CURRENT CONCEPTS IN DERMATOLOGY

Karthik Krishnamurthy, D.O., FAOCD
Activity Chair
Acknowledgement of Commercial Support

2017 American Osteopathic College of Dermatology Corporate Members

Diamond Level
Galderma • Pfizer

Platinum Level
Lilly USA, LLC

Gold Level
AbbVie • Valeant Pharmaceuticals

Bronze Level
Allergan • Dermpath Lab of Central States

Pearl Level
Aclaris Therapeutics • Dermpath Diagnostics • Novartis • Sun Dermatology

Sponsors/Unrestricted Educational Grants
Dermpath Lab of Central States • Lilly USA, LLC • Sagis Diagnostics • Valeant Pharmaceuticals

Product Theater
AbbVie • Lilly USA, LLC • Pfizer • Valeant Pharmaceuticals

2017 American Osteopathic College of Dermatology Spring Meeting Exhibitors

3Gen, Inc.  Dermpath  Pfizer/Eucrisa
AbbVie  D-Path  ProPath Services LLP
Aclaris Therapeutics, Inc.  Encore Dermatology  Ra Medical Systems, Inc.
Advanced Dermatology & Cosmetic Surgery  Galderma Laboratories  Sagis Diagnostics
Allergan  Heartland Payment Systems  Sensus Healthcare
Anne Arundel Dermatology  Hill Dermaceuticals, Inc.  Skin Path Solutions
Aurora Diagnostics  Janssen Biotech, Inc.  Strata Skin Sciences
Bayer Healthcare  Leo Pharma  Sun Dermatology
Celgene  Lilly USA, LLC  Valeant Pharmaceuticals
Dermpath Diagnostics  Medimetriks Pharmaceuticals
Dermpath Lab of Central States  Novartis

Continuing Medical Education Statements

This activity will change your practice and improve patient outcomes!

AOA Statement:
The American Osteopathic College of Dermatology is accredited by the American Osteopathic Association to provide osteopathic continuing medical education for physicians. This activity anticipates being approved for 26 hours of AOA Category 1-A credit pending approval by the AOA CCME and will report CME and specialty credits commensurate with the extent of the physician's participation in this activity. March 29-April 1, 2017

AAD Statement:
The American Osteopathic College of Dermatology Current Concepts in Dermatology (Program #698100) is recognized by the American Academy of Dermatology for 26 AAD Recognized Credit(s) and may be used toward the American Academy of Dermatology's Continuing Medical Education Award. March 29-April 1, 2017

ACCME Statement:
The American Osteopathic College of Dermatology is currently seeking accreditation by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. March 29-April 1, 2017
The Continuing Medical Education Program of the American Osteopathic College of Dermatology will support, enhance and advance new models of academic excellence and community health care.

The objectives of this organization are:
1. To maintain the highest possible standards in the practice of dermatology
2. To stimulate study and to extend knowledge in the field of dermatology
3. To promote a more general understanding of the nature and scope of the services rendered by osteopathic dermatologists to the other divisions of medical practice, hospitals, clinics and the public.
4. To contribute to the best interests of the osteopathic profession by functioning as an affiliated organization of the American Osteopathic Association

Purpose
The purpose of the CME program is to provide AOA-accredited continuing medical education activities to inform the dermatologist physician. The program will provide a mechanism by which its constituents can improve competency, maintain board certification and cultivate lifelong learning. CME will provide physicians with the opportunity to further develop their knowledge through individual and group learning activities. The Continuing Medical Education Committee will monitor the quality of all programs conducted by the AOCD.

Accreditation:
The AOCD is accredited by the American Osteopathic Association. This activity anticipates being approved for 26 hours of AOA Category 1-A credit pending approval by the AOA CCME.

The American Osteopathic College of Dermatology Current Concepts in Dermatology (Program #698100) is recognized by the American Academy of Dermatology for 26 AAD Recognized Credit(s) and may be used toward the American Academy of Dermatology’s Continuing Medical Education Award.

The American Osteopathic College of Dermatology is currently seeking accreditation by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

This meeting will provide a diversified CME presentation focusing on the art and science of Dermatology. Information will be presented through lectures and scientific paper presentations. The activity actively encourages members to develop enduring materials as an evolving tool for continuing education. The College is committed to exploring the development of its capacity to expand resources in other educational techniques, including Web-based activities and point-of-care technologies.

Commercial Support Disclosure
AOCD CME will identify relevant financial relationships prior to awarding AOA Category 1A and/or AMA PRA Category 1 Credit™ for CME activities. All persons in a position to influence or control CME content (course directors, program planning committee members, speakers, authors and staff) will complete a standardized disclosure form. Information about funding will be requested to identify CME activities at higher risk for commercial bias.

All AOCD CME activities will be evaluated by learners and possibly peer reviewers to determine if the content was free of commercial bias. All those identified as having influence and/or control of CME content perceived as either manifesting conflicts of interest or being biased may be disqualified from consideration as resources (planning group member, authors, faculty, etc) in subsequent CME activities.

Learners will be provided with information on identified COI from any of the above categories of persons that affect the content of CME, and that information will be positioned in course materials such that it is read by learners prior to the execution of the CME activity. Speakers for the AOCD will be required to provide disclosure information to meeting attendees during their introduction of their topic. Additionally, disclosure statements are provided in the program schedule given to each meeting attendee and is available online at www.aocd.org.
In accordance with the ACCME’s Standards for Commercial Support of Continuing Medical Education, the Policy on Collection of Financial Relationships and Resolution of Conflicts of Interest (COI) exists to provide guidance for staff, instructors, planners, reviewers and managers of CME activities sponsored by The American Osteopathic College of Dermatology, (AOCD). This policy addresses the underlying philosophy of disclosure to learners, mechanisms to collect disclosure information and the parties from whom financial disclosure shall be collected, the mechanisms to resolve COI, and requirements to make disclosure to learners prior to the start of an activity.

Professional Practice Gap Statement:
Physicians need to understand, update and manage changes in dermatology in order to provide optimal patient care. Dermatologists in private practice may not have immediate access to new updates in therapies and treatments. This activity will help to close gaps in physician’s areas of state rules, regulations and compliance mechanisms, updates in skin cancers, melanomas, rheumatology-dermatology, dermoscopy updates, urticaria, pediatric dermatology, male and female pattern hair loss, therapeutic updates and the use of radiation in treating skin cancers.

Expected Outcomes:
As a result of participation in the AOCD/CME activity, practicing clinicians will improve competency; maintain specialty board certification; and cultivate lifelong learning. It is expected that attendees of this meeting will improve their diagnostic competence regarding a wide range of dermatologic conditions. In addition to increased diagnostic competence, enhanced concepts of therapy and treatment in dermatologic care will be gained for implementation in everyday practice.

- Attendees will learn new treatment options for pediatric dermatology issues.
- Attendees will be able to recognize clues to determining the causes of localized contact dermatitis.
- Attendees will learn the epidemiology of HIV as it pertains to dermatology.
- Attendees will learn the cutaneous manifestations of HIV infection.
- Attendees will be able to identify what an ethical dilemma is and how it can be analyzed.
- Attendees will gain more knowledge about conflicts of interest and how they apply to in-office dermatopathology laboratories.
- Attendees will gain an understanding of the appropriate coding guidelines and concepts using easy to understand methodologies of code selection and application.
- Attendees will learn how to identify appropriate dermatology codes and correct use/application of such codes for services procedures performed in your practice to ensure accurate claim submission as well as proper code identification.
- Attendees will gain an understanding of the quality of life impact of hyperhidrosis.
- Attendees will learn the known pathogenesis and treatment of hyperhidrosis.
- Attendees will be able to correlate clinical manifestations of disease with rational treatment selection and progress monitoring.
- Attendees will gain an awareness of the current state of acne, rosacea, eczema, psoriasis in patients and correlate with management plan.

The overall result being improved physician/provider performance and increased positive patient outcomes.

These objectives will be achieved in a setting which is evidence-based, culturally sensitive and free of commercial bias. The AOCD is committed to the practice of continuing program improvement. The AOCD will actively explore new educational technologies, develop collaborative relationships with other CME providers and seek to build the capacity to evaluate competency-based outcomes among the clinicians we serve. CME will provide physicians with the opportunity to further develop their knowledge through individual and group learning activities.

Needs Assessments:
The activity was developed based upon the needs of physicians within the association identified through:
- An evaluation/survey provided to meeting participants at both our annual and midyear meeting
- Consensus of faculty members within a department or service area
- New advances in dermatologic treatment identified in major publications or research studies
- New methods of diagnosis or treatment
- Availability of new medication(s) or indication(s)
- Development of new technology
- Acquisition of new facilities or equipment
- Input from experts regarding advances in medical knowledge
- Legislative, regulatory, or organizational changes effecting patient care
- Epidemiological data
The AOCD Continuing Medical Education Committee works to assure the inclusion of appropriate Osteopathic content in the Continuing Medical Education activities presented by AOCD, and to assure that the Continuing Medical Education Programs of the AOCD will achieve the stated objectives of each meeting in a setting which is evidence-based, culturally sensitive and free of commercial bias.

The Continuing Medical Education Committee of the AOCD will monitor the quality of all activities conducted.

Content Areas:
The AOCD approves the CME activities based upon needs assessment data to ensure that all offerings present current, up to date and cutting edge information. Specific areas of emphasis include, new advances in dermatologic treatment, new methods of diagnosis or treatment, availability of new medication(s) or indication(s), development of new technology, advances in medical knowledge and legislative, regulatory, or organizational changes effecting patient care. The Osteopathic Core Competencies of Osteopathic Philosophy, Principles, Practice and Manipulative Medicine, Medical Knowledge, Patient Care, Interpersonal and Communication Skills, Professionalism, Practice-Based Learning and Improvement and System-Based Practice will also be incorporated into all CME activities.

Target Audience:
The primary target audience of the CME activities conducted by the AOCD are the dermatologist physician members. The College also serves community physicians, volunteer clinical faculty, academic clinicians and students affiliated with the AOCD. The activity will also actively seek to broaden its audience through developing affiliations with CME providers on the national level.

Faculty Disclosure:
As a sponsor accredited by the AOA, it is the policy of the AOCD to require the disclosure of anyone who is in a position to control the content of an educational activity. All relevant financial relationships with any commercial interests and/or manufacturers must be disclosed.

Disclosure of Commercial Support of CME:
As you undoubtedly know from the national media, there has been much discussion concerning the relationships between CME sponsors, faculty and commercial companies providing support of CME.

Both the American Osteopathic Association and the Committee on Continuing Medical Education have adopted regulations for ethical actions in this area which the American Osteopathic College of Dermatology endorse and have adopted for all our educational activities.

Please be assured that having an affiliation with a company does not imply in any way that something is wrong or improper; however, we want to inform attendees that such a relationship exists.

Should you have any questions regarding the facilities, handouts, activity content, or concerns about CME compliance with the AOA “Uniform Guidelines,” feel free to contact the AOCD representative:

Marsha A. Wise, BS
Executive Director
P.O. Box 7525
Kirkville, MO 63501
660-665-2184
800-449-2623

Unresolved issues regarding compliance with the AOA “Uniform Guidelines” can be brought to the attention of the AOA Division of CME by calling: 800-621-1773, or by writing:

AOA CME Office
142 East Ontario Street
Chicago, IL 60611
Resident Poster Presentations
Extragenital Bullous Lichen Sclerosis on the Anterior Lower Extremities: Report of a Case and Literature Review
Nichelle Arnold, D.O.
SCS/MSUCOM/Botsford Hospital

Establishment of Clinic-Based Biorepository
Sarah Belden, D.O.
MWU/OPTI/Affiliated Dermatology

A Proposed Method for Upper Eyelid and Infrabrow Tightening Using a Transcutaneous Temperature Controlled Radiofrequency Device With Opaque Plastic Eye Shields
Lauren Boudreaux, D.O.
OPTI-West/Silver Falls Dermatology

Locally Advanced Basal Cell Carcinoma: A Severe Case Presentation and Review
Liza Brown, D.O.
NSUCOM/Larkin Community Hospital

Congenital Psoriasis: A Rare Entity
Isaac Bryan, D.O.
Texas OPTI/Bay Area Corpus Christi Medical Center

Darier-Roussy Variant of Sarcoidosis
Stephen Cahill, D.O.
KCU-GMEC/Tri-County Dermatology

Challenges in the Treatment of Chromoblastomycosis: A Case Report from Kenya
Stephanie Campbell, D.O.
KCU-GMEC/Tri-County Dermatology

Undifferentiated Pleomorphic Sarcoma of Skin: Clinical and Histopathologic Emulator of Atypical Fibroxanthoma, Distinction Imperative
Michael Carletti, D.O.
Texas OPTI/UNTHSC

A Case of Urticaria Pigmentosa
Vanita Chand, D.O.
LECOMT/St. John's Episcopal Hospital, South Shore

Skin Cancer Awareness, Prevention, and Education in Adults Over Age 40
Sasha Chediak, D.O.
NSUCOM/Broward Health Medical Center

A Case of Chordoma Catus Following Recurrence of L3 Chordoma
Kylee Crittenden, D.O.
CORE/O'Bleness Memorial Hospital

Pyoderma Faciale: A Case Report
Amelia Damse, D.O.
KCU-GMEC/Dermatology Residency of Orlando

A Case of Henoch-Schonlein Purpura in an Adult
Lisa Diaz, D.O.
NSUCOM/Broward Health Medical Center

Cyclosporine Ophthalmic Solution Inducing Hair Hyperpigmentation
Chelsea Duggan, D.O.
SCS/MSUCOM/Oakwood Healthcare System

Case Report: Sebaceous Carcinoma of the Areola in an Immunosuppressed Patient
Michelle Elway, D.O.
RMOPTI/Colorado Dermatology Institute

Resolution of Subacute Cutaneous Lupus with Belimumab
Michael Garone, D.O.
NSUCOM/Largo Medical Center

A Rare Case of Erythema Elevatum Diitini
John Gay, D.O.
OMNEE/LewisGale Hospital - Montgomery

An Atypical Pediatric Case Presentation of Erythema Elevatum Diitini
Evelyn Gordon, D.O.
LECOMT/St. John's Episcopal Hospital, South Shore

Subcutaneous Sarcoidosis as a Manifestation of HAART-Induced Immune Reconstitution Syndrome
Brittany Grady, D.O.
NYCOMEC/Palisades Medical Center

Chelitis Granulomatosa & Differential Case Report and Discussion
Bryan Gray, D.O.
SCS/MSUCOM/Botsford Hospital

A Case Analysis and Update of Small/Medium Pleomorphic T-cell Lymphoma
Gabriel Guerrero, D.O.
Still OPTI/Northeast Regional Medical Center

Porphyria Cutanea Tarda: A Case Presentation and Discussion
Jordan Harris, D.O.
OPTI-West/Aspen Dermatology

Multiple Eruptive Eccrine Hidrocystomas
Stephanie Howerton, D.O.
OPTI-West/Silver Falls Dermatology

Goldenhar Syndrome
Peter Jajou, D.O.
SCS/MSUCOM/Oakwood Healthcare System

Case of Acquired Epidermodyasplasia Verruciforms
Carmen Julian, D.O.
PCOM/North Fulton Hospital Medical Campus

Radiation-Induced Breast Angiosarcoma: A Case Report
Franz Kerdel, D.O.
NSUCOM/Larkin Community Hospital
Treatment with the Q-Switched, Nd-Yag Laser in the Wavelengths of 532nm and 1064nm for the Treatment of Post-Endovenous Ablation and Post-sclerotherapy Hyperpigmentation: A Retrospective Case Series

Angela Macri, D.O.
OMNEE/Sampson Regional Medical Center

Brooke-Spiegler Syndrome
Sarah Malarich, D.O.
Texas OPTI/South Texas Osteopathic Dermatology

A Rare Case of SCC in a Pediatric Patient with NF-1
Christopher Mancuso, D.O.
NYCOMEC/St. Barnabas Hospital

Dermal Melanoma: A Rare Subtype of Melanoma
Brianna McDaniel, D.O.
OMNEE/Sampson Regional Medical Center

Atypical Fibroxanthoma Invading the Parietal Bone
Miesha Merati, D.O.
LECOMT/University Hospitals Regional Hospitals

Epidermolysis Bullosa Acquisita: A Case Presentation
Kiran Mian, D.O.
OPTI-West/Chino Valley Medical Center

Multiple Mastocytomas : A Case Report and Discussion
Kevin Miller, D.O.
MWU/OPTI/Affiliated Dermatology

Neutrophilic Eccrine Hidradenitis Spectrum
Leslie Mills, D.O.
CEME/Palm Beach Consortium for GME

Stewart-Treves Syndrome – Endangered Not Extinct
Jessica Newburger, D.O.
OMNEE/Park Avenue Dermatology

Diffuse Hypopigmented Rash on an Eight-Year Old Girl
Sheena Nguyen, D.O.
OPTI-West/Chino Valley Medical Center

A Rare Case of SCLE Presenting with EM-like and SJS/TEN-like Lesions: A Review of Rowell Syndrome
Danielle Nicolazzo, D.O.
NSUCOM/Larkin Community Hospital

Systemic Nickel Allergy Syndrome
Jessica Perkins, D.O.
NSUCOM/Largo Medical Center

Cytokeratin AE1/AE3 a More Sensitive Merkel Cell Carcinoma Marker: A Retrospective Case Series
Nickolas Poulos, D.O.
NSUCOM/Larkin Community Hospital

Case Report: Eruptive Xanthoma in a 14-Year-Old Boy
Ryan Proctor, D.O.
OPTI-West/Aspen Dermatology

Extensive Locally Invasive Cutaneous Tumors
Kelly Quinn, D.O.
PCOM/Lehigh Valley Health Network

Nevus Lipomatosus Cutaneus Superficialis
Heather Reagin, D.O.
Texas OPTI/UNTHSC

Argyria Secondary to Systemic and Topical Absorption of Colloidal Silver Through Natural Mineral Supplementation
Veronica Rutt, D.O.
PCOM/Lehigh Valley Health Network

An Unusual Presentation of a Congenital Myofibroma: A Case Report
Pamela Sheridan, D.O.
NSUCOM/Broward Health Medical Center

A Challenging Case of Pyoderma Gangrenosum
Christine Sickles, D.O.
OMNEE/LewisGale Hospital - Montgomery

A Case of Unilateral Linear and Whorled Nevoid Hypermelanosis
Louis Siegel, D.O.
LECOMT/St. John's Episcopal Hospital, South Shore

A Unique Presentation of Metastatic Melanoma Appearing Ten Years After the Primary Lesion That Highlights the Usefulness of SOX-10 In Identifying Melanomas of Metastatic Origin
Natalie Steinhoff, D.O.
NSUCOM/Largo Medical Center

Metastatic Merkel Cell Carcinoma
Nicole Swenson, D.O.
KCU-GMEC/Dermatology Residency of Orlando

Intervally Collected Granular Safety Data Throughout Treatment with Polypodium leucotomos Extract for 56 days in 40 Adult Patients
Richard Winkelmann, D.O.
CORE/O’Bleness Memorial Hospital

Successful Re-Treatment of Generalized Granuloma Annulare with Adalimumab
Michael Zaycosky, D.O.
KCU-GMEC/Dermatology Residency of Orlando
Extragenital bullous lichen sclerosis on the anterior lower extremities: report of a case and literature review

Nichelle Arnold DO, Mitch Manway DO, Sean Stephenson DO, Howard Lipkin DO
Department of Dermatology  ■  Beaumont Hospital, Farmington Hills, MI

INTRODUCTION

Lichen sclerosis (LS) is a benign, chronic, inflammatory skin disease with a predilection for the anogenital region in women. Although males can also be affected, the ratio of female to male incidence has been reported to be as high as 6:10:1 and possesses a bimodal age distribution of pre-pubertal girls and postmenopausal women [1,2]. Afflicted skin usually manifests as polygonal papules that coalesce into porcelain white plaques and can be associated with edema, telangiectasias, and comedo-like plug formation [3].

Lichen sclerosis can be debilitating for some patients causing significant pruritus, pain, dysuria, and dyspareunia [4]. Rarely, lichen sclerosis appears in various extragenital areas, however most cases are relatively asymptomatic [5]. Even more uncommon, as displayed in this case report of a 69 year old female, LS can present exquisitely with a bullous or hemorrhagic appearance [5].

CASE REPORT

The patient is a 69 year old female who presents with a chief complaint of a skin rash located on her left and right perineal regions. The lesions have been present for one year and are associated with bleeding, blistering, itching, and pain. She states that the spots come and go but never completely resolve. She has not used any topical or oral treatments. She denies a history of skin lesions on her legs or elsewhere on her body prior to this episode. The patient is on many medications, none of which were started around the onset of the rash. She is otherwise well, denying any recent illnesses or significant changes in her health status.

Review of symptoms is negative for fever, chills, joint pain, muscle pain, nausea, vomiting or headache.

Past medical history includes: diabetes (type 2), hypercholesterolemia, hypertension, and chronic obstructive pulmonary disease. Her daily medications include: fluticasone propionate, Aspirin, leg for hemolysin and eosin (H&E) as well as direct immunofluorescence (DIF).

The time of initial examination two 3 mm punch biopsies were completed on the left anterior lower leg for hemolysin and eosin (H&E) as well as direct immunofluorescence (DIF). Pathology: The biopsy for H&E demonstrated hyperkeratosis with follicular plugging and atrophy of the epidermis {figures 3 and 4}. There is separation between the epidermis and dermis exhibiting a superficial perivascular predominantly lymphocytic inflammatory cell infiltrate. DIF was negative.

The skin disease morphea, which possesses many similar clinical and histological features, is not actually a separate entity but is actually a presentation along the same disease spectrum [5]. Extragenital disease most commonly appears on the thighs, buttocks, breasts, back, chest, axillae, shoulders, and elbows. However, many unique presentations have been reported, including cases of infantile and internal LS [1,2,7]. Although the clinical presentation is somewhat variable, LS usually begins as slightly elevated papules which coalesce overtime into erythematous plaques with increasing atrophic and wrinkled appearance. Advanced features include follicular plugging, telangiectasia formation, as well as bullae and hemorrhagic lesions which are caused by the fragility of a flattened epidermal-dermal interface [2,4]. Histologic features include epidermal atrophy, tunnels/hyperkeratosis, follicular plugging, adenoid homogenized superficial dermis, dilated blood vessels, loss of rete ridges, hydropic degeneration of the basal layer, and a dermal lymphohistiocytic inflammatory cell infiltrate. Lichen sclerosis et atrophicus can be present. That being said, Histologic characteristics are not definitive alone and a combination of clinical and pathologic information must be considered for proper diagnosis. Dermoscopic evaluation may reveal scales, keratic plaques, erosions, and chrysalis structures [5]. On the other hand, immunohistochecanical studies have shown downregulated immunoreactivity to CD 68 and CD 11 [7]. The differential of extragenital bullous LS includes bullous morphea, bullous lichen plaques, criscutal bullous pemphigoid, bullous scleroderma, and cicatricial lichen planus [6].

Some reports have shown an increase in risk of squamous cell carcinoma development in anogenital forms of LS, but no strong association has been shown with extragenital cases [13]. Treatment is aimed at relieving symptoms of dryness, pruritus, and improvement in appearance. Unfortunately, there are very few well-designed randomized clinical trials, and therefore treatment options are based upon limited observations [4]. Ultra-potent topical corticosteroids such as clobetasol propionate 0.05% cream are first line and will be effective in most patients, but not all [14]. Length of treatment with this method has varied from 12-24 weeks [15]. Should this treatment prove ineffective or if long-term steroid use is undesirable due to possible adverse effects, other potential treatments may include injection of corticosteroids, topical calcium-channel blockers such as pimecrolimus or tacrolimus, vitamin D derivatives such as vitamin D systemic retinoids, and UV phototherapy [5,16]. Use of hormone therapies such as topical testosterone or progesterone have shown good efficacy and should be avoided [16]. Regrettably, there is no permanent cure for lichen sclerosis and relapses may transpire [6].

CONCLUSION

In conclusion, we will continue to follow our patient with regular examinations to ensure that her lesions are remaining under control and that she has no signs of malignancy. Although rare, this case is a reminder that lichen sclerosis should remain on the differential for a patient presenting with a blistering dermatosis.

REFERENCES

Abstract
The incidence of skin cancer (squamous cell carcinoma, basal cell carcinoma and melanoma) has been increasing over the past several years. It is expected that there will be a parallel demand for cutaneous tumor samples for biomedical research studies. Tissue availability, however, is limited due to the cost of establishing a biorepository and the lack of protocols available for obtaining clinical samples that do not interfere with clinical operations. A protocol was established to collect and process cutaneous tumor and associated blood and saliva samples that has minimal impact on routine clinical procedures on the date of Mohs surgery. Tumor samples are collected and processed from patients undergoing their first layer of Mohs surgery for biopsy-proven cutaneous malignancies by the Mohs histotechnologist. Adjacent normal tissue (ANT) is collected at the time of surgical closure. Additional samples that may be collected are whole blood and buccal swabs. Tumor and blood tissue may also be collected from melanoma patients. By utilizing tissue samples that are normally discarded, a biorepository was generated that offers several key advantages for being based in the clinic versus the laboratory setting. These include a wide range of samples collected, access to de-identified patient records including pathology reports, and, for the typical donor, access to additional samples during follow-up visits. The samples have been tested in downstream applications (explant culture, RNA isolation, western blot analysis, cell cultures, and histological evaluation) and have been validated.

Outline of Sample Collection & Processing

Figure 1. Flowchart depicting general overview of patient sample collection, processing, and the potential stored samples generated from consented Mohs patients. The final downstream applications are described on the type of sample collected from the patient.

Mojhs Tumor Tissue Samples

Evaluate size of tumor removed from patient
(B) Liquid biopsy technique for circulating tumor cells isolation

Collect pre-Mohs tissue in culture medium
Remove a 0.5mm3 fragment

Remaining tumor used for Mohs processing

Microscopic tissue analysis

Remaining tissue used for downstream applications

Transfer to biorepository

Figure 2. Mohs procedure & processing of tissue for analysis

Establishment of Clinic-Based Biorepository
Sarah Belden1, Chandana Uppalapati2, Agnes Pascual3, McKale Montgomery3, Kathryn Leyva2, Elizabeth Hull3 & Richard Averitte1
1Affiliated Dermatology Residency Program/Midwestern University Osteopathic Postdoctoral Training Institute, 2Department of Microbiology & Immunology/AZCOM, 3Biomedical Science Program, College of Health Sciences/Midwestern University

Explant Culture and RNA Isolation

Immunocytochemistry Analysis of SCC Sample

Figure 3: (A) Immunocytochemistry on SCC sample showing expression of known markers for SCC. (B) Representative western blots of MUC1 and p40 are shown.

RNA Integrity

Figure 4: (A) Assessment of RNA size and integrity by gel electrophoresis. (B) BioRepository. Immunocytochemistry markers and the expression of known markers for SCC were examined by Western blot (C) Representative western blots of MUC1 and p40 are shown.

Analysis of Proteins extracted from ANT and SCC

SCC Markers are Differentially Expressed in Tumor Tissue

Figure 5: (A) Total protein was isolated from ANT and SCC samples and the expression of known markers for SCC in examined by Western blot. (B) Representative western blots of MUC1, p40, and the expression of known markers for SCC in ANT and SCC samples.

Circulating Tumor Cells (CTCs) Isolated from Culture

Figure 6: (A) Presumptive CTC’s isolated from patient donor tissue sample. (B) CTCs isolated from patient donor blood sample.

Discussion
To the author’s knowledge, this protocol is the first of its kind that focuses on the clinical procurement of cutaneous tissue samples in both a cost-effective and quick approach on the day of Mohs surgery. Each sample type has been tested in downstream applications to validate collection procedures:

- Tumor and adjacent normal tissue have been successfully used in protein and RNA isolation, and can potentially be used for DNA isolation
- Viable explants established from the tissue sections have been evaluated by microscopy while stored histological slides have been used for immunohistochemistry and immunofluorescence
- Circulating tumor cells have been isolated from patient donor blood samples

We hope that the clinic-based biorepository model may be utilized to help alleviate the shortage of patient samples in biomedical research

- Melanoma samples may also be obtained and stored in the biorepository on the date of excision

Future Directions

- By following the protocol described here, it is possible to extend this model to other dermatology clinics, other tumor types (such as melanoma), and other surgical specialties and practices to provide human tissue samples for multifaceted research into human cancers
- Melanoma and blood samples (liquid biopsy) could be utilized for liquid biopsy analysis, a technique useful for identifying DNA from tumor cells in the early detection of cancer

Acknowledgements
This work was supported by funds from Midwestern University College of Health Sciences Research Foundation Grant awarded to ESH and Midwestern University Office of Research and Sponsored Programs Intramural Grant award to K.L. Additional support was provided by Affiliated Laboratories and Affiliated Dermatology. All experiments on human tissue samples were approved by Western IRB (IRB#2015-033), Midwestern Institutional Review Board approved the validation work with clinic-based biorepository samples at Midwestern University (4407). We thank Sarah Yackich, Jami Sue, Stallen Fawkes, Cody Jordan, Heather Klaes, and Ali Zaidi for their technical assistance.
ABSTRACT

Laxity of the eyelid and periorbital areas, a common manifestation of aging, is usually addressed via blepharoplasty and/or fat transfer. Given the trend toward safer, less invasive treatments preferred by those patients reticent to undergo more invasive procedures, nonablative radiofrequency (RF) therapy represents a safe and effective alternative. Transcutaneous temperature controlled radiofrequency (TTCRF) integrates nonablative superficial RF treatment with automatic temperature feedback to control energy deposition, as a stimulant of overall collagen remodeling and tightening. Infrared thermal imaging is employed for this purpose. A proposed method for upper eyelid and infrabrow tightening using TTCRF with opaque plastic eye shields provides a safe and effective alternative to upper lid and periorbital tightening.

INTRODUCTION

Laxity of the eyelid and periorbital region is a universal and early manifestation of aging which increases over time, often addressed by blepharoplasty and/or fat transfer. Many younger patients may be reticent to undergo these invasive procedures, especially in the presence of safe, effective alternatives with minimal risk and downtime. A brief review of the available non-invasive methods follows. Carruthers and Carruthers used a small-tip RF device in a 2007 study, and used opaque black plastic shields to protect the globe of the eye during treatment. Safety was demonstrated but outcomes were described as mild to moderate at best. Opaque black haptic contact lenses containing autoclavable plastic shields designed for blepharoplasty procedures protect the globe of the eye from heat and RF energy. Any mask-up, false eyelashes, and contact lenses were removed prior to treatment. The subject is placed in a supine position with the RF grounding pad placed on exposed clean skin (shaved of excessive hair) on the upper back. Eyes were shielded with soap and water followed by chlorhexidine 5% pads before autoclaving prior to treatment, and were inspected thoroughly for rough or jagged edges before placement. The suction cup applicator was placed on the convex surface of the shield for placement and one drop of lubricant (mineral oil 42.5%, petrolatum 57.5%) was applied to the concave inner surface of the shield. A single drop of preservative free 0.5% ophthalmic solution was applied on the treated eyelid after 10 to 20 seconds. The subject was then gently lifted using gaze and while the subject looked downward, the fabricated shield was placed onto the globe of the eye under the upper, then lower lid using the suction applicator handle. After shield insertion, the patient closes their eyes and the applicator handle is removed by applying light pressure to the upper lid and easily dislodged from the suction cup, then removed from the shield. The small diameter RF probe is then inserted and held between 30 and 45 degrees. FLIR thermal imaging was used to monitor temperature and maximum safe energy deposition. For transcutaneous applications forward-looking infrared (FLIR) thermal imaging is employed for this purpose.

While RF may seem to be an ideal modality for the periorbital area, the eyes are among tissues known to be extremely susceptible to damage by RF energy; any RF should therefore be peripheral to the area in question, where it has to account for this. Carruthers and Carruthers used a small-tip RF device in a 2007 study and used opaque black plastic shields to protect the globe of the eye during treatment, safety was demonstrated but outcomes were described as mild to moderate at best. Opaque black haptic contact lenses containing autoclavable plastic shields designed for blepharoplasty procedures, protect the globe of the eye from heat and RF energy. Any mask-up, false eyelashes, and contact lenses were removed prior to treatment. The subject is placed in a supine position with the RF grounding pad placed on exposed clean skin (shaved of excessive hair) on the upper back. Eyes were shielded with soap and water followed by chlorhexidine 5% pads before autoclaving prior to treatment, and were inspected thoroughly for rough or jagged edges before placement. The suction cup applicator was placed on the convex surface of the shield for placement and one drop of lubricant (mineral oil 42.5%, petrolatum 57.5%) was applied to the concave inner surface of the shield. A single drop of preservative free 0.5% ophthalmic solution was applied on the treated eyelid after 10 to 20 seconds. The subject was then gently lifted using gaze and while the subject looked downward, the fabricated shield was placed onto the globe of the eye under the upper, then lower lid using the suction applicator handle. After shield insertion, the patient closes their eyes and the applicator handle is removed by applying light pressure to the upper lid and easily dislodged from the suction cup, then removed from the shield. The small diameter RF probe is then inserted and held between 30 and 45 degrees. FLIR thermal imaging was used to monitor temperature and maximum safe energy deposition. For transcutaneous applications forward-looking infrared (FLIR) thermal imaging is employed for this purpose.

A Proposed Method for Upper Eyelid and Infrabrow Tightening Using a Transcutaneous Temperature Controlled Radiofrequency Device With Opaque Plastic Eye Shields

Lauren Boudreaux, DO, and Douglas Key, MD

a: GSMC/Silver Falls Dermatology, Salem, OR, b: Laser Institute for Cosmetic and Regenerative Medicine, Portland, OR

PATIENTS AND METHODS

Subjects (n=6, 36 women and 4 men, age range: 33-72) presented with mild to moderate laxity of the eyelid and infrabrow. Exclusion criteria included any anatomically nearby metallic implants or microelectronic devices, such as pacemaker, cochlear implant, or glaucoma drainage device. Good Clinical Practice Guidelines and informed consent was obtained from all subjects prior to treatment.

Any mask-up, false eyelashes, and contact lenses were removed prior to treatment. The subject is placed in a supine position with the RF grounding pad placed on exposed clean skin (shaved of excessive hair) on the upper back. Eyes were shielded with soap and water followed by chlorhexidine 5% pads before autoclaving prior to treatment, and were inspected thoroughly for rough or jagged edges before placement. The suction cup applicator was placed on the convex surface of the shield for placement and one drop of lubricant (mineral oil 42.5%, petrolatum 57.5%) was applied to the concave inner surface of the shield. A single drop of preservative free 0.5% ophthalmic solution was applied on the treated eyelid after 10 to 20 seconds. The subject was then gently lifted using gaze and while the patient looked downward, the fabricated shield was placed onto the globe of the eye under the upper, then lower lid using the suction applicator handle. After shield insertion, the patient closes their eyes and the applicator handle is removed by applying light pressure to the upper lid and easily dislodged from the suction cup, then removed from the shield. The small diameter RF probe is then inserted and held between 30 and 45 degrees. FLIR thermal imaging was used to monitor temperature and maximum safe energy deposition. For transcutaneous applications forward-looking infrared (FLIR) thermal imaging is employed for this purpose.

There were no major adverse events recorded. Treatment was safe and tolerable for all subjects. Figures 1 and 2 represent before and after photographs of patients undergoing treatment as per study protocol. One of the challenges with this study was obtaining consistent clinical photography to record and measure improvement in lid laxity and brow ptosis. Challenges with comparative photography in matching upper lid laxity are affected by facial expression, brow position, and consistent lighting and positioning of the subject.

Further refinement of safe methods for studying TTCRF for upper lid and infrabrow laxity would benefit from validated objective methods to accurately rate improvement, given the small size of the area treated and possible variability of the outcomes. A study by Javate and colleagues used nonablative, non-invasive superficial RF to the periorbital area. Subsequent evaluation of 2.05 mm and average superior eyelid crease elevation of 0.98 mm after treatment, with average 3.52 mm and 1.84 mm eyebrow lifting and superior eyelid crease elevation, respectively, at 6-week follow-up. Results were statistically significant. Future study using this or similar techniques to objectively document subject results for areas such as the periorbit would be the logical next step, although these modalities may not be available in every practice.

RESULTS AND DISCUSSION

There were no major adverse events recorded. Treatment was safe and tolerable for all subjects. Figures 1 and 2 represent before and after photographs of patients undergoing treatment as per study protocol. One of the challenges with this study was obtaining consistent clinical photography to record and measure improvement in lid laxity and brow ptosis. Challenges with comparative photography in matching upper lid laxity are affected by facial expression, brow position, and consistent lighting and positioning of the subject.

Further refinement of safe methods for studying TTCRF for upper lid and infrabrow laxity would benefit from validated objective methods to accurately rate improvement, given the small size of the area treated and possible variability of the outcomes. A study by Javate and colleagues used nonablative, non-invasive superficial RF to the periorbital area. Subsequent evaluation of 2.05 mm and average superior eyelid crease elevation of 0.98 mm after treatment, with average 3.52 mm and 1.84 mm eyebrow lifting and superior eyelid crease elevation, respectively, at 6-week follow-up. Results were statistically significant. Future study using this or similar techniques to objectively document subject results for areas such as the periorbit would be the logical next step, although these modalities may not be available in every practice.

REFERENCES


AUTHOR CORRESPONDENCE

Lauren Boudreaux, DO, ... boudreaux@silverfallskern.com

Figures

Figure 1: Digital photographs of a woman (age, 54 years) before (left) and after (right) 6 treatments one month apart with TTCRF for the eyelid and infrabrow, using opaque black plastic eye shields to protect the eye during treatment. Photos courtesy of Douglas Key MD.

Figure 2: Digital photographs of a woman (age, 60 years) before (left) and after (right) 6 treatments one month apart with TTCRF for the eyelid and infrabrow, using opaque black plastic eye shields to protect the eye during treatment. Photos courtesy of Douglas Key MD.

CONCLUSIONS

The use of autoclavable opaque plastic eye shields provides a safe method of treating the upper lid eye and infrabrow using TTCRF.
Basal cell carcinoma (BCC) is a common skin malignancy comprising 80% of non-melanoma skin cancers (NMSCs). Over 2.6 million cases are estimated to be diagnosed in the United States alone each year. Advanced Basal cell carcinomas (aBCCs) are comprised of BCCs that have metastasized to local or distant lymph nodes or organs (mBCC), or locally advanced BCCs that are extensive and infiltrative vital structures such as eyes, nose or brain (laBCC). LaBCC tumors represent roughly 1-10% of all previous medical treatments including Mohs, surgery and radiation. Management of BCC depends on tumor histological type, location, size, comorbidities, previous treatment and preference of patient. Aggressive and infiltrative subtypes are best treated with Mohs surgery. Giant tumors defined as those >5 cm in diameter pose a significant challenge to treatment as surgery has high risk of treatment failure and recurrence and can pose significant morbidity and disfigurement. In laBCC, seen in the above case, at the time of presentation, surgery was simply not a treatment option. In laBCC, not suitable for surgery or where surgery is not desired by the patient secondary to impairment in quality of life, alternative treatment modalities include radiation therapy, either palliative or curative, chemotherapeutics such as cisplatin (for metastatic disease) or oral chemotherapeutics such as cyclophosphamide. Newer chemotherapeutics such as vemurafenib and dabrafenib are currently undergoing human trials targeting BCCs.2 The first FDA approved HPI for aBCC was approved in 2012, known as Vismodegib. Phase II trials of Vismodegib in the ERIVANCE study included 71 patients with mBCC, as well as 33 aBCC patients. Mean objective response rate was 43%, in aBCC with average tumor progression free survival (PFS) of 9.5 months.3 For those patients that had a biopsy to confirm response, 54% were clear of tumor.4 Side effects of this medication in order from most common to least include muscle spasms, alopecia, dysgeusia, weight loss, diarrhea and fatigue as discussed previously in the above case discussion.

Although treatment of BCC with HPIs has shown promising results, PFS is limited secondary to resistance of Smo Inhibition resulting in new tumor development and expansion of previously treated tumors, seen in our above case. Resistance of Smo was found secondary to mutations in Smo signaling pathway. The case described above shows what a devastating physical, psychological and financial burden these tumors can have, with multidisciplinary care through dermatologists, Mohs surgeons, radiation oncologists, plastic surgeons, psychiatrists and primary care physicians is needed to provide adequate care for this growing group of patients with challenging aBCCs.

CONCLUSION

Locally aBCCs are extremely challenging to treat. Future therapies may include inhibitors of protein down-stream to the hedgehog signaling pathway. The case described above shows what a devastating physical, psychological and financial burden these tumors can have, with multidisciplinary care through dermatologists, Mohs surgeons, radiation oncologists, plastic surgeons, psychiatrists and primary care physicians is needed to provide adequate care for this growing group of patients with challenging aBCCs.

REFERENCES

The diagnosis of congenital psoriasis is rare. Nationally, the prevalence of adults with psoriasis can be as high as 3% while estimations for psoriasis in the pediatric population is 1%. Psoriasis is an immune-mediated inflammatory process that produces activation of T cells that lead to abnormal keratinization. Certain genetic factors have been described, the most strongly associated human leukocyte antigen type is Cw6. We present a case of a biopsy proven psoriasis since birth. We review the literature and comorbidities associated with psoriasis for consideration in pediatric patients with this chronic disease.

**INTRODUCTION**

A three-week old female presented having pink patches and plaques with a fine scale to the intertriginous areas and scalp that were present since birth. She was born full term via spontaneous vaginal delivery without complications during pregnancy or delivery. On exam there were pink patches and plaques with a fine scale to the axilla, neck, inguinal folds and scalp. She had previously been treated with mometasone 0.1% cream daily for one week with little improvement. Family history was negative. A punch biopsy was obtained to ascertain if there was an underlying systemic process due to the presentation and poor response to potent topical steroids. One week following the biopsy the patient presented with an acute flare of erythematous patches and plaques to the body. The patient was admitted to the hospital for observation, treated with topical corticosteroids and wet wraps. Rheumatology was consulted and long term treatment options were discussed with the parents. The patient was started on acitretin.

**DISCUSSION**

**Congenital Psoriasis**

Rare presentation of an autoimmune, chronic skin disorder

**Clinical Presentation**

Erythematous plaques and patches with adherent scale over a wide distribution. Typically involves the face and scalp and spares the diaper area

**Histology**

Parakeratosis overlying a thickened epidermis and absent granular layer. Elongated rete ridges with dilated capillary loops and collections of neutrophils in the epidermis

**Pathogenesis**

Inflammatory cascade of T cells (Th2 and Th17) and the production numerous inflammatory cytokines leading to systemic inflammation, rapid keratinocyte turnover and systemic involvement. Triggers for psoriasis can be infectious, traumatic, stress or idiopathic. Genes implicated in psoriasis reside on chromosome 6 more commonly PSOR1. HLA types Cw6, B13, B17

**COMORBIDITIES**

**HISTOLOGY**

Elongated rete ridges with dilated capillary loops and collections of neutrophils in the epidermis.

**CASE REPORT**

A three-week old female presented having pink patches and plaques with a fine scale to the intertriginous areas and scalp that were present since birth. She was born full term via spontaneous vaginal delivery without complications during pregnancy or delivery.

On exam there were pink patches and plaques with a fine scale to the axilla, neck, inguinal folds and scalp. She had previously been treated with mometasone 0.1% cream daily for one week with little improvement. Family history was negative. A punch biopsy was obtained to ascertain if there was an underlying systemic process due to the presentation and poor response to potent topical steroids.

One week following the biopsy the patient presented with an acute flare of erythematous patches and plaques to the body. The patient was admitted to the hospital for observation, treated with topical corticosteroids and wet wraps. Rheumatology was consulted and long term treatment options were discussed with the parents. The patient was started on acitretin.

Two weeks into treatment visual improvement was seen.

**REFERENCES**


**CONCLUSION**

Congenital psoriasis is a less commonly encountered disease. That requires a skin biopsy for a definitive diagnosis and better directed therapy. Treatment can be fraught with complications and patient education. In pediatric patients rheumatology or pediatric dermatology involvement will help to maximize patient outcome. A great deal of education for parents of these children is required to understand expectations as well as the prognosis and future comorbidities.

**HISTOLOGY**

Pathology:
- Psoriasiform hyperplasia
- Folliculitis
- Granulomatous inflammation
- Inflammatory infiltrate
- Psoriatic epidermal hyperplasia
- Dermal vasculitis
- Granulomas

**COMORBIDITIES**

**CONCLUSION**

Congenital psoriasis is a less commonly encountered disease. That requires a skin biopsy for a definitive diagnosis and better directed therapy. Treatment can be fraught with complications and patient education. In pediatric patients rheumatology or pediatric dermatology involvement will help to maximize patient outcome. A great deal of education for parents of these children is required to understand expectations as well as the prognosis and future comorbidities.

**REFERENCES**


**COMORBIDITIES**

**DISCUSSION**

**CONCLUSION**

**REFERENCES**

Darier-Roussy Variant of Sarcoidosis

Stephen C. Cahill, DO
Resident Physician, Tricounty dermatology
Kansas City University of Medicine and Biosciences Consortium
Cuyahoga Falls, Ohio

Schield Wikas, DO
Program Director, Tricounty dermatology
Kansas City University of Medicine and Biosciences Consortium
Cuyahoga Falls, Ohio

Abstract

Darier-rousy disease (subcutaneous nodular sarcoidosis) is a rare variant of sarcoidosis. Classically, lesions present as asymptomatic, firm, mobile, subcutaneous nodules without epidermal changes.

We report a case of darier-rousy disease and pulmonary sarcoidosis that presented with lesions involving the hands and extremities. A biopsy of the left arm was taken. The biopsy revealed a normal epidermis and a deep dermal inflammatory infiltrate comprised of well-demarcated "naked granulomas" embedded in a dense fibrotic stroma.

Our case represents the clinicopathologic spectrum on which sarcoidosis can present and underscores why sarcoidosis is often known as the "great imitator."

Case Report

58 year old Caucasian female presented to the dermatology office with complaints of masses over her hands and upper and lower extremities. The lesions developed over the past 4-6 weeks. The patient complained of mild to moderate shortness of breath. All other review of symptoms were negative. Patient denied recent travel or new medications. Past history is significant for asthma, COPD, atrial fibrillation, hypercalemia or hypercalciuria, so a serum calcium and 24 hour urine calcium may be warranted. Chest radiograph, pulmonary function test and electrocardiogram may also be helpful. Past history is significant for sarcoidosis. Other therapies include methotrexate, thalidomide, minocycline, isotretinoin, allopurinol, cyclophosphamide or hydroxychloroquine. Our patient was established with a pulmonologist. She was started on prednisone which improved her cutaneous and pulmonary symptoms. She is continued to be followed clinically.

Discussion

Sarcoidosis is a disease that can affect all ages, gender, and ethnicities. With peak incidence distribution in a bimodal pattern; age 25-35 and 45-65. The most common presentation is in African American women in their fourth decade. While the pathogenesis of sarcoid is unknown, it is believed to be immune-mediated. The noncaseating granulomas seen in sarcoid are made up of CD4 helper T-cells. Patients are also noted to have elevated levels of IFN-gamma and IL-2 with a Th1 type immune response.

Cutaneous sarcoidosis can present clinically with a variety of cutaneous scenarios and is often known as "a great imitator". Approximately 25% of patient with sarcoidosis will have cutaneous findings. A majority of patients have systemic manifestations that can affect the lungs, peripheral lymph nodes, heart, kidneys, gastrointestinal tract, nervous system, liver, spleen, endocrine glands, muscle, and bone. One of the most common findings is lung involvement, affecting approximately 90% of patients. There is no definitive diagnostic test for sarcoidosis. Although, roughly 30% of patient will have an elevated anti-nuclear antibody (ANA), and 60% of patients will have an elevated serum angiotensin-converting enzyme (ACE) level. Many patients may have hypercalemia or hypercalciuria, so a serum calcium and 24 hour urine calcium may be helpful.

The mainstay of therapy is corticosteroids. Other therapies include methotrexate, thalidomide, minocycline, isotretinoin, allopurinol, cyclophosphamide or hydroxychloroquine. Our patient was established with a pulmonologist. She was started on prednisone which improved her cutaneous and pulmonary symptoms. She continues to be followed clinically.

Conclusion

Our case exemplifies the clinicohistologic spectrum on which sarcoidosis can present. The constellation of clinical findings was histologically confirmed to be manifestations of the darier-rousy disease variant. When lesions suspicious for darier-rousy disease present it is helpful to perform multiple biopsies and include underlying subcutaneous and adipose tissue.

Sarcoidosis often has systemic manifestations that can affect almost every organ in the body. The clinician should remain a high clinical suspicion of any abnormalities found with a review of systems. One of the most common findings is pulmonary involvement affecting approximately 90% of patients. There are several clinically relevant subtypes and syndromes of sarcoidosis, including darier-rousy disease, lupus pernio, Lofgren syndrome, and Heerfordts syndrome.

The mainstay of treatment for sarcoidosis is treatment with corticosteroids. If a steroid sparing regimen is needed methotrexate or antimalarials are common effective alternatives.

References

Discussion

Chromoblastomycosis, also known as chromomycosis, is a verrucous dermatosis commonly present on the lower extremities in individuals who live in the tropics or subtropics. There are 6 causative organisms involved, the most common of which being Fonsecaea pedrosoi. Risk factors include exposure to contaminant soil, previous site of injury for inoculation, and male gender. The fungi prefer to live in areas of high humidity and decaying materials; and farm workers or individuals who live within this environment are at particular risk. Long term sequelae of untreated lesions may include secondary infection with hematologic dissemination, lymphedema, and squamous cell carcinoma within the lesion. Therefore, treatment is paramount. Chromoblastomycosis has been known to be relapsing with a low cure rate. Fortunately, our patient did not had any of these consequences despite the presence of this lesion for over 10 years.

Although there is a wide array of treatment options, no gold standard exists for the treatment of chromoblastomycosis. Current therapy includes oral anti-fungal agents, surgical excision, electrodessication, cryotherapy, topical chemotherapeutic agents, photodynamic therapy, and topical heat (Table 1). Some authors are proponents of combination therapy; e.g. itraconazole + cryotherapy or itraconazole + terbinafine. Pulse therapy has also been reported to prevent relapse.

A 31-year-old Kenyan male presented with extensive verrucous ulcerated plaques above the medial aspect of the right ankle. The lesion was present for over 10 years and had gradually ulcerated and extended superiorly on his leg. Patient admitted to frequent walks over muddy soil with bare feet especially during the rainy seasons. Patient denied any pertinent review of systems, medical history, or surgical history. He could not account for any previous injury to his legs.

Prior treatments included ibuprofen, polysporin, iodine solution for daily cleansing, warm compresses, bacitracin, neomycin, loratadine, and oral fluconazole, none of which provided much improvement. Patient was next started on oral terbinafine 250mg daily which he took over the course of nearly two years. During this period of time, he did have a hiatus in therapy for several months. Over three years, the lesion had slowly improved, as illustrated in the comparison photos (Figs. 1 & 2). The option to treat with terbinafine was due to its higher availability and lower cost.

Histopathology

A punch biopsy was performed and revealed granulomatous inflammation with pigmented yeast, also referred to as Medlar bodies or sclerotic bodies (Fig. 3 & 4) consistent with chromoblastomycosis.
Undifferentiated Pleomorphic Sarcoma of Skin: Clinical and histopathologic emulator of atypical fibroxanthoma, distinction imperative

Michael Carletti DO1, Peter Malouf DO2, Zachary Ingersoll MS-III1, Greg Hosler MD, PhD2, Stephen Weis DO1
1 University of North Texas Health Science Center, Forth Worth, TX; 2 ProPath, Dallas, TX

History

90 year old Caucasian man with history of several non-melanoma skin cancers, presented with a 4.0 x 2.5 cm ulcerated, friable, exophytic mass on the left mid frontal scalp of two months duration.

The patient had previously presented two months earlier with non-healing scalp lesion. At that time, the lesion was a 0.9 cm ulcerated, erythematous, papule. A shave biopsy of the lesion was performed however the histopathology was non-diagnostic and demonstrated marked parakeratosis, fibrosing granulation tissue in the upper dermis, with a massive neutrophilic infiltrate.

A repeat biopsy was performed of the exophytic mass for diagnostic and de-bulking purposes. The histopathology of the re-biopsy demonstrated an ulcerated tumor filling the dermis. The tumor cells were pleomorphic, spindled, arranged in vague fascicles, and extended to the deep margin. The cytology was markedly atypical, with large irregular nuclei, prominent nucleoli, and numerous mitoses, including atypical forms. Immunohistochemical analysis was performed. The tumor cells were diffusely positive for CD10 and weakly positive for CD68. Cytokeratin AE1/AE3, desmin, S-100, EMA, diffusely positive for CD10 and weakly positive for cytology was markedly atypical, with large irregular fascicles, and extended to the deep margin. The margins were free of tumor however the patient was referred to oncology for further evaluation and consideration of adjuvant therapy. The patient and family declined oncology referral, and as of four months post-excision, there was no evidence of recurrence.

Discussion

Undifferentiated pleomorphic sarcoma (UPS) of skin can clinically and histopathologically mimic atypical fibroxanthoma (AFX). Distinguishing between the two is important, as the prognoses of these tumors are vastly different. UPS follows more of a benign course, typically recurs only after incomplete excision, and rarely metastasizes. UPS, previously grouped into the malignant fibrous histiocytoma (MFH) category, is more aggressive in nature, and has a high rate of recurrence along with malignant/metastatic potential.

Clinically, UPS presents as a rapidly growing solitary nodule on sun-damaged, actinic skin of the elderly, usually on the head and neck region. UPS is considered a soft tissue tumor but can occur superficially in the skin, with a presentation mimicking AFX.

Histologically, UPS and AFX consist of spindle shaped cells arranged in a fascicular pattern and can exhibit multinucleation, pleomorphism, and mitotic figures. UPS is distinguished from AFX by deep subcutaneous involvement, perineural and/or lymphovascular invasion, and necrosis. Immunohistochemically, both stain negative for S-100/SOX-10, cytokeratin, CD31/CD34, and desmin/myosin allowing differentiation from other pleomorphic tumors in the skin, such as melanoma, squamous cell carcinoma, angiosarcoma, and leiomyosarcoma. AFX and UPS are diagnoses of exclusion, requiring broad lineage-specific immunohistochemical analysis to exclude other poorly differentiated tumors.

There is significant overlap between AFX and UPS of skin clinically, morphologically, and immunohistochemically. Histologically, there are identifiable differences found on excision of the lesion. Distinguishing the two requires complete excision to evaluate for aggressive features, specifically the tumor’s extent of invasion, with AFX designated to tumors restricted to the dermis. UPS of skin invades deeply into subcutaneous tissue and can demonstrate tumor necrosis, perineural or lymphovascular invasion. These features are consistent with its more aggressive course including recurrence and metastatic potential.

Undifferentiated pleomorphic sarcoma is a rare entity with confusing, misleading, and changing nomenclature previously named malignant fibrous histiocytoma. Undifferentiated pleomorphic sarcoma of skin is a diagnosis of exclusion made after complete excision with histology aided by immunohistochemistry. The correct diagnosis is crucial to optimal outcome, preventing mismanagement of an aggressive and potentially fatal tumor.

Physical Exam

Clinically, UPS presents as a rapidly growing solitary nodule on sun-damaged, actinic skin of the elderly, usually on the head and neck region. UPS is considered a soft tissue tumor but can occur superficially in the skin, with a presentation mimicking AFX.

Histologically, UPS and AFX consist of spindle shaped cells arranged in a fascicular pattern and can exhibit multinucleation, pleomorphism, and mitotic figures. UPS is distinguished from AFX by deep subcutaneous involvement, perineural and/or lymphovascular invasion, and necrosis. Immunohistochemically, both stain negative for S-100/SOX-10, cytokeratin, CD31/CD34, and desmin/myosin allowing differentiation from other pleomorphic tumors in the skin, such as melanoma, squamous cell carcinoma, angiosarcoma, and leiomyosarcoma. AFX and UPS are diagnoses of exclusion, requiring broad lineage-specific immunohistochemical analysis to exclude other poorly differentiated tumors.
A Case of Urticaria Pigmentosa

Vanita Chand, DO*, Sergey Petrosian, DO**, Suzanne Sirota Rozenberg, DO, FAOCD***

*2nd Year Resident, St. John’s Episcopal Hospital-Dermatology Residency Program, Far Rockaway, NY
**Intern, St. John’s Episcopal Hospital, Far Rockaway, NY
***Program Director, St. John’s Episcopal Hospital-Dermatology Residency Program, Far Rockaway, NY

---

Abstract

We present a case of the most common form of cutaneous mastocytosis in children, Urticaria Pigmentosa (UP).

Introduction

Mastocytosis is a group of rare disorders involving excess proliferation and accumulation of mast cells. It is divided into two entities: cutaneous mastocytosis involving the skin, and systemic mastocytosis, which affects multiple organs (1). We present a case of the most common form of cutaneous mastocytosis in children, Urticaria Pigmentosa.

Case Presentation

A 3-month-old male presented to dermatology clinic for a rash that started a few weeks after birth. Mom stated the brown spots appeared on the arms initially, and then gradually involving the abdomen, chest, back, legs, and face. ID ruled out rash secondary to congenital infection with negative serology for Rubella, CMV, RPR. On review of systems, the patient had intermittent episodes of respiratory distress. The patient was reaching developmental milestones and growing appropriately per the pediatrician. On physical examination, the patient appeared comfortable. There were multiple dark brown-red macules and patches on the face, arms, legs, chest, abdomen, and back (Figure 1). Darier sign was positive. 2 mm punch biopsy revealed a proliferation of mast cells with +CD117 marker, consistent with Urticaria Pigmentosa. On follow up, we learned that the patient was scheduled to have surgery for umbilical hernia repair.

Discussion

UP is the most common form of cutaneous mastocytosis in childhood. It presents in the first few weeks of life as 5 to 15 mm pink to brown colored, urticarial, macules, papules, vesicles, or nodules. Lesions are more commonly found on the trunk and generally spare the central face, palms, and soles. The lesions exhibit the classic Darier’s sign, which is urtication upon local rubbing of a lesion. Most children with UP will have a limited course with spontaneous resolution by adolescence. However, 10-15% of cases may persist into adulthood (1). Diagnosis of UP can be confirmed with biopsy. On histology, there is a dense dermal collection of uniformly spaced mast cells. Eosinophils are also commonly found within the dermis (Figure 2). Staining with Leder stain will show red colored mast cells, while with the Giemsa stain mast cell granules will stain a metachromatic purple color. Toluidine blue, trypase and CD117 stains (c-kit tyrosine kinase) may also be used (Figure 3). Further workup may be considered if the patient exhibits systemic symptoms (2).

Treatment is largely focused on symptom relief and prevention of mast-cell degranulation by avoiding triggers. Exacerbating factors include exercise, heat, friction of skin, and ingestion of hot spicy foods. Systemic agents that can cause mast-cell degranulation include alcohol, narcotics, NSAIDs, polymyxin B, and anticholinergic medications. There are several systemic anesthetic drugs that can actually precipitate an anaphylactic reaction in mastocytosis. Lidocaine, however, is safe when used as a local anesthetic. Safe systemic anesthetics include fentanyl, sufentanil, remifentanil, midazolam, propofol, ketamine, desflurane, sevoflurane, cisatracurium, pancuronium and vecuronium bromide. Antihistamines, both first and second generation, are a mainstay of treatment. Topical, intralesional and oral steroids can be used depending on disease severity. Psoralen with UVA (PUVA) along with other light therapies have shown benefits as well (3,4).

Conclusion

We present a case of Urticaria Pigmentosa in a patient who was scheduled for a surgical procedure requiring systemic anesthetics. It was imperative to advise and counsel our patient about the risks associated with anesthetics i.e, an anaphylactic reaction (4). Thus, this case exemplifies the importance of counseling patients with mastocytosis about medication and lifestyle-related triggers to prevent symptoms.

References

5. James, William D., MD; Berger, Timothy G., MD; Elston, Dirk M., MD. Andrews’ Diseases of the Skin. Published January 1, 2016. © 2016.
INTRODUCTION

• According to the EPA and CDC, the most prevalent diagnosed cancer in the United States is skin cancer. One in five Americans will be diagnosed with skin cancer in their lifetime.  

• The American Cancer Society estimated that 76,699 people would be diagnosed with melanoma in 2013, of which Florida represents 5,330 of these new cases, the second highest population behind California.

• Nonmelanoma skin cancers (NMSCs) include basal cell carcinoma and squamous cell carcinoma. These are the most commonly diagnosed forms of cancer in the United States, making up 1.3 million cases annually.

• They are usually diagnosed after the age of 55, and although the death rates due to NMSCs are low, they represent about 5% of all Medicare cancer expenditures.

• Direct sun exposure, blistering sunburns in childhood, and family history are risk factors for this type of skin cancer.

• Malignant melanoma is the deadliest form of skin cancer and can develop from pre-existing moles or on normal skin.

• The risk factors for melanoma include a light complexion, a large number of moles, blistering sunburns during childhood, sun exposure, and a family history.

• If caught early, melanoma can be curable, thus it is important to raise awareness and concern about skin cancer and had more skin cancer screenings.5

METHODS

• Participants were recruited from the waiting room of the internal medicine and geriatric section of the Ziff Clinic at Nova Southeastern University.

• Inclusion criteria to participate in the study were 40 years of age and older, male or female, all races, English speaking, and those who could provide voluntary consent.

• Forty-seven patients were willing to participate and were then given a consent form and survey.

• The survey consisted of 18 questions answered by the patients. The questions determined education about skin cancer, skin cancer screening habits, skin cancer treatment options, sun-safe practices, and beliefs about skin cancer and sun exposure.

• Data was then analyzed using Excel software to give averages and percentages for each question on the survey.

RESULTS

• Forty-seven patients were willing to participate and were then given a consent form and survey.

• Five participants in this group could identify the most dangerous form of skin cancer: 95% (n=6) reported that they were aware of the different treatment options for skin cancers.

• 79% (n=17) reported that they avoided the sun between 10:00am and 4:00pm.

• They were not performing skin self-examinations at home but they performed skin self-examinations at home regularly. Of those, 47% (n=7) stated that they performed skin self-examinations at home regularly.

• The majority of the participants who did report using sunscreen stated that they applied it to their face, neck, and arms in addition to most other parts of their body.

• 50% (n=4) stated that they had a skin cancer screening in the last 12 months, 9% (n=2) had been there or were at an increased risk of developing skin cancer. Only 32% (n=3) stated that they performed skin self-examinations at home regularly.

• 51% (n=11) stated that they had sorely neglected what to look for, which is in the ABCs of suspicious moles—Asymmetry, Border irregularities, Color variation, and a new lump.

• 85% (n=9) stated that they would seek medical attention for a changing mole. 15% (n=1) stated that they had a family member with skin cancer, and of those, only two participants knew what type of skin cancer their family member had.

• Are you aware of the different types of skin cancers?

• 60% (n=12) stated that they thought there was a lack of knowledge and information available to the public on sun protection.

• 56% (n=10) stated that they had known then what they know now about skin cancer and sun damage.

• Do you use sun protection?

• 74% of participants (n=35) stated that they would have avoided the sun in their youth if they had known then what they know now about skin cancer and sun damage.

• The survey consisted of 18 questions answered by the patients. The questions determined education about skin cancer, skin cancer screening habits, skin cancer treatment options, sun-safe practices, and beliefs about skin cancer and sun exposure.

• Data was then analyzed using Excel software to give averages and percentages for each question on the survey.

• 91% (n=18) reported that they had a skin cancer screening in the last 12 months.

• 36% (n=6) had been there or were at an increased risk of developing skin cancer.  32% (n=6) stated that they performed skin self-examinations at home regularly.

• 34% (n=6) stated that they had sorely neglected what to look for, which is in the ABCs of suspicious moles—Asymmetry, Border irregularities, Color variation, and a new lump.

• 79% (n=15) stated that they would seek medical attention for a changing mole. These patients were not performing skin self-examinations at home but they performed skin self-examinations at home regularly. Of those, 47% (n=8) stated that they performed skin self-examinations at home regularly.

• 71% (n=13) stated that they had a family member with skin cancer, and of those, only two participants knew what type of skin cancer their family member had.

• Are you aware of the different types of skin cancers?

• 60% (n=11) stated that they thought there was a lack of knowledge and information available to the public on sun protection.

• 56% (n=10) stated that they had known then what they know now about skin cancer and sun damage.

• Do you use sun protection?

• 74% of participants (n=35) stated that they would have avoided the sun in their youth if they had known then what they know now about skin cancer and sun damage.

DISCUSSION

• The majority of participants had not had a skin cancer screening, nor had they had a physician discuss skin cancer with them.

• They were not performing skin self-examinations at home but would seek medical attention for a changing mole. These outcomes imply that there may be a lack of emphasis on the importance of skin cancer screening among primary care physicians (PCPs).

• PCPs should be encouraged to discuss skin cancer prevention and diagnosis with their patients and to provide their patients with literature concerning this common, and potentially deadly, disease.

• PCPs should be encouraged to pursue continuing education regarding dermatological diseases in order to better recognize when to refer their patients to a dermatologist.

• PCPs should instruct their patients on how to properly perform a self-examination, how to identify suspicious moles, and encourage them to use sunscreen and sun protection every day, regardless of their time in direct sunlight.

• For the 47% of participants who do not protect themselves properly when exposed to the sun, they may be difficult to motivate since sun damage can take decades to appear and is often viewed as an imminent problem. Most skin cancers are only skin deep, with rarely associated symptoms or internal manifestations, so patients may not take it seriously.

• Skin cancer is the most common form of cancer in the United States, and malignant melanoma is responsible for one death every hour.

• Skin cancer educational efforts through the media are the most prominent form of raising awareness, thus information regarding skin cancer prevention, detection, and treatment should continue to be distributed by the media. However, behavioral change is not shown over the long term, necessitating implementation of more patient education from PCPs.

• There are several public health initiatives working to raise skin cancer awareness. Skin cancer costs billions of dollars a year to treat. These initiatives are critical to public health and will hopefully, in the long run, help to save lives and to lower the yearly cost created by skin cancer in the United States.

• It is imperative that PCPs talk with their patients about skin cancer, and that people are educated through media and public initiatives about the facts concerning skin cancer, performing skin self-examinations, and implementing sun-safe practices into their daily lives.

REFERENCES


A Case of Chordoma Cutis Following Recurrence of L3 Chordoma

Kylee N. Crittenden, DO, Austin Longberg, DO, Shannon C. Trotter, DO, Sara B. Peters, MD, PhD
The James at Martha Morehouse Medical Plaza, Columbus, OH

A 67-year-old male reported to the outpatient dermatology clinic for skin surveillance. Past medical history was significant for uveal melanoma, squamous cell carcinoma (SCC) of the tongue, and conventional type chordoma of L3. The chordoma was diagnosed four years prior and was treated with surgery followed by radiation and imatinib and sirolimus. At the time of presentation to our clinic, the chordoma had recurred and the patient was re-started on imatinib and sirolimus. On physical exam, a friable, pink nodule measuring 1.0 centimeter was noted in the patient’s low back near the laminectomy incision site (Figure 1). The nodule was asymptomatic. A shave biopsy was performed and pathology revealed a lesion present in the dermis composed of cords and strands of vacuolated cells in a myxoid stroma, consistent with chordoma cutis (Figure 2). Lesional cells stained positive for epithelial membrane antigen (EMA) and negative for S100. Imatinib and sirolimus were continued for treatment of his metastatic chordoma. Follow-up scans to assess the efficacy of the treatment are pending.

Chordomas are rare bone tumors that originate from the embryonic notochord and may occur in the skull base, the cervical, thoracic, and lumbar spine, as well as the sacral region. Chordoma cutis is the term for extension of a chordoma to the skin, either by direct extension or metastasis.

Chordoma is a neoplasm that typically affects those between 55 and 68 years of age. Due to its derivation from the notochord, locations affected by chordoma lie along the spine, with approximately 50% of tumors occurring midline in the sacrococcygeal region. Chordomas often progress to an advanced disease stage before the onset of symptoms, which classically begin with insidious onset of pain followed by paresthesias and other neurological sequelae.

Given the name by Su in 1993, ‘chordoma cutis’ refers to the cutaneous form of chordoma. Chordomas can also metastasize to the lungs, liver, lymph nodes and brain. Nodular cutaneous lesions in patients with a history of chordoma should be investigated thoroughly with a high suspicion for chordoma cutis. In rare cases, a skin lesion can be the initial presentation rare tumor derived from embryonic notochord that comprises 1-4% of all malignant tumors of the bone. It is a slow growing, locally invasive disease, leading to the diagnosis of a chordoma.

Histologically, the hallmark finding is the presence of vacuolated cells with an eccentric, hyperchromatic nucleus, known as physaliferous or bubble cells, within a myxoid or mucinous stroma (Figure 2). The classic triad of stains include S100, cytokeratin, and vimentin.

Numerous reported cases have demonstrated that the primary tumor expresses S100 positivity, while the secondary cutaneous tumor does not.

This case represents a rarely reported occurrence of cutaneous metastasis accompanying a recurrent chordoma. Further research is needed to improve morbidity and mortality in patients with chordoma. Surgical excision remains the treatment of choice for chordomas; however, positive margins are common due to the tumor’s proximity to nervous tissue, size of tumor at the time of diagnosis, and invasion into surrounding tissues and recurrence rates are as high as 75%.

In cases of chordoma cutis, Mohs micrographic surgery has been utilized and is an option that may provide the highest cure rate. Chemotherapeutic agents, such as tyrosine kinase inhibitors imatinib and sorafenib after surgical excision, have been documented with minimal success. In addition, radiotherapy has shown minimal to moderate usefulness as adjunctive therapy. With increased awareness of chordoma and chordoma cutis, prompt diagnosis and surgical excision may improve survival of these patients.

References


Acknowledgements

Thank you to Stephanie Deming and Alleen Center for your help with acquiring the clinical and histologic images for this poster.
Pyoderma Faciale: A Case Report
Amelia Damse, DO, MPH, Asmi Sanghvi, MS IV
Orlando Dermatology Residency / KCU GME / Orlando, FL

INTRODUCTION
Pyoderma faciale is an inflammatory condition that classically affects the mid-facial region in women in their 20s and 30s. While its true epidemiology is unknown, it may be confused with other granulomatous, infectious and inflammatory conditions that affect the face in this population. Making the distinction is important in order to promptly initiate appropriate therapy. We review some of the conditions that should be considered in the differential, and discuss how to make the distinction between these entities.

CASE: A 24-year-old female presents to clinic concerned about a rash on her face that started one month prior to the visit. The rash began on her right cheek, right paranasal area, and chin as erythematous papules and pustules which coalesced in some areas to form erythematous plaques. It rapidly progressed to involve both cheeks and her chin. Upon further questioning she admitted to nail and subjective fevers. She had no prior treatment for this condition. Her past medical history was remarkable for hypothyroidism for which she was taking Synthroid 50 mcg daily. Her past surgical, social, and family histories were not remarkable. A discussion about initiating treatment with isotretinoin was held with the patient but she initially declined, so she was given a prednisone taper and started on doxycycline. Upon completion of the steroid taper her rash flared again and she agreed to initiate isotretinoin treatment at her one-month follow up visit. She presented a prednisone taper and started on isotretinoin 10 mg daily, which was increased to 20 mg at her next visit since her condition had improved.

DISCUSSION: The first line treatment for pyoderma faciale is isotretinoin. This drug is an effective medication in the treatment of many dermatologic conditions including nodulocystic acne, recalcitrant inflammatory acne, pyoderma faciale, acne fulminans, and gram negative folliculitis. It is also related to vitamin A and serves many functions including normalization of keratinization, causing atrophy of sebaceous glands and reducing sebum production, inhibits collagenase, and downregulates proliferative keratin. The goal cumulative dose when using isotretinoin is 120-150 mg/kg.

While being an effective treatment, the side effect profile of isotretinoin is extensive. The most common side effects of isotretinoin therapy observed are xerosis, xerophthalmia, and xerostomia. Most of the side effects are tolerable, but in severe cases they may be managed by decreasing the dosage of isotretinoin. Pseudotumor cerebri has been described as a side effect of isotretinoin use, and it is important to note that concurrent use of isotretinoin and tetracyclines increases the risk of this complication.

Granulomatous perifollicular dermatitis is another granulomatous condition that may resemble pyoderma faciale both in morphology and distribution. It is characterized by pink to flesh-colored papules that erupt in the perioral and periorbital regions, with a few cases reporting lesions outside of the facial area, including extremity, trunk, and a few reported cases on the labia majora. Histology reveals a dense granulomatous infiltrate with prominent lymphocytes. While pyoderma faciale typically affects middle-aged women, granulomatous perifollicular dermatitis is most commonly found to affect prepubertal black children particularly those with a Caribbean or African descent, occasionally affecting Caucasians as well. Topical steroids are heralded as either the cause of this condition or a major exacerbating factor. Therapy involves systemic antibiotics such as metronidazole in young patients or tetracycline in patients over 18 years of age.

CONCLUSION
Pyoderma faciale is an inflammatory condition that affects middle-aged women, and presents as inflammatory papules and fluctuant nodules involving the central area of the face, particularly in the perioral and periorbital areas. It is characterized by fibrosis and telangiectasia of the skin, and the diagnosis is made by exclusion. We discuss how to distinguish this entity from other granulomatous, infectious and inflammatory conditions that may resemble it.

REFERENCES:


Tinea faciei is an inflammatory condition that affects middle aged women, and presents as inflammatory papules and fluctuant nodules involving the central area of the face. Typically, it presents with telangiectasia and erythema. The condition may be confused with other granulomatous, infectious and inflammatory conditions that affect the face in this population. Making the distinction is important in order to promptly initiate appropriate therapy. We review some of the conditions that should be considered in the differential, and discuss how to make the distinction between these entities.

CASE: A 24-year-old female presents to clinic concerned about a rash on her face that started one month prior to the visit. The rash began on her right cheek, right paranasal area, and chin as erythematous papules and pustules which coalesced in some areas to form erythematous plaques. It rapidly progressed to involve both cheeks and her chin. Upon further questioning she admitted to nail and subjective fevers. She had no prior treatment for this condition. Her past medical history was remarkable for hypothyroidism for which she was taking Synthroid 50 mcg daily. Her past surgical, social, and family histories were not remarkable. A discussion about initiating treatment with isotretinoin was held with the patient but she initially declined, so she was given a prednisone taper and started on doxycycline. Upon completion of the steroid taper her rash flared again and she agreed to initiate isotretinoin treatment at her one-month follow up visit. She presented a prednisone taper and started on isotretinoin 10 mg daily, which was increased to 20 mg at her next visit since her condition had improved.

DISCUSSION: The first line treatment for pyoderma faciale is isotretinoin. This drug is an effective medication in the treatment of many dermatologic conditions including nodulocystic acne, recalcitrant inflammatory acne, pyoderma faciale, acne fulminans, and gram negative folliculitis. It is also related to vitamin A and serves many functions including normalization of keratinization, causing atrophy of sebaceous glands and reducing sebum production, inhibits collagenase, and downregulates proliferative keratin. The goal cumulative dose when using isotretinoin is 120-150 mg/kg.

While being an effective treatment, the side effect profile of isotretinoin is extensive. The most common side effects of isotretinoin therapy observed are xerosis, xerophthalmia, and xerostomia. Most of the side effects are tolerable, but in severe cases they may be managed by decreasing the dosage of isotretinoin. Pseudotumor cerebri has been described as a side effect of isotretinoin use, and it is important to note that concurrent use of isotretinoin and tetracyclines increases the risk of this complication.

Granulomatous perifollicular dermatitis is another granulomatous condition that may resemble pyoderma faciale both in morphology and distribution. It is characterized by pink to flesh-colored papules that erupt in the perioral and periorbital regions, with a few cases reporting lesions outside of the facial area, including extremity, trunk, and a few reported cases on the labia majora. Histology reveals a dense granulomatous infiltrate with prominent lymphocytes. While pyoderma faciale typically affects middle-aged women, granulomatous perifollicular dermatitis is most commonly found to affect prepubertal black children particularly those with a Caribbean or African descent, occasionally affecting Caucasians as well. Topical steroids are heralded as either the cause of this condition or a major exacerbating factor. Therapy involves systemic antibiotics such as metronidazole in young patients or tetracycline in patients over 18 years of age.

Acne conglobata is an inflammatory condition that also resembles pyoderma faciale. The clinical morphology includes numerous comedones and large abscesses with interconnecting sinuses, cysts, and inflammatory nodules generally affecting young males around 16 years of age. Lesions appear on the face, back, buttocks, chest, anterior neck, and shoulders. Therapy with isotretinoin is recommended early on to reduce the risk of scarring. Additional treatments include oral antibiotics, intralesional and systemic steroids. Other therapeutic options include CO2 laser for sinuses tractus, and fractional laser for scars (16). The subpopulation affected, the presence of comedones, and the distribution of the lesions allows the clinician to differentiate between these two diseases.

One case report describes rosacea fulminans with ocular involvement. Slt was exam was consistent with keratitis and conjunctivitis, with multiple central opacities and cell deposit. One simple KOBD deep can be performed in the office to look for dematoophytes in order to differentiate between the two conditions. Treatment of choice is topical antifungal drugs such as azoles (17). It is an important diagnosis to consider because misdiagnosing this condition and treating with steroids will exacerbate tinea faciei.
A Case of Henoch-Schonlein Purpura in an Adult

Lisa M. Diaz, D.O. (PGY-3)1, Carlos H. Nousari, M.D.2
1) Dermatology Resident, Department of Dermatology, Broward Health Medical Center 2) Program Director, Department of Dermatology, Broward Health Medical Center, Graduate Medical Education Department, Fort Lauderdale, FL 33316

BACKGROUND

Henoch-Schönlein Purpura (HSP), or IgA Vasculitis, is characterized by the clinical tetrad of palpable purpura, arthralgia/arthritis, abdominal pain, and hematuria. The majority of cases, approximately 90%, are diagnosed in children. There is a male predominance and an increase in number of cases during the winter season. The incidence of HSP in children is approximately 20 cases per 100,000. It is less common in adults with textbooks reporting an incidence of 14 cases per million.

Triggers of HSP include medications, infections, malignancies, inflammatory disorders, and idiopathic causes. The most common triggers in children are infectious, particularly viral infections, streptococcal pharyngitis, and mycoplasma. In adults, medications are the most common trigger. Virtually every class of medication can induce HSP, and the time from introduction to reaction may vary from hours to years. Therefore, it may be difficult to determine which drug is responsible.

In order to diagnose HSP the patient must demonstrate palpable purpura plus one of the following: arthritis/arthralgia, diffuse abdominal pain, a biopsy demonstrating IgA deposition or renal involvement manifested as hematuria or proteinuria.

CASE PRESENTATION

A 59-year-old previously healthy Caucasian woman presented with a one-month history of a bilateral progressive lower extremity rash associated with polyarthralgia and dependent edema (Figures 1-3).

Over the past month, she had been seen at two urgent care centers and two emergency rooms and each time was diagnosed with cellulitis and discharged on oral antibiotics and a prednisone taper. Her symptoms would improve slightly but then would flare once her prednisone taper was completed.

Review of systems was positive for arthralgia in the bilateral knees and ankles, fatigue, and burning and pain in the area around the lesions. Pertinent negatives included lack of abdominal pain or melena.

Her vitals were stable except for her systolic blood pressure which was persistently elevated in the 170s to 190s. A CBC was notable for a leukocytosis of 18,500. A CMP was significant for an elevated creatinine of 1.2. A subsequent urinalysis revealed moderate hematuria and proteinuria.

Work-ups for systemic lupus erythematosus, immunofluorescence with electrophoresis, total serum immunoglobulins, and beta 2 microglobulin were negative. Further studies of medium vessel vasculitides and viral serology (including EBV, VZV, HIV, and a hepatitis panel) were all negative. Lower extremity wound cultures were positive for E. coli and S. aureus. Ultrasound of the bilateral lower extremities was unremarkable. Magnetic resonance imaging demonstrated diffuse edema and enhancement of the soft tissue consistent with cellulitis.

CLINICAL IMAGES

Figures 1-3: Violaceous erythematous non-blanchable papules distributed over the extremity surfaces of the bilateral lower and upper extremities.

PATHOLOGY

Punch biopsies were performed and submitted for histopathological and direct immunofluorescence (DIF) examination. Hematoxylin & eosin (H&E) staining of the specimens revealed leukocytoclastic vasculitis (Figures 4 & 5). DIF revealed perivascular IgA, C3, and fibrin deposits consistent with IgA Vasculitis (Figure 6).

These biopsy results in the setting of the clinical findings of palpable purpura, arthralgia, proteinuria, hematuria, and hypertension confirmed the diagnosis of adult Henoch-Schönlein Purpura.

TREATMENT & MANAGEMENT

Due to severity of disease, renal involvement and joint involvement the following therapy was initiated:

- Solumedrol pulse therapy: 500 mg IV daily infusion x 3 days
- Mycophenolate Mofetil 1,500 mg twice daily
- Prednisone 80 mg qAM

The patient was instructed to follow up with a dermatologist, nephrologist, rheumatologist, and internist at an academic center so that her care could be more easily managed between the different specialties.

REFERENCES


Cyclosporine Ophthalmic Solution Inducing Hair Hyperpigmentation

Chelsea Duggan DO*, Steven Grekin DO**
*Dermatology Resident, **Dermatology Program Director, Beaumont Health-Trenton

Introduction

Hair follicles are important adnexal structures that have both ectodermal (hair) and mesodermal (dermal papillae) derivation.1 Hair cycles through various phases including anagen (growth) catagen (regression) and telogen (resting phase).2 Involved in the cycling includes various cytokines and growth factors such as FGF-5/7 (fibroblast growth factor), TGF-β/α (transforming growth factor), BMP-2/4 (bone morphogenetic protein), vitamin D receptor, RXR-α (retinoid X receptor-α), PTHRp (parathyroid hormone-related peptide), TNF-α (tumor necrosis factor), IL-1α (interferon-γ) among others.2 Cyclosporine is a calcineurin inhibitor that was identified in 1976 to have potent immunosuppressive effects. Cyclosporine was originally approved for organ rejection in the United States in 1983 and then reformulated in 1995 to have better bioavailability.1 Cyclosporine has many adverse effects but of interest to this case report include hypertrichosis and hyperpigmentation. A literature search of cyclosporine ophthalmic drops revealed no case reports of hyperpigmentation of the scalp hairs secondary to this treatment. However, oral cyclosporine has many reported cases of both of the above side effects.

Case Study

A 69-year-old female presented to the clinic complaining of her hair darkening in color. She stated this began after beginning treatment with cyclosporine ophthalmic solution for ocular dryness. The patient has had gray hair since approximately the age of 60 but did have blonde hair as a child. Patient admits to dying her hair blonde after she had significant amounts of gray hair. She denied hypertrichosis, denied pruritus, or pain of the scalp. She states the change in hair color happened over a period of several months. The hairs that are hyperpigmented grow in a patchy pattern diffusely throughout her scalp. Her past medical history includes only seasonal allergies. She admits to only using cyclosporine ophthalmic solution twice a day and taking a women’s daily vitamin. She denies any other medication and denies any herbal supplements. On physical examination, patient had no apparent areas of hair loss, no erythema and no scale of the scalp.

Discussion

The mechanism of action of cyclosporine has not been fully delineated yet it is known to inhibit production of interleukin-2 (IL-2) via inhibiting calcineurin which reduces the activity of a transcription factor, nuclear factor of activated T-cells (NFAT-1).3 Cyclosporine has many adverse reactions but of interest is hypertrichosis and hyperpigmentation. S Lan et al. report that caspase-dependent apoptosis pathways play a vital role in transition of hair from anagen to catagen and cyclosporine decreases this cycling.3 Similarly, a study by Gafter-Guili et al. revealed cyclosporine may induce hair growth by increasing the amount of follicles.4 Cyclosporine via an intra-ocular route has not been reported in the literature to our knowledge of causing hyperpigmentation of scalp hairs. However, it has been reported as an oral preparation to cause hyperpigmentation of both the skin and hair in patients as well as hypertrichosis. Lee et al. report a microarray analysis in which they showed NFAT-2 was upregulated in white compared to black hair. Cyclosporine reduces the activity of NFAT which enhances tyrosinase activity and melanogenesis.5 Authors Sadighha and Zahed report a patient that was receiving cyclosporine for the treatment of psoriasis developing hair darkening as well as hair growth two months after the initiation of treatment.6

Conclusions

Many studies have focused on the mechanisms involved in melanogenesis to unveil new treatments for greying hair and a way to delay the aging process. Our case study may be the first report of ophthalmic cyclosporine causing hair hyperpigmentation. Further studies are needed to elucidate the exact mechanism in which cyclosporine can induce hair darkening. This is a challenging feat in that the exact mechanism of action of cyclosporine has yet to be fully understood. It is interesting as well that our patient was able to have systemic effects from a locally applied i.e. ophthalmic solution. Further research in this case report that may yield valuable information is elucidating the amount of systemic absorption via testing our patients scalp hairs for cyclosporine.

References

Sebaceous carcinoma (SC) is a rare, aggressive skin cancer derived from the epithelium of the sebaceous glands typically found in a perifollicular distribution.1-4 Few cases have reported extracutaneous locations, to date. We present an unusual case of extracutaneous SC on the areola of the breast. Our case report is unique, given the rarity of the neoplasm, uncommon location, mode of occurrence, and chronic immunosuppressed state of our patient, secondary to renal transplantation. Moreover, an association with sporadically occurring SC in both renal transplant recipients (RTR) and chronic immunosuppression has been reported in a limited number of cases.5,6

Case Report

A 65-YO immunosuppressed Asian male with a medical history significant for polyzystic kidney disease, with two subsequent renal transplants, presented complaining of a wart-like growth on his right nipple. (Figure A).

The lesion had been present for approximately six months, and had been bleeding and pruritic as well as significantly grown. An attempt was made to treat the lesion at home with OTC wart removal, without resolution.

PMH was remarkable for HTN, and PCDX. Surgical history included renal transplant x 2 in addition to a removal of benign bladder growth and oral pharyngeal lesion.

Chronic immunosuppressive treatment for approximately 10 years, with a regimen of tacrolimus, myfortic (mycophenolic acid), prednisone, and recently, IVIG.

Past exposure to routine x-rays, CT scans, and dental x-rays.

Declined history of skin or any other cancer. Family history significant only for two daughters with PCDX and a sister deceased from ovarian cancer.

The skin exam revealed a 3 cm friable, erythematous and pulsatile, well-circumscribed mass on the right areola, clinically concerning for SCC versus pyogenic granulomas.

A chief biopsy of the entire demonstrated biopsies of enlarged atypical sebaceous tissue emanating from the dermoeperidermal junction and transected broadly at the deep surgical edge.

Multiple mitotic figures, including atypical radial forms were apparent. (Figure B, C). Immunostains were positive for adipophilin. Given the large number of mitotic figures and apparent size of the process, there was a reasonable concern for a superficial variant of SC.

Upon referral to general surgery, it was noted that the biopsy performed 2 weeks earlier which had amputated the entire growth on the surface had since returned, growing even larger than it was originally. (Figure D) Clearly, it was behaving as an aggressive, rapidly growing process.

The lesion was excised via a right maeastomy with radical dissection and sentinel lymph node (SN) staging with lymph node biopsy x4.

All four of the right SNs of the axilla were negative for metastatic SC by morphology, together with ERMA and pan-cytokeratin immunohistochemical (IHC) exams to rule out Muir-Torre Syndrome.

Therefore, the pathology was without evidence of stage III metastasis. (Figure E)

The patient was then referred to Oncology even though there is neither literature clearly supporting a clear-cut rule for adjuvant radiation or chemotherapy, nor are there randomized prospective trials to guide the treatment.

Given the patient’s chronic immunosuppression and kidney disease, and the potential additional risk with any therapy, it was determined that our patient would forego adjuvant therapy.

The patient then began additional testing and follow-up for continued surveillance of recurrence or metastasis.

He is currently one year post-op, and is in remission in regards to his renal transplant rejection, with no metastases or new lesions found on subsequent follow-up visits.

Clinical and Histologic Findings

A. Lesion of right areola on initial presentation prior to biopsy.

B. Right nipple. Multiple mitotic figures including atypical radial forms and clear differentiation.

C. Right nipple biopsy. Multiple mitotic figures are evident including atypical radial forms and clear differentiation.

D. SP Pos F1 right mastectomy with radical dissection and sentinel lymph node biopsy with lymph node biopsy x4.

E. Immunostains were positive for adipophilin. Given the large number of mitotic figures and apparent size of the process, there was a reasonable concern for a superficial variant of SC.

Muir-Torre Syndrome (MTS)

SC, renal or venous associated extracutaneous internal malignancies is the hallmark of Muir-Torre Syndrome (MTS). It is the triad of benign venous polyposid cutaneous tumors, renal and cutaneous internal malignancies in renal transplantation. 

The initial presentation of Muir-Torre Syndrome is usually a solitary primary cutaneous or cutaneous mucosal tumor. It is associated with a high rate of internal malignancies and represents a syndrome related to the founder effect of heritable defects in DNA mismatch repair genes.

There is often a family history with the presenting feature of a solitary, SN, low grade intraductal tumor for patients. Although diagnosis of adenocarcinoma tumor, in clinical and radiological features, are similar to those in MTS, including the presence of variable features of hyperpigmentation, multifocal disease, extracutaneous internal malignancy, and an increased association with colorectal cancer.

HCC-associated tumour like MTS.

PERICILLARY IMMUNOHISTOCHEMICAL STAINING-

Novel Follow-Up Protocol for Our Case

Given the treatment protocols and surveillance. It is important for dermatologists, oncologists, and nephrologists to have a low threshold for identifying these neoplasms, especially in immunosuppressed RTR patient populations. More research must be conducted to better determine the risk factors and treatment options for patients in this population, as well as for patients with extracutaneous SC in general, since there are virtually no treatment protocols to follow, to date. We must draw on what we currently know about SC overall until more is known.

Even more important, as providers, we must report cases we see. Further surveillance over a greater time period will, perhaps, yield more information about SC in unusual locations.

References

5. Sung D, Kaltreider SA & Gonzalez-Fernandez F. Early Onset Sebaceous Carcinoma.  Diagnostic Pathology 2011, 6:81
9. PCKD and renal transplant rejection

Conclusion

Extracutaneous SC is a rare entity. Given the general behavior of ocular SC, it is not clear as of yet if extracutaneous SC behaves similarly and requires the same treatment protocol and surveillance. It is important for dermatologists, dermatopathologists, and nephrologists to have a low threshold for identifying these neoplasms, especially in immunosuppressed RTR patient populations. More research must be conducted to better determine the risk factors and treatment options for patients in this population, as well as for patients with extracutaneous SC in general, since there are virtually no treatment protocols to follow, to date. We must draw on what we currently know about SC overall until more is known. Even more important, as providers, we must report cases we see. Further surveillance over a greater time period will, perhaps, yield more information about SC in unusual locations.
Belimumab is a novel monoclonal antibody that targets human B cells. It was FDA approved in 2011 for the treatment of systemic lupus erythematosus (SLE).

This case represents one of only a few previous case reports describing the effectiveness of Belimumab on the cutaneous lesions of subacute cutaneous lupus erythematosus (SCLE).

Lesions can have an annular appearance with red raised borders and central clearing, or they can appear eczematous. The latter was seen in our case.

SCLE lesions typically do not scar, as was the case with our patient.

SCLE can be drug-induced, though our patient was on no medications which have been linked to SCLE

Roughly 50% of patients who are diagnosed with SCLE will meet ACR criteria for SLE1

Up to 15% of SCLE patients will eventually develop significant internal disease2

Antibodies to SSA (Ro) are commonly present in SCLE, however our patient failed to demonstrate this.

Belimumab is a human monoclonal antibody that inhibits the formation of a B cell survival factor.

There are currently 2 major trials demonstrating the safety and efficacy of Belimumab3,4

This case report provides further validity to the safety and efficacy of Belimumab in treating lupus erythematosus.

46-year-old male presented to the dermatology clinic with a 3 month history of fatigue, hair loss, and a progressive rash primarily located on sun-exposed areas.

Physical Exam: erythematous, scaly plaques on the face (Figure A), chest and back in a V distribution, shoulders, and forearms. Patchy alopecia of the scalp was present (Figure B). No oral or nasal ulcers noted. No joint pain, swelling, or effusions noted.

Lab data: Laboratory evaluation was significant for +ANA (1:320), +SM/RNP antibodies, and mild neutropenia. SSA and SSB antibodies were negative.

2 biopsies were taken, one was sent for immunofluorescence

Histopathology: band-like lymphohistiocytic infiltrate at the dermal-epidermal junction (Figure C). Scattered necrotic keratinocytes and extravasated erythrocytes were present. Increased mucin was present in the dermis. Direct immunofluorescence showed IgG and IgA deposits in a band-like pattern along the basement membrane zone.

The patient met criteria for SLE and the cutaneous findings were consistent with SCLE.

The patient was not a candidate for hydroxychloroquine or prednisone due to a recent diagnosis of central serous retinopathy.

He was also not a candidate for methotrexate due to heavy alcohol consumption.

The patient was started on Belimumab with a loading dose followed by monthly injections.

The patient had resolution of cutaneous lesions (Figure D), as well as improvement of his fatigue and neutropenia.

The only side effect noted was flu-like symptoms for 3 days following the injections.

SCLE is typically a very photosensitive eruption. It is interesting to note that the mid facial skin is often spared in favor of lateral facial involvement, which can be seen in our patient. The upper trunk and extensor upper extremities are often involved.

REFERENCES


A RARE CASE OF ERYTHEMA ELEVATUM DIUTINUM
Trent Gay, DO; Daniel Hurd, DO.
LewisGale Hospital Montgomery, Blacksburg, VA;

Introduction:
Erythema elevatum diutinum (EED) is a rare chronic form of cutaneous leukocytoclastic vasculitis affecting small vessels with only a few hundred cases reported in the literature. The disease is commonly associated with various inflammatory and infectious diseases. Lesions are cutaneous and typically present on extensor surfaces as purple-violaceous papules, plaques, and nodules. We report the case of a 60 year-old male patient with cutaneous lesions consistent with EED.

Case Report:
A 60 year old male presented to our dermatology clinic with a 2.5 year history of erythematous, raised, asymptomatic papules and plaques on the bilateral hands and elbows. (FIG 1, FIG 2) The lesions occur in flares and persist for months before slowly resolving. The patient never completely cleared the eruption since it started. He was previously diagnosed with granulomatous annulare and was treated with topical class 1 steroids with no improvement. Based on the chronicity and appearance of the lesions, erythema elevatum diutinum was suspected and a biopsy was performed. The histopathology revealed a moderate infiltrate in the superficial to mid dermis consisting of numerous neutrophils, histiocytes, and scattered lymphocytes with prominent leukocytoclasia. (FIG 3, FIG 4) These findings were consistent with EED. A workup was performed to evaluate if there was an identifiable cause. A CBC, ASO titer, SPEP, ANA, anti-histone and G6PD level was performed with no abnormalities observed. A thorough history with the patient identified no risk factors for HIV or viral hepatitis exposure so these labs were not performed. The patient was prescribed oral dapsone 100mg daily. He has been on this medication for over two months and in a more recent follow up over the phone he reports he is doing well.

Discussion
Erythema elevatum diutinum (EED) was first described in the late 1800’s separately by Hutchinson1 and Bury2,3. It was not until 1892 that Crocker and Williams found similarities in their cases and those described by Hutchinson and Bury that they reclassified the condition as erythema elevatum diutinum4,5. The Latin name describes the characteristics of the lesions seen in EED; red (erythema), elevated (elevatum), and persistent (diutinum). EED is a rare dermatosis with only a few hundred cases reported in the literature. It affects both sexes with no known racial predilection5. It can occur at any age but most commonly affects adults in the age range 30 to 60 years4,5,6.

The lesions tend to occur in a symmetrical distribution on the extensor surfaces and skin overlying joints6. The lesions first manifest as red-brown, or purple papules, plaques or nodules that are soft lesions from edema and tissue destruction6. The lesions become firmer as they fibrose and turn a yellow to brownish hue with resolution7. EED cutaneous manifestations are generally asymptomatic but may be tender to touch, pruritic, burn or sting particularly in onset of newer lesions. Other associated symptoms include arthralgia (40% of cases), fever, and other constitutional symptoms7. EED lesions tend to have a prolonged course with variable periods of flares or persistence with no change. The disease course has an average of 5-12 years before resolution. The lesions sometimes recur after treatment has been stopped7.

FIGURE 1: Characteristic EED lesions on the hands bilaterally.
FIGURE 2: Lesions on the bilateral extensor elbows.
FIGURE 3: Histopathology of specimen at 4x demonstrating the superficial to mid dermal localization of the infiltrate.
FIGURE 4: Histopathology of specimen at 20x demonstrating the mixed infiltrate of histiocytes, lymphocytes and neutrophils with leukocytoclastic vasculitis.

The etiology of EED is unknown, but is believed to be a form of chronic recurrent leukocytoclastic vasculitis resulting from immune complex deposition in vessel walls8. The trigger to the immune reaction is theorized to be from an unknown antigen. EED has a strong association with certain autoimmune, neoplastic and infectious processes. Associated autoimmune diseases include celiac disease9, rheumatoid arthritis10, relapsing polychondritis11, and type I diabetes mellitus12. Neoplastic diseases that have been reported in association with EED include hematologic malignancies, prostate carcinoma, testicular lymphoma13, lung cancer14 and breast cancer15. Hematologic malignancies account for 30% of associated EED cases and include: myelodysplasia, myeloproliferative alterations, multiple myeloma, cryoglobulinemia and immunoglobulin G (IgG) or immunoglobulin A (IgA) paraproteinemias16,17,18. There are also some reported infectious associations including streptococcus19, hepatitis, tuberculosis and HIV20,21.

Histopathologically acute lesions present with a wedge-shaped infiltrate of polymorphonuclear cells, leukocytoclastic debris, macrophages, histiocytes and rarely eosinophils surrounding blood vessels forming a leukocytoclastic vasculitis2. The proportion of histiocytes in the infiltrate increases and the appearance of a leukocytoclastic vasculitis diminishes as the course progresses. Chronic lesions show dermal fibrosis with a proliferation of dermal spindle cells and occasionally an increase of multinucleate giant cells and finally a granulation response with healing22. The histopathology is not pathognomonic but is highly suggestive of EED.

First-line treatment of EED is dapsone or sulfonamides2. Due to the disease’s chronic nature, stopping treatment may cause the skin lesions to recur. Therapy is found to be more effective in earlier lesions and less effective in chronic fibrotic lesions. In patients with an associated disease, treatment is more successful if the underlying disease is also targeted such as treating HIV with an antiretroviral, or celiac’s disease with a gluten free diet23.

Conclusion
EED is a chronic and recurrent leukocytoclastic vasculitis diagnosed by a combination of clinical and histopathologic findings. The disease etiology is thought to be due to immune-complex deposition in small vessels. EED is associated with many autoimmune disorders, infectious diseases and malignancies and thus effective treatment requires targeting both the underlying disorder and the lesions themselves.
ABSTRACT
Erythema elevatum diutinum (EED) is a rare, chronic dermatosis that presents with red-violet to red brown papules, plaques, and nodules on the extensor surfaces. Circulating immune complexes with repeated deposition and associated inflammation is thought to play a role in its pathogenesis and it is associated with various systemic diseases including infectious, autoimmune, and hematologic disorders. We report an interesting case of EED in a 6-year old patient who presented with an itchy rash and abdominal pain for 2 weeks and was later found to have Crohn’s disease.

CASE PRESENTATION
A 6-year old Caucasian male presented with his mother for a 2-week history of a pruritic rash on his left lower leg, lower arms, and buttocks along with intermittent abdominal pain.
- PMH: None
- PSH: None
- Meds: None
- Allergies: NKDA

Clinical Course: The patient had complained of pruritus and his mother had been applying over the counter hydrocortisone cream with no improvement. He also experienced bouts of abdominal pain with diarrhea and constipation over the last two weeks and denied fever, chills or night sweats. The patient presented to our dermatology clinic and a shave biopsy was taken of a lesion on the right lower leg.
- Biopsy results: The biopsy results showed a mildly hyperkeratotic epidermis, a grenz zone noted in the dermis, a perivascular and diffuse infiltrate composed of neutrophils and eosinophils.
- The biopsy diagnosis was a neutrophilic dermatitis with a differential diagnosis including EED, a lesion related to Crohn’s disease, Behcet’s disease, or urticaria.

CLINICAL PICTURE 1

Differential Diagnosis
- The clinical and histological differential diagnosis of EED depends on the stage of the lesion.
- Clinically, early stage lesions resemble neutrophilic dermatoses, such as Sweet’s syndrome, purpuric vasculitis of the dorsal hands, and rheumatoid neutrophilic dermatitis. Late stage lesions resemble granuloma annulare, tuberculous xanthomas, rheumatoid nodules, fibrous nodules of Borrelia, and multicentric reticulohistiocytosis.
- Histologically, the differential diagnosis for early stage lesions resemble leukocytoclastic vasculitis with prominent intravascular neutrophils. Late stage lesions resemble tuberculous xanthomas, fibrotic disorders or tumors such as DFSP, fibrotic nodules of Borrelia, Kaposis sarcoma, and bacillary angiomatosis.

CLINICAL PICTURE 2

REFERENCES

DISCUSSION
Variable | EED
--- | ---
Epidemiology | Very rare, several hundred cases have been reported. Equally affects males and females most commonly middle or older age. No racial predilection is seen

Skin findings | Early lesions- erythematous or red/violaceous petechiae and purpura which progress to become firm lesions. Various presentations including: annular plaques with raised border, verrucous plaques on the soles, Skin colored nodules usually seen on palmar/plantar region usually in HIV infected patients. Often asymptomatic but can be pruritic or burning in nature

Extra-cutaneous findings | Arthritis, glomerulonephritis, nodular sciatic, panuveitis and blindness

Distribution | Symmetrical to the extensor surfaces of the elbows, knees, hands, and feet. Additional sites may include: face, trunk, analis, buttocks, genitalia, and Achilles tendon

Associated conditions: Infectious: Hep B, HIV, TB. Syphilis and beta-hemolytic streptococcal infections
Autoimmune: Wegner’s granulomatosis, inflammatory bowel disease, celiac disease, relapsing polychondritis, SLE, RA. and dermatitis herpetiformis
Hematological: plasma cell dyscrasias, myelodysplasia, myeloproliferative disorder and hairy cell leukemia

Pathogenesis: Unknown but likely to be immune complex deposition resulting in complement activation, neutrophil recruitment and the release of destructive enzymes resulting in fibrin deposits around dermal vessels secondary to the presence of persistent circulating immune complexes.

Histologic features: Nodular and diffuse infiltrates of neutrophils and nuclear dust, eosinophils, histiocytes and plasma cells that extend to subcutaneous fat. Has a classic onion-skin like perivascular fibrosis. Mixture of plasma cells and lymphocytes are the hallmark

Treatment | Dapsone, tetracycline, nicotinamide, sulfapyridine, cholchicine, intravenous/sysemic corticosteroids, topical dapsone or surgical excision

Clinical course | Relapsing and remitting. Majority resolve within 5 years

DERMATOPATHOLOGY
Histologic features of EED - A dense psovacular infiltrate of neutrophils mixed with lymphocytes and histiocytes seen in an early lesion. B. Minimal perivascular infiltrate and marked perivascular fibrous thickening resembling “onion skinning” in a late-stage lesion of EED.

CONCLUSION
EED is a rare, chronic fibrosing leukocytoclastic vasculitis that presents with orange to yellow papules and plaques over the joints and the extensor surfaces of the elbows, knees, hands and feet. Multiple infectious, hematological and autoimmune conditions are associated with EED likely secondary to the presence of persistent circulating immune complexes leading to fibrin deposition around dermal vessels. The exact pathogenesis is unknown but thought to be associated with circulating immune complexes. It tends to have a relapsing and remitting course which can last multiple years and the mainstay of treatment is dapsone.
Subcutaneous sarcoidosis (Darier-Roussy disease) most often presents as skin-colored, firm, mobile subcutaneous nodules in the absence of epidermal change. These lesions most frequently involve the extremities and may be tender or asymptomatic. Subcutaneous sarcoidosis is commonly associated with visceral disease involvement.1,2

For patients infected with HIV, combination antiretroviral therapy has shown to significantly decrease morbidity and mortality associated with the disease by suppressing viral replication and improving host cellular immunity. Immune reconstitution syndrome is a significant complication associated with immune restoration following initiation of combination retroviral therapy. 4

Here we describe the case of a 44-year old Hispanic HIV positive male who developed subcutaneous sarcoidosis associated with pulmonary involvement after receiving antiretroviral therapy for the past year. The patient had no prior history of sarcoidosis. We describe the clinical, histopathological, radiographic, and laboratory evidence that led to his diagnosis.

Case Presentation

A 44-year old Hispanic HIV positive male presents to the clinic with a history of painful subcutaneous masses involving bilateral upper and lower extremities for the past 5 days with an associated fever. Figures 1-2 show the lesions as they were seen and palpated at the patients’ initial visit to our clinic. The patient denies a recent history of joint pain, cough, or shortness of breath. The patient had been on a fixed-dose combination therapy for HIV which included abacavir, dolutegravir, and lamivudine for the past year, which was tolerated well.

Physical Examination

On physical examination, there were multiple, skin-colored, mildly tender subcutaneous nodules involving the upper and lower extremities. There was no cervical, axillary, or inguinal lymphadenopathy appreciated.

Histopathology

A 4 mm punch biopsy was performed from the right upper arm to rule out morphea versus panniculitis versus other. Microscopic analysis of the specimen revealed discrete collections of epithelioid histiocytes within the subcutis rendering a diagnosis of sarcoidal granulomatous panniculitis. The Fite and GMS stains were negative.

Laboratory Data

- CBC/CMP- within normal limits
- Quantiferon-TB Gold- negative
- ACE: 147 U/L
- ESR: 12 mm/hr
- Absolute CD4 cells: 137 cells/mL
- HIV 1 RNA- undetectable on PCR

Radiology

PA and lateral chest X-ray- bilateral hilar enlargement suspicious for lymphadenopathy.

Discussion

Sarcoidosis is characterized by an upregulation of CD4+ T helper cells that contribute to the formation of granulation tissue in response to antigen(s). The precise antigens leading to sarcoidosis are uncertain; however, both autoimmune and infectious etiologies have been proposed. Given that the hallmark of human immunodeficiency virus (HIV) is deficiency of functioning CD4+ lymphocytes, it rarely co-occurs with sarcoidosis.5,3

Immune reconstitution syndrome most commonly presents as the reactivation of opportunistic infections, and less commonly autoimmune disease, in patients receiving combination antiretroviral therapy. 4

Recognizing immune restoring therapies as a potential cause of cutaneous, subcutaneous, and/or visceral sarcoidosis can help the clinician initiate the appropriate work up, with the goal of prompt diagnosis and treatment of this disease.

References


Correspondence

Brittany Grady DO
Hackensack UMC-Palisades
emailbygrady@gmail.com
Chelitis Granulomatosa & Differential Case Report and Discussion
Bryan Gray DO, Sonam Rama DO, Howard Lipkin, DO

LEARNING OBJECTIVES
Chelitis Granulomatosa (CG) is a rare, idiopathic disorder characterized by persistent swelling of the lips. When present with facial nerve palsy and fissured tongue, it is referred to as Melkersson-Rosenthal syndrome. Histologically, it’s granulomatous inflammation it appears identical to sarcoidosis and Crohn’s so these disorders must be ruled out. It is important to have knowledge about not only this entity, but its differential in the setting of non-acute lip swelling.

CLINICAL AND PATHOLOGIC PHOTOGRAPHS

CASE SUMMARY
A 62-year-old Caucasian male with recurrent periodontal infections presented with a 1-year history of progressive upper and lower lip swelling. Patient denied pruritus or pain, but admitted to difficulty in speaking as well as eating. He was previously treated by an allergist with no improvement. Patient had required multiple dental extractions in the past and also had a history of TZDM and hypertension for which he took amlodipine. Clinically, the patient was found to have non-pitting, non-tender, irregular edema of both the upper and lower lips as well as poor dentition. Labwork was obtained that showed no pertinent positives. Punch biopsy of the lower labial mucosa was performed which revealed granuloma formation in the lamina propria with no organisms found on special stains. Due to the histological appearance and exclusion of Crohn’s and sarcoidosis based upon negative labwork and review of systems, the patient was diagnosed with chelitis granulomatosa. The patient was treated with intralesional kenalog starting up to 12.5mg/cc. Patient noticed mild improvement, however, lip edema remained and the patient reported “flares” of swelling that would recur then remit. Oral treatment was then initiated with doxycycline, which also yielded only mild improvement.

DISCUSSION OF CHELITIS GRANULOMATOSA
Chelitis granulomatosa (CG) is an uncommon disease that presents with persistent or recurrent lip swelling. It is considered a manifestation of orofacial granulomatosis (OFG), a clinical term describing orofacial swelling caused by noncaseating granulomatous inflammation in the absence of systemic disease. Other signs include ulceration, gingival enlargement, mucosal tags and lymphadenopathy. CG is a monosymptomatic form of Melkersson-Rosenthal syndrome which includes CG, facial nerve palsy and fissured tongue. Both sarcoidosis and Crohn’s have very similar histology, so these conditions must be excluded.

The incidence of CG has been estimated at 0.08% in the general population, being more common in the second decade of life with slight female predominance. The precise etiology is unknown for CG. Some theorized etiological factors include and immune response to infections (Mycobacterial), food/preservative allergies (cinnamon/benzoate) and dental materials. There is a significant increase of IFN-y expression in oral lesions together with increased levels of IL-12. Increased levels of Th1 chemokines (RANTES/MIP-1a) and chemokine receptors (CCR5, CXCR3) have also been noted.

Some skin conditions share similar features to CG. These include other granulomatous diseases such as a foreign body reaction, mycobacterial infection, sarcoidosis, Crohn’s disease, Wegener’s granulomatosis, and histoplasmosis. Other conditions that should be considered include amyloidosis and angioedema, which is caused by a hypersensitivity reaction to certain allergens, medications including ACE inhibitors, or hereditary deficiency of C1 esterase inhibitor.

WORKUP/MANAGEMENT
Histology of CG is characterized by noncaseating granuloma formation with epitheloid and Langerhan type giant cells and admixed lymphocytic infiltrate. Mycobacterial stains as well as polarization must be completed to rule out other types of granulomatous inflammation. Cutaneous crohn’s disease as well as sarcoidosis should be excluded and appropriate referrals made if symptomatology is present. Management includes removal of offending agents if one is found and often intralesional corticosteroids to relieve edema. Systemic therapy may be necessary in resistant cases which includes doxycycline, clofazimine, sulfasalazine, hydroxychloroquine, TNF-alpha, infliximab, thalidomide and steroids. Surgically, cheloplasty has shown effectiveness in chronic cases resistant to therapy.

CONCLUSIONS
Recognition of Granulomatous Chelitis and other clinical entities similar can aid the general dermatologist be more prepared to treat less common mucosal disorders.

REFERENCES
A Case Analysis and Update of Small/Medium Pleomorphic T-cell Lymphoma

Gabe Guerrero, DO, PGY3; Nathan Cleaver, DO, FAOCD

Introduction

Cutaneous T-cell lymphomas (CTCLs) are a heterogenous group of lymphomas that make up approximately 80% of primary cutaneous lymphomas. CTCLs include mycosis fungoides (MF), Sézary syndrome, and cutaneous CD30+ T-cell lymphoproliferative disorders among others.

Based on the 2005 World Health Organization–European Organisation for Research and Treatment of Cancer (WHO-EORTC) classification, CD4+ primary cutaneous small/medium-sized pleomorphic T-cell lymphoma (PCSM-TCL) was listed as a provisional entity of CTCLs. Currently the 2016 WHO classification, a revision to the 2008 WHO classification also keeps PCSM-TCL as a provisional entity but will rename the entity primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (SMT-LPD) as it is considered a limited clonal response to an unknown stimulus as opposed to an overt lymphoma.

PCSM-TCL is a rare type of lymphoproliferative disorder that clinically presents as a solitary plaque, module, or tumor most commonly on the face or the neck. It generally runs an indolent course with an excellent prognosis. Histologically, it has dense, diffuse or nodular infiltrates in the dermis, with a predominance of CD4+ small/medium-sized pleomorphic T-cells. A small proportion (<30%) of large pleomorphic cells may be present. Immunophenotyping demonstrates CD3+, CD4+, CD8- and CD30- neoplastic cells.

It was recently found that the atypical T cells in CD4+ PCSM-TCL express PD-1, BCL6 and CXCL13, suggesting that these cells originate from T-folliclar helper cells (TFHs). CD4+ T-cells, B-cells, histiocytes, plasma cells and eosinophils can also be found in differing proportions in the infiltrate. It is imperative to distinguish CD4+ PCSM-TCL, which is generally indolent in nature, from other lymphoid disorders in order to offer the most appropriate treatment and management.

Case

46-year-old male with no significant past medical history presented with a reddish-brown plaque on his left inferior postauricular neck that had been present for about five months. The patient complained that it was increasing in size along with burning and itching. The lesion was at the site of a previous biopsy that was diagnosed as a inflamed lentigo.

The histologic sections demonstrated an atypical lymphoid infiltrate extending from the papillary dermis into the reticular dermis with contiguous extension along follicular epithelium. Numerous atypical mitoses, hyperchromatic and pleomorphic lymphocytes were noted within the atypical infiltrate. Immunostaining demonstrated a high proliferative atypical T-cell infiltrate with a predominant 10:1 CD4 to CD8 ratio with diffuse expression of PD-1. With the continued clinical and histological findings, the patient was diagnosed with CD4+ primary cutaneous small/medium-sized pleomorphic T-cell lymphoma. The lesion was excised and a PET scan and hematology/oncology consultation did not reveal any systemic involvement.

Discussion

As PCSM-TCL has similar histological features with cutaneous lymphomas such as mycosis fungoides (MF), angioimmunoblastic T-cell lymphoma (AITL), lymphomatoid papulosis (LyP), subcutaneous panpaniculitis-like T-cell lymphoma (SPTCL), and marginal zone B-cell lymphoma, it imperative to differentiate between these entities due to the therapeutic and prognostic implications. PCSM-TCL demonstrates a CD3+, CD4+, CD8-, CD30- immunophenotype. In addition, it has also been shown to originate from follicular T helper cells by demonstrating a positive staining pattern for PD-1, BCL-6, and CXCL13. PD-1 is found in a subset of T-cells within the germinal center and helps promote B-cell survival and differentiation. Although PD-1 is not specific for TFHs, it can be helpful when differentiating PCSM-TCL from other lymphomas. The follicular helper T-cell origin may also explain the admixture of B-cells. Of note, a new marker, calcineurin/nuclear factor of activated T-cells c1 (NFAc1), has shown a nuclear staining pattern that is very sensitive and specific for PCSM-TCL allowing differentiation from some histologically similar lymphomas such as MF which demonstrates a cytoplasmic staining pattern.

Histologically, PCSM-TCL may have worrisome features. It may mimic tumor stage MF even demonstrating foci of epidermotropism. MF may also stain positive for PD-1, but clinically there is no history of patches and plaques. PCSM-TCL may also mimic AITL, which is a lymphoma derived from TFHs. Like MF, AITL differs from PCSM-TCL clinically with systemic findings such as generalized lymphadenopathy. A positive PD-1 also helps differentiate PCSM-TCL from LyP and anaplastic large cell lymphoma. PCSM-TCL has been shown to involve the subcutis, therefore the generalized lesions of SPTCL help distinguish the two along with the CD3+, CD4+, CD8+ phenotype of SPTCL.

Lastly, it is debatable whether PCSM-TCL and T-cell pseudolymphoma represent two separate entities. Both present with a solitary plaque or nodule and both may stain for PD-1. In addition, not all cases of PCSM-TCLs are monoclonal. But T-cell pseudolymphoma is different in that it lacks an aberrant immunophenotype and is usually polyclonal. However, T-cell pseudolymphoma has at times demonstrated a monoclonal phenotype. The lines between PCSM-TCL and T-cell pseudolymphoma may be blurred and of little use prognostically.

Due to the indolent nature of PCSM-TCL, surgical excision is the treatment of choice. For cases with recurrence or with multiple lesions, radiation or chemotherapy has been used with success. In most cases, toxic treatment should be avoided and staging evaluation is not necessary.

References


Porphyria Cutanea Tarda: A Case Presentation and Discussion
Jordan Harris, DO, Craig Parson, OMS IV, Michael Eyle, DO, FAOCO
Aspen Dermatology Residency Program/OPTI-West

Introduction

Porphyria cutanea tarda (PCT) is a complex and multifactorial disease. PCT results from a decreased rate of hepatic heme biosynthesis and an increased rate of heem degradation. This is often caused by a mutation in the enzyme uroporphyrinogen decarboxylase (UROD), which catalyzes the formation of uroporphyrinogen III from coproporphyrinogen III. PCT is classified into two main types: type I and type II. Type I PCT is associated with chronic liver disease and type II PCT is associated with inherited mutations in the UROD gene. PCT is often precipitated by alcohol, cigarette smoking, and other drugs. It is the most common type of porphyria and is estimated to affect between 10 and 20 people per million in the general population. It is important to recognize and manage PCT as it can lead to significant skin damage, scarring, and even skin cancer.

Case Report

A 57-year-old female presented to our outpatient dermatology clinic with complaints of blisters and blemishes on her hands for three months. She noted the lesions were located on her fingers and hands, and were present during all seasons. Her past medical history was significant for lupus erythematosus, myeloproliferative diseases, and thyroid disease. She was also prescribed a daily dose of postmenopausal hormone replacement therapy (HRT). She denied any family history of porphyria and had no history of liver disease or alcohol or tobacco use.

Physical exam revealed multiple blisters and bullae on her hands and fingers. The blisters were located on the palmar aspects of her hands and fingers, and were present on both the palms and fingers. She also had mild hypertrichosis on her hands and fingers. The blisters were painful and were located on the extensor surfaces of her hands and fingers. She denied any fever, chills, or malaise.

Laboratory workup, including a CBC, complete metabolic profile, iron studies, hepatitis B and C serologies, HCV, MRIs, and Pap, was unremarkable except for mildly elevated AST/ALT to 2 x normal and a significantly elevated ferritin at 637 mg/dL (reference interval: 15 to 150 mg/dL). A strong porphyrin screen was performed, which showed considerably elevated uroporphyrins (225.4 mg/g (normal ≤ 42 mg/g)) and porphobilinogen (11.6 mg/g (normal ≤ 4 mg/g)), with mild elevations in coproporphyrins (34.8 mg/g (normal ≤ 18 mg/g)). A strong porphyrin screen was performed, which showed considerably elevated uroporphyrins (374.5 mg/g (normal 5.0 mg/g to 11.5 mg/g)) and porphobilinogen (22.3 mg/g (normal 1.0 mg/g to 7.4 mg/g)), with mild elevations in coproporphyrins (119.3 mg/g (normal ≤ 18 mg/g)).

The patient was referred to gastroenterology and gastroenterologist for further evaluation. Further workup, including liver ultrasound and abdominal CT scan, showed a fatty liver. Smooth muscle antibodies, liver-kidney microsomal antibodies, mitochondrial (M2) antibodies, alpha-1-antitrypsin, and complement levels were all within normal limits. Hematology started the patient on prednisone every other week. At the patient’s two-month follow-up, she reported no new lesions. Her liver enzymes and ferritin had returned to normal despite continuing, though reportedly decreasing, her alcohol intake.

Discussion

Porphyria cutanea tarda (PCT) is the most common porphyria, presenting with various cutaneous findings including painless blisters, atrophic scars, hypertrichosis, hyperpigmented scars, and milia in sun-exposed areas. Since it was first described by Waldenstrom in 1937, there has been increasing interest in the relationship between PCT, iron overload, UROD activity, and the possible role in hereditary hemochromatosis.

Case Report cont.

Laboratory workup, including a CBC, complete metabolic profile, iron studies, hepatitis B and C serologies, HCV, MRIs, and Pap, was unremarkable except for mildly elevated AST/ALT to 2 x normal and a significantly elevated ferritin at 637 mg/dL (reference interval: 15 to 150 mg/dL). A strong porphyrin screen was performed, which showed considerably elevated uroporphyrins (225.4 mg/g (normal ≤ 42 mg/g)) and porphobilinogen (11.6 mg/g (normal ≤ 4 mg/g)), with mild elevations in coproporphyrins (34.8 mg/g (normal ≤ 18 mg/g)). A strong porphyrin screen was performed, which showed considerably elevated uroporphyrins (374.5 mg/g (normal 5.0 mg/g to 11.5 mg/g)) and porphobilinogen (22.3 mg/g (normal 1.0 mg/g to 7.4 mg/g)), with mild elevations in coproporphyrins (119.3 mg/g (normal ≤ 18 mg/g)).

The patient was referred to gastroenterology and gastroenterologist for further evaluation. Further workup, including liver ultrasound and abdominal CT scan, showed a fatty liver. Smooth muscle antibodies, liver-kidney microsomal antibodies, mitochondrial (M2) antibodies, alpha-1-antitrypsin, and complement levels were all within normal limits. Hematology started the patient on prednisone every other week. At the patient’s two-month follow-up, she reported no new lesions. Her liver enzymes and ferritin had returned to normal despite continuing, though reportedly decreasing, her alcohol intake.

Discussion cont.

Porphyria cutanea tarda (PCT) is the most common type of porphyria and is estimated to affect between 10 and 20 people per million in the general population. It is important to recognize and manage PCT as it can lead to significant skin damage, scarring, and even skin cancer. PCT is often precipitated by alcohol, cigarette smoking, and other drugs. It is the most common type of porphyria and is estimated to affect between 10 and 20 people per million in the general population. It is important to recognize and manage PCT as it can lead to significant skin damage, scarring, and even skin cancer.
Multiple Eruptive Eccrine Hidrocystomas
Stephanie S. Howarter, DO1; John Young, MD2
1 – Dermatology Resident, PGY3, Good Samaritan Regional Medical Center, Silver Falls Dermatology, Salem, OR
2 – Dermatology Program Director, Good Samaritan Regional Medical Center, Silver Falls Dermatology, Salem, OR

ABSTRACT
The Robinson variant of eccrine hidrocystomas involves several facial lesions and is relatively uncommon. These lesions are benign, and treatment for them is difficult and often not satisfactory. We report a case of this rare entity involving the nose and upper cutaneous lip of a 75 year old female.

BACKGROUND
Eccrine hidrocystomas are divided into two groups – the more common, solitary type known as the Smith variant and the rare type involving several lesions on the face known as the Robinson variant. These cystic lesions are benign and of sweat gland origin. They also tend to affect women more frequently than men. Associations with increased sweating and high temperatures are often reported. To date, there has not been a designated consistently efficacious therapy; although anecdotal improvement has been found with such treatments as excision, dermabrasion, electrocuterry, botulinum toxin, topical and oral anticholinergic agents, and pulsed-dye laser.

CASE HISTORY
A 75 year old female presented to the clinic with concerns regarding new eruption of several translucent-to-slightly blue papules of the nose and upper cutaneous lip, present for several months. The lesions were asymptomatic. She denied personal or family history of prior similar lesions. She also denied any recent change in medication or activity that may have correlated with lesion onset.

PATHOLOGY
Eccrine hidrocystomas appear histologically as cysts with thin-walls comprised of 2 layers of cuboidal epithelial cells in the mid- and reticular dermis

REFERENCES
Goldenhar Syndrome

Peter Jajou DO

PGY-3 Dermatology Resident; Beaumont Health; Trenton, MI

Case Presentation

A 2-year-old Caucasian female was born with right aural atresia and microtia, dermoid cyst of the iris, and accessory tragus. The patient was born via C-section to a 28-year-old, G3P2 mother, at 40 weeks gestation. All fetal ultrasounds were unremarkable throughout the pregnancy, and the subsequent delivery was uncomplicated. The patient failed her newborn BAERS hearing screen on the right and passed on the left.

At the time of birth, no family history of birth anomalies were apparent. Past medical history is unremarkable.

At six months of age, pediatric geneticists at a tertiary care center evaluated the patient. A clinical diagnosis was rendered and genetic testing was ordered.

Examination: The patient displayed appropriate milestones for her age. The right ear displays aural atresia and microtia. Additionally, the right preauricular region showed a firm, flesh colored nodule, consistent with an accessory tragus. The left eye displayed a yellowish-white, elevated mass on the iris at the 5-o’clock position, consistent with epibulbar dermoid cyst.

 Labs: Chromosomal Microarray (CMA), Full Spine Xray, Echocardiogram

Discussion

Goldenhar syndrome as described by the French ophthalmologist Maurice Goldenhar in 1952 consisted of a clinical triad of features including accessory tragus, mandibular hypoplasia, and ocular epibulbar dermoids. In 1963 Gorlin et al., observed additional vertebral anomalies in association with Goldenhar’s syndrome and termed it oculo-auriculo-vertebral dysplasia. Subsequently, both terms have been used interchangeably. The syndrome has a heterogeneous phenotype with patients presenting with a varying spectrum of anomalies affecting the eyes, ears, and vertebrae. Mandibular hypoplasia has also been observed. Abnormalities are found only unilaterally in 85% of cases and bilaterally in 10-33%.

Classically the features of this syndrome can include ocular changes such as epibulbar dermoids, epibulbar epidermolysis, microphthalmia, and coloboma. Aural features may include pre-auricular skin tags, hearing loss, atresia of the external meatus, and microtia. Vertebral anomalies consist of scoliosis, cervical fusion, atlas-occipitalisation and hemivertebrae.

While the exact etiology remains largely unknown, it is known that the syndrome is a congenital anomaly affecting the first and second branchial arches. Abnormal embryonic vascular supply and disrupted mesodermal migration have been proposed as causes. Autosomal dominant, autosomal recessive and multifactorial inheritance patterns have also been suggested. Ingestion of drugs during pregnancy such as thalidomide, retinoic acid, tamsofen, heavy alcohol, and cocaine have been suggested along with maternal diabetes, rubella, and influenza as etiologic factors. One case of the syndrome reported vitamins A toxicity in the mother. A daily dose of 25000 IU produces a teratogenic effect on neural crest cell formations which are necessary for proper pharyngeal arch development.

When considering the diagnosis of Goldenhar syndrome, the physician has to be aware that 50% of patients will have other systemic involvement. Renal agenesis, pulmonary agenesis, cardiac structural defects, cleft lip and palate, macrostomia, micrognathia, tracheoesophageal fistula, umbilical hernia, cognitive developmental delays, and webbing of the neck are all known associations. The most common cardiac defects are tetralogy of fallot and ventricular septal defects. Other syndromes associated with multiple pre-auricular tragi to consider in the differential diagnosis include Treacher-Collins syndrome, Wolf-Hirschhorn syndrome, Nager’s acrofacial dysostosis, Trethew-Brocks syndrome, and Delleman syndrome.

Treatment options vary based on age and systemic involvement and are mainly coexistent in most complicated cases. More severe cases will require aggressive surgical intervention early on to avoid vision and hearing loss. Reconstructive surgery can be performed on the external ear at age 6-8 and the jaw in early teens. Epibulbar dermoids should be surgically excised. A multidisciplinary approach including otolaryngology, ophthalmology, pediatrics, and dermatology is necessary. Progress is good in uncomplicated cases with minimal systemic involvement.

Patient Course & Therapy

At one year of age, the accessory tragus was removed, but currently, it seems to be regrowing in the same location. The patient visits her ophthalmologist every three months for close monitoring. To date, reports show her vision is unaffected. She also visits with otolaryngologist every three months for auditory monitoring. A CT of the right temporal bone is planned when she is 5-years-old in order to examine the internal structures of the ear, and determine if opening the external auditory canal is worth pursuing. Additionally, she sees cranofacial surgical specialists once a year.

The need for close and diligent follow up is required in order to evaluate new or changing phenomena as she progresses and develops in age. To date, all her developmental milestones have been achieved.

No family history of birth anomalies were noted at the time of her birth. However, this past year, a first cousin was born with a dermoid cyst above her eyebrow. Whether these events are related or not remains to be determined.

Conclusion

Goldenhar syndrome is a rare congenital developmental anomaly affecting the first and second branchial arches. Classic features of the syndrome include ocular, aural, and vertebral developmental defect. Failed newborn screens can be the key clue for rare syndromes and they should be pursued with a thorough work-up. A multidisciplinary approach may be required.

References


www.PosterPresentations.com

RESEARCH POSTER PRESENTATION DESIGN © 2012

32
Case of Acquired Epidermodysplasia Verruciforms
Carmen A. Julian, D.O., Marcus B. Goodman, D.O. FAOCDD
PCOM/North Fulton Hospital Medical Campus, Roswell, GA

Abstract
Acquired type epidermodysplasia verruciformis (EDV) has historically been linked to individuals infected with human immunodeficiency virus (HIV) (1) and those on chronic immunosuppressant therapy for solid organ transplant (2). Recently, with the expansion of immunosuppressant drugs being used to treat a variety of immune mediated diseases, there has been an increase in EDV like syndrome presentations in case reports and literature. The trend is evident in an increasing number of adult and pediatric patients treated with biologic agents and immunosuppressant drugs for a variety of conditions such as atopic dermatitis (3), graft-versus-host disease (GVHD) (4), leukemia (5), and in this case systemic lupus erythematosus (SLE) (6). There is no standardized treatment of EDV and/or acquired EDV, which is primarily case based and often delivers variable unsatisfactory results (1).

Case Report
A 36 y.o. African American female with a 12-year history of adult and pediatric patients treated with biologic literature. The trend is evident in an increasing number of EDV like syndrome presentations in case reports and immunosuppressant drugs being used to treat a variety of transplant (2). Recently, with the expansion of chronic immunosuppressant therapy for solid organ EDV is a rare autosomal recessive disease associated with mutations of EVER1 and EVER2 genes on chromosome 17(7). These mutations downregulate cell-mediated immunity via zinc transport proteins with mutations of EVER1 and EVER2 genes on (8), which are not pathogenic in particular susceptible to the beta subgroups HPV (9). Patients with EDV are human papilloma virus (HPV). Patients with EDV are particularly susceptible to the beta subgroups HPV 5, 8, which are not pathogenic in immunocompetent hosts (8). Inherited forms present with recalcitrant flat warts in childhood that later develop flat topped pityriasis versicolor like patches/plaques which progress to non-melanoma skin cancers in sun exposed areas starting at the third and fourth decade (9). The disease is difficult to manage and often disfiguring and disabling, advising those affected to strict sun protection and domiciles in cloudy climates as UV radiation plays a pivotal role in malignant transformation of lesions (10).

Discussion
EDV is a rare autosomal recessive disease associated with mutations of EVER1 and EVER2 genes on chromosome 17(7). These mutations downregulate cell-mediated immunity via zinc transport proteins and predispose those affected to all subtypes of the human papilloma virus (HPV). Patients with EDV are particularly susceptible to the beta subgroups HPV 5, 8, which are not pathogenic in immunocompetent hosts (8). Inherited forms present with recalcitrant flat warts in childhood that later develop flat topped pityriasis versicolor like patches/plaques which progress to non-melanoma skin cancers in sun exposed areas starting at the third and fourth decade (9). The disease is difficult to manage and often disfiguring and disabling, advising those affected to strict sun protection and domiciles in cloudy climates as UV radiation plays a pivotal role in malignant transformation of lesions (10).

Histopathology
hyperkeratosis, hypergranulosis, and acanthosis

large keratinocytes with vacuolated sea-blue cytoplasm

characteristic keratinocytes with distinct bluish-grey cytoplasm and a peri-nuclear halo

Discussion
Acquired type EDV has increased in frequency proportionally with increased use of a variety of immunosuppressant agents, as historically it was limited primarily to HIV infected individuals and renal transplant patients (11). The challenges associated with cutaneous malignancies is similar to inherited type and current management is anecdotal and positive results vary with any treatment plan. Many patients requiring immunosuppressant therapy cannot discontinue the offending agent. If a situation exists when the drugs can be stopped, often patient’s cutaneous involvement persists even months after stopping any immunosuppressant (3). Management and prevention of malignant transformation will require some trial and error and may depend on the comfort level of the patient and clinician with regard to safety and associated side effects. Treatment is focused on the reduction of wart like lesions and more importantly to prevent their transition into malignancy.

A combination approach is often needed and will require modifications due to side effects, poor results and to tailor for patient skin types or tolerability. No single treatment modality has been shown to be effective at controlling or remitting disease. A review of most literature would suggest a regimen of oral retinoids, PDT and topical imiquimod may present the most promising likelihood at controlling verrucous-like lesions and progression to squamous cell carcinoma(2,12). The rarity of the disease, whether inherited or acquired, limit any possibility of a controlled comparison study to be plausible. The initial treatment plan in this case was chosen with regard to limit side effects, not interfering with her SLE management and would be compatible with a Fitzpatrick IV skin type.

References
Radiation-Induced Breast Angiosarcoma: A Case Report

Franz Kerdel, DO,* Danielle Nicolazzo, DO,** Stanley Skopit, DO, MSE, FAOCD, FACD****

*Dermatology Resident, 3rd year, Larkin Community Hospital/NSU-COM, South Miami, FL
**Dermatology Resident, 1st year, Larkin Community Hospital/NSU-COM, South Miami, FL
***Program Director, Dermatology Residency Training Program, Larkin Community Hospital/NSU-COM, South Miami, FL

Introduction

Angiosarcoma is a rare, aggressive tumor of endothelial derivation, which represents 1-3% of all soft tissue sarcomas.1 Angiosarcomas of the breast can be classified into separate entities: primary and secondary forms. A form of secondary angiosarcoma of the breast includes post radiation induced angiosarcoma, which prevalence has increased by the use of breast conservation therapy (partial mastectomy with adjuvant breast radiation therapy), although the incidence still remains low (0.0% to 20% in patients treated).2 Women who received radiation therapy in treatment of breast cancer are at a 9-16 fold increase in the relative risk of developing angiosarcoma when compared to those treated with other modalities.3 Radiation induced angiosarcoma may carry a worse clinical outcome than equivalent primary breast sarcomas. There is usually delay in diagnosis, which attributes to the poor prognosis.4

Case Report

We report a case of an 81-year-old Caucasian female that presented to our outpatient clinic on November 2015 for an indurated erythematous rash on her left breast for approximately 2 months. The patient’s medical history included a T1bN0M0 infiltrating ductal carcinoma, 8mm in diameter that was treated with lumpectomy and sentinel lymph node biopsy in July of 2008. Post operatively she underwent adjuvant radiation therapy (34 treatments) to the left breast (dosimetry records unavailable), as well as adjuvant Letrozole for five years, completing treatment regimen in 2013. The patient had undergo mammogram and ultrasound of bilateral breast in 2014, demonstrating BI-RADS 2 with no evidence of disease recurrence. Prior to the consultation in our office, the patient was seen by her dermatologist in September of 2015 who performed a skin biopsy of the lesion demonstrating subtle interface alteration with superficial chronic inflammation, consistent with drug reaction.

Upon evaluation in November 2015, patient presented with an erythematous, indurated, ill-defined dermal plaque. Seven years post radiation therapy, a usual presentation of post radiation induced angiosarcoma. However, with a diagnosis was determined by histological examination of the biopsy. Biopsy results showed a high-grade angiosarcoma measuring 4.5cm in greatest dimension involving the nipple, skin, and breast parenchyma. Single daily fractions of radiation therapy were done at 200 cGy, 24 sessions (total dose 5,000 cGy) over 33 days. Patient was able to complete treatment without any unexpected side effects.

Clinical Photos

Figure 1a. Radiation-induced angiosarcoma in an 81 year old woman. Erythematous, indurated, ill-defined dermal plaque. Seens years post radiation therapy.

Figure 1b. Marks demonstrate biopsy sites. 2 done skin punch performed.

Pathology

Two punch biopsies showed atypical vascular proliferation with dilated vascular structure at the superficial dermis. Atypical cells intersecting collagen bundles and invading the reticular dermis and subcutaneous tissues.

Immunohistochemical stains showed a CD31, CD45 (margin) and p53 (nuclear) positive phenotype, CD34 staining was only focal.

Correlation of the clinical features and microscopic findings were consistent with the diagnosis of lymphangiosarcoma.

Treatment

A simple left breast Mastectomy followed by reconstructive surgery with a rectus abdominus myocutaneous flap for wound closure was performed in December of 2015. Pathology showed a high-grade angiosarcoma measuring 4.5cm in greatest dimension involving the nipple, skin, and breast parenchyma. Single daily fractions of radiation therapy were done at 200 cGy, 24 sessions (total dose 5,000 cGy) over 33 days. Patient was able to complete treatment without any unexpected side effects.

Discussion

Over the past few decades breast conservation therapy, which refers to conserving surgery, followed by moderate dosed radiation therapy has become the preferred method of treating breast cancer over the conventional radical mastectomy. The equivalency in the survival between the two approaches has been demonstrated by prospective, randomized clinical trials revealing little difference in the 5-year breast cancer mortality.5 As more patients elect for breast conservation therapy, the incidence of angiosarcoma, although still rare, may increase. Angiosarcoma have been described in an array of clinical presentations including: bruise like patches of skin, blue pitted nodules, erythematous patches, and at advanced stages as a nodular, violaceous plaque with an ill-defined nodular appearance.3 Less common presenting findings include eczematoid changes, ulcerations, bloody nipple discharge and non-pigmented macules. Lesions should be differentiated from recurrent breast carcinoma, atypical hemangiomma, and radiation dermatitis.6 An accurate diagnosis of angiosarcoma may be made with simple skin tissue sampling, such as a punch biopsy. Thus we recommend that multiple biopsies be taken at different areas of the lesion to prevent false negative reports.

The standard treatment for post-radiation angiosarcomas includes a total mastectomy. In regards to radiation induced angiosarcoma which have been treated with surgery alone, recurrence rates have been cited as high as 50 to 70%.6 Due to these high recurrence rates, patients may benefit from adjuvant treatments including chemotherapy and radiation therapy.7 Recently there has been success with the use of radiotherapy and chemotherapy in combination to treat these tumors. In a study of 14 patients, the 5-year survival rate of those treated in this manner was was 86 percent.8 Other treatment options may include adjuvant chemotherapy, however results are limited and its use is not clearly defined. The use of sorafenib, bevacizumab, endostar, docetaxel has been administrated in addition to combination therapy in case studies.9 However, for patients that cannot undergo surgery, chemotherapy as a palliative treatment option can extend survival rates. Toxicity and anthracyclines are usually the most used agents.8

References


Contact

Franz R. Kerdel
Larkin Community Hospital
Dermatology@NSU.COM
Email: F.kerdel@gmail.com
Treatment with the Q-switched, Nd-Yag Laser in the wavelengths of 532nm and 1064nm for the Treatment of Post-endovenous Ablation and Post-sclerotherapy Hyperpigmentation: A Retrospective Case Series.

Angela Macri DO, MS, PGY-3  Dermatology Resident at Sampson Regional Medical Center
Mojgan Hosseinipour DO, PGY-1  Traditional Rotating Intern at Sampson Regional Medical Center
Jaimie Nuckolls DO, PGY-1  Traditional Rotating Intern at Sampson Regional Medical Center
Kamran Goudarzi MD, FACS, FICS  Attending at DermOne Dermatology, Cosmetic, and Scarless Vein Center
Jonathan Crane DO, FAOCD, FAAD  Dermatology Program Director, Sampson Regional Medical Center

**The authors declare that there are no conflicts of interest**

Introduction

Varicose veins can be very problematic to patients causing a great deal of medical and cosmetic concern. Treatment of varicose veins by either sclerotherapy or endovenous ablation causes obliteration of the lumen of the vessel, fibrosis, and an inflammatory reaction that allows leakage of red blood cells into the perivascular space. When red blood cells are broken down by macrophages hemosiderin is deposited in the dermis. These procedures also cause inflammation in the epidermis and dermis, creating a reactive melanogenesis. The accumulation of hemosiderin and melanin from these mechanisms leads to unwanted hyperpigmentation of the skin. Hyperpigmentation is an important concern to patients undergoing these procedure as it can take several years to resolve, if ever. Many treatment modalities have been attempted in the past including compression stockings with topical corticosteroids, mechanical evacuation of thrombi, pulsed dye laser, Q-switched ruby laser, and intense pulsed light (IPL), all with varying results. Our study shows that the Q-switched Nd-Yag laser is an effective treatment option for post-sclerotherapy and post-endovenous ablation hyperpigmentation.

Methods

This was a retrospective case series of a data set from the DermOne Scarless Vein care center in Wilmington, NC. Eight patients that had post-sclerotherapy and/or post-endovenous ablation hyperpigmentation of the legs were treated with the Nd-Yag laser in 11 different locations total. Patients with Fitzpatrick skin type 2 or 3 were treated with the 532nm laser and patients with Fitzpatrick skin type 4 were treated with the 1064nm laser. Patients with skin type 1, 5, or 6 were not treated. Laser settings for the 532nm Nd-Yag included a spot size of 3 or 4, energy of 1.5-3, and Hz of 10. Laser settings for the 1064nm ND-Yag included spot size of 6, energy of 4, and Hz of 10. Treatments were spaced anywhere from 2-5 months apart. Two clinicians graded the improvement in hyperpigmentation of the legs using a Clinical Global Impression scale of no improvement/worse, minimal improvement, moderate improvement, marked improvement, or complete resolution. Patients were asked if they had pain during the procedure. Aquaphor was applied to the treatment sites and patients were instructed to use ice packs after the procedure.

Results

All locations showed improvement where 1 had minimal, 2 had moderate, and 6 had marked improvement while 2 had complete resolution. Two locations required only one treatment to get a complete resolution. Four sites obtained a marked improvement after 2 treatments, however, one other site with marked improvement did require 3 treatments. Two locations had a moderate amount of improvement after 2 treatments and one site had a minimal amount of improvement after only one treatment.

Discussion

Both hemosiderin and melanin contribute to post-sclerotherapy hyperpigmentation. Hemosiderin has an absorption spectrum that peaks at 410 to 415 nm, followed by a gradually sloping curve throughout the visible spectrum. Melanin has an absorption spectrum from 250-1200 nm.\(^1\) The ND-Yag laser has been known to treat pigmented lesions and has a frequency doubling device to reduce the 1064 nm light wavelength by half to 532 nm.\(^2\) Although the laser does not target the peak absorption spectrum for hemosiderin there seemed to be enough photomechanical destruction of hemosiderin to improve the hyperpigmentation in our patients. The patients in our study all showed improvement with 72% having marked to complete resolution. Treatment to one half of a hyperpigmented site was done in location 8 to show that the pigment goes away quicker with a laser treatment than with no laser treatment. The laser was well tolerated by all patients. Fitzpatrick skin types 1 and 5 were excluded to ensure patients would not burn, scar, or worsen their hyperpigmentation. In some patients the erythema lasted several months but eventually faded with time.

Conclusion

Although this was a small study subset, we believe that the Q-switched, Nd-Yag laser in the wavelengths of 532nm and 1064nm in patients with Fitzpatrick skin types 2-4 is an efficacious treatment for post-endovenous ablation.
Brooke-Spiegler Syndrome

Sarah Malerich, DO, PGY3; Alpesh Desai, DO, FAOCD
University of North Texas Health Science Center / South Texas Osteopathic Dermatology, Houston, Texas

Abstract
Brooke-Spiegler Syndrome (BSS) is a rare inherited autosomal dominant genodermatosis characterized by the development of multiple adnexal cutaneous tumors including spiradenomas, cylindromas, trichoepitheliomas, epidermoid cysts and milia.

Case Report
An 84 year old female with a past medical history of multiple firm, pink nodules with surface telangiectasias involving the forehead, external ears, and scalp (figure 1) presented with a chief complaint of painful lesions on her scalp. The patient has a family history of similar lesions in her brother, sister and mother. A 1.6 x 0.5 cm biopsy was taken from the largest lesion and histologic findings showed multiple nests of basaloid cells forming a jigsaw-like pattern with scant stroma surrounded by eosinophilic, hyaline-rich sheaths, consistent with cylindroma (figures 2, 3).

The patient subsequently returned to our clinic 2 weeks later complaining of continued growth of the lesion with increased pain. An excision was performed, measuring 2.7 x 2.2 x 1.3 cm. Pathology report described at dermopathology consensus conference was read as adnexal neoplasm, favoring cylindroma with re-excision required to rule out malignant transformation of the benign tumor. During the visit, three additional biopsies were taken from sites the patient deemed bothersome with two diagnosed as spiradenomas and one as cylindroma.

Histopathological examination revealed a lymphocytic cell population with basaloïd cells arranged in rosettes, characteristic of spiradenomas, while the other tumor exhibited discrete nests in a jigsaw puzzle pattern, representing a cylindroma. The patient was diagnosed with Brooke-Spiegler syndrome (BSS) given the patient’s presentation of multiple adnexal cutaneous tumors, family history, and autosomal dominant inheritance of this genodermatosis.

Discussion
Brooke-Spiegler Syndrome results from mutations in the CYLD gene whose product encodes a deubiquitinating enzyme that negatively regulates nuclear factor kappa-B, an adrenal proliferator inducer or tumor regulator protein. Nonsense mutations are associated with the highest phenotypic variability and recurrence rate, while missense mutations often result in the multiple familial trichoepitheliomas phenotype. Marked phenotypic variability between and within families with the same germline mutation is well documented. Referral for genetic testing may be considered to confirm the diagnosis as this will allow the clinician to educate on inheritance pattern, which may impact family planning.

Clinical Appearance
Clinically tumors favor the head and neck, presenting around puberty and enlarge and proliferate in number throughout life. Often asymptomatic, although pain has been reported in 50% of patients and may be attributed to nerve compression. Malignant transformation is estimated to occur in 5-10% of BSS patients and should be suspected if lesions rapidly enlarge, change in color, bleed, or ulcerate. Subjective complaint of painful tumors is indication for excisional removal.

Histopathology
Cylindromas are well-circumscribed dermal nodules formed by monomorphic basaloïd cells arranged in a jigsaw puzzle pattern and surrounded by eosinophilic basement membrane, hyaline material. Central cells are paler than palisading peripheral cells, creating duel epithelial cells. In contrast, spiradenomas are comprised of lymphocytes and lack the jigsaw arrangement typical of cylindromas. Spiradenomas are dermal nodules composed of small, dark, basaloïd epithelial cells arranged in a rosette pattern. The other prominent cell type is large, pale-colored cells found at the center of the tumor nests. Trichoepitheliomas are characterized by basaloïd palisading cells forming nests or cribiform patterns surrounded by fibroblast and collagen bundle rich stroma.

Table 1. Common neoplasms present in patients with Brooke-Spiegler Syndrome

<table>
<thead>
<tr>
<th>Trichoepithelioma</th>
<th>Cylindroma</th>
<th>Spiradenoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Appearance</strong></td>
<td>Flesh-colored, translucent papules</td>
<td>Firm, rubbery, pink nodules with telangiectasias</td>
</tr>
<tr>
<td><strong>Typical body location</strong></td>
<td>Central face</td>
<td>Scalp and face</td>
</tr>
</tbody>
</table>

References

Table 1. Common neoplasms present in patients with Brooke-Spiegler Syndrome

<table>
<thead>
<tr>
<th>Trichoepithelioma</th>
<th>Cylindroma</th>
<th>Spiradenoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Appearance</strong></td>
<td>Flesh-colored, translucent papules</td>
<td>Firm, rubbery, pink nodules with telangiectasias</td>
</tr>
<tr>
<td><strong>Typical body location</strong></td>
<td>Central face</td>
<td>Scalp and face</td>
</tr>
</tbody>
</table>

Figure 2. Cylindroma
Figure 3. Cylindroma

Treatment
Aimed at improving cosmesis; includes resurfacing modalities such as thermal electrodecoagulation, cryotherapy, dermabrasion, trichloroacetic acid, retinoic acid, and erbium-YAG/carbon dioxide (CO2) laser. Resurfacing therapy is most appropriate and effective for trichoepitheliomas, however, recurrence is common. Current literature for treatment of malignant cutaneous tumors indicates wide surgical excision with a minimum of 2 cm laterally and 1 cm basal margins with subsequent radiotherapy to decrease risk of tumor recurrence. Patients should receive early treatment to minimize disfigurement secondary to tumor development and regular dermatologic evaluation to monitor lesions and detect potential malignancies.

Causative therapy for BSS remains under current investigative efforts. Recent studies have revealed impaired tropomyosin kinase (TRK) signaling associated with CYLD mutations, as well as overexpression of TRK in cylindroma cells. Utilization of a TRK inhibitor molecule, lestaurtinib, may serve as a novel causative treatment option for BSS patients. Continued genetic studies are necessary to further develop effective, causative therapies that significantly improve patient outcomes beyond symptomatic relief provided by current treatment modalities.
A Rare Case of SCC in a Pediatric Patient with NF-1

Christopher Mancuso, DO*, Mojan Hosseinipour**, MSIV DO, Craig Austin**, MD, Charles Gropper***, MD, Cindy Hoffman****, DO

Abstract

We present a case of a pre-adolescent female with Neurofibromatosis type 1 (NF1) who developed squamous cell carcinoma (SCC) on the dorsum of the nose. This rare presentation has been reported in the literature only twice and in both instances involved adult patients. SCC itself is very rare in children and is usually seen in those with a predisposing condition like immunosuppression, radiation exposure or genodermatoses of which our patient did not have. We also discuss the possible pathogenesis of epithelial tumor development in patients with NF1, a historically non-epithelial tumor producing disorder.

Introduction

Neurofibromatosis type 1 is an autosomal dominant genetic disorder characterized by the presence of café-au-lait macules, plexiform neurofibromas, nerve sheath tumors, lisch nodules and freckling in the cutaneous squamous cell carcinoma.

Patients by age 8 years and in 100% of patients by age 20 years. Patients are characterized by the presence of café-au-lait macules (CALMs), neurofibromas, nerve sheath tumors, lisch nodules and freckling in the cutaneous squamous cell carcinoma. Another study in mice by Ahi et al. showed further evidence for NF1’s role in epithelial carcinogenesis. They studied mice who were heterozygous for null mutations in NF1, exposing them to known carcinogens. Heterogeneous mice developed papillomavirus growth as well as sustained increases in keratinocyte proliferation, while wild type mice with the same exposure did not. In addition, all mice with papillomas were shown to have activation of RAS, a crucial step in the process of carcinogenesis, supporting its involvement in epithelial tumors. There are very few reported cases of epithelial tumors, specifically cutaneous squamous cell carcinoma (SCC), in patients with NF1. Ishida and Okabe reported a case of SCC of the forehead in an 80 year old female patient with a history of NF1.7 Friedman et al. reported a case of SCC arising on the sole of the foot in a 67 year old male patient with NF1.8 Interestingly, NF1 also appears to have some relationship with cutaneous melanomas. In a study of 11 patients with melanomas and concurrent NF1 patients a mean Breslow depth of 3.2mm, considerably deeper than their non-NF1 counterparts. In fact, NF1 is the third most affected gene in melanomas.9

Squamous cell carcinoma is the second most common cutaneous malignancy in adults. Classically it occurs in older adults on chronically sun exposed areas as well as in those with radiation exposure, chronic wounds, arsenic exposure and immunodeficiency. Children rarely develop any cutaneous cancers, with the exception of up to 1/10000 children. One study by a large pediatric hospital showed that out of 398 dermatology patients, 53 cutaneous malignancies were diagnosed. Of that number 6% were squamous cell cancer. They are most commonly seen in association with underlying skin conditions like albinism, xeroderma pigmentosum, and epidermolysis bullosa. Although all of the classic predisposing factors can come into play.10 According to one article, pediatric squamous cell cancer of all types appears to be increasing in prevalence over the past two decades. They believe it to be caused by multiple factors including recurrence of SCC from radiation treatments years later and increased HPV infection prevalence.11 Cutaneous malignancy should be considered early on in any child with predisposing factors and atypical presentation.12 It is important to use a dermatopathologist comfortable with diagnosing pediatric lesions. Clinicians may also consider performing a second wider biopsy, so as to not miss or delay diagnosis. At times an adult dermatopathologist may be better suited in diagnosis of these classically late presenting lesions. Treatment of these lesions is recommended and full excision is warranted as squamous cell cancers in children have poor prognosis.13 Our patient underwent Mohs micrographic surgery for full evaluation of tumor margins and best cosmetic outcome on this young female’s face. Months out she has shown no signs of recurrence and is happy with her cosmetic appearance. She is being followed by ophthalmology, radiology, dermatology, and has been offered genetic counseling for her underlying NF1. We expect to have her follow up once a year for a full skin exam to monitor for further skin cancer development.

Case Report

An 11 year old female with a past medical history of NF1 and positive family history of NF1 including mother and sibling, presented to the dermatology clinic for evaluation of a lesion on her nose that was present for the past 6 months (Figure 1). There was no bleeding, pain or change in size. She denied similar lesions elsewhere. On physical examination the lesion measured 7 mm in diameter on the dorsum of the nose with overlying scale-crust, as well as multiple well-defined brown patches and macules on the trunk and extremities. Differential diagnosis included: verruca vulgaris, actinic keratoses, and molluscum contagiosum, and pyogenic granuloma. Cryotherapy using liquid nitrogen was performed on the lesion for presumed verruca vulgaris. Three weeks later the patient returned for clinical checkup with the lesion having grown in size since the last visit. The patient then had a shave biopsy of the nasal lesion which showed atypical squamous cell proliferation invading the dermis consistent with SCC. The patient then underwent Mohs micrographic surgery for complete surgical removal.

Dermatopathology

Figure 2 & 3: Shave biopsy from patient’s nasal dorsum shows atypical keratinocytes invading the dermis with overlying parakeratosis and peripheral pseudohorn cyst formation.

Discussion

In conclusion, this is the third reported case of cutaneous SCC in a patient with NF1, and the first reported case in a pre-adolescent patient. To our knowledge, this is the first documented case of SCC of the nose diagnosed in a patient with NF1. Due to the rarity of the condition, we were not able to find guidelines for management of pediatric squamous cell cancer and perhaps with its increasing incidence this issue may be addressed in the future. Our case along with prior studies conducted, suggest an increase in risk for developing epithelial tumors in patients with NF1 warranting further study in this topic. With this knowledge, clinicians can be more informed about all the risks pertaining to NF1 and will hopefully consider SCC when they come across any abnormal lesions that are found in predisposed individuals.

References


Conclusions


Correspondence

Chris Mancuso, DO
Saint Barnabas Hospital
Bronx, NY
mancusoderm@gmail.com
Dermal Melanoma: a rare subtype of melanoma

Brianna McDaniel1, D.O., PGY-3; Jonathon Crane1,2, D.O.

1Sampson Regional Medical Center, Dermatology Residency Program, Clinton, NC; 2Dermatology Residency Program Director

Introduction

• Benign subcutaneous masses such as lipomas and cysts are common and often go untreated.
• Primary dermal melanoma may be clinically unrecognizable as an atypical melanocytic process because of its resemblance to a subcutaneous cystic or vascular process.
• The term primary dermal melanoma has been used to describe a subtype of melanoma confined to the dermis or to the subcutaneous tissue without evidence of trauma, regression, or systemic disease. (3)
• Here we present a case of a presumed lipoma, excised at the request of the patient, and found on pathology to be a dermal melanoma.

Case Presentation

• A 77 year-old male presented for excision of a flesh-colored subcutaneous tumor on his left upper arm present for six months and presumed to be a lipoma due to its appearance and his past history of multiple lipomas.
• Excision revealed a dermal/subcutaneous melanoma with out epidermal changes and consisting almost entirely of markedly atypical epithelioid cells growing in a sheet-like fashion. Marked pleomorphism was present with numerous mitotic figures.
• Immunoperoxidase staining was positive for S-100 and Melan-A, and negative for CKAE 1/3, supporting the histopathologic diagnosis. The greatest thickness was 15 mm with deep margin involvement.
• Whole body PET scan showed left axillary metastasis without distant metastasis. MRI of the brain was negative for metastatic disease.
• Left axillary sentinel lymph node biopsy revealed metastatic melanoma and re-excision of the remainder of the tumor revealed a deep dermal/subcutaneous circumscribed melanoma with no melanoma in situ or upper dermal melanoma noted.
  • The greatest thickness of the residual tumor was 25 mm, extending to within 1.2 mm of the deep margin with negative peripheral margins.
• Subsequent left axillary lymph node resection was negative for metastatic disease. Medical oncology recommended no adjuvant therapy. All subsequent PET and CT scans have not shown further evidence of metastasis.
• Dermal melanoma was originally considered in transit (stage IIIB) or stage IV melanoma, but is now recognized as a separate entity because of the significantly higher survival rate compared to stage III and IV melanoma.
• Outcomes in dermal melanoma correlate more closely with cutaneous melanoma of a similar thickness versus dermal metastasis with similar depth. (2)
• Management of dermal melanoma consists of wide local excision as well as a sentinel lymph node biopsy.
• Sentinel lymph node biopsy is a cost effective way to increase disease-free survival and has been associated with a lower recurrence rate. (4)
  • A large case series of 83 patients demonstrated a positive sentinel lymph node biopsy was associated with a 5 year disease-free survival of 61% compared to lymph node negative 5-year survival of 81%. (2)
• A positive lymph node biopsy should be followed up with a complete lymph node dissection and discussion of adjuvant therapies.

Conclusion

• Primary dermal melanoma is a rare entity that represents less than 1% of all melanomas.
• Histologically, primary dermal melanoma appears identical to metastatic melanoma. (1)

References

Atypical Fibroxanthoma Invading the Parietal Bone

Miesha Merati, DO, Jeffrey Scott, MD, Jeremy Bordeaux, MD, MPH, Chad Zender, MD

Department of Dermatology, University Hospitals Cleveland Medical Center/Case Western Reserve University School of Medicine. Cleveland, OH, USA.

**History & Clinical Course**

Eighty-six year-old male with multiple medical co-morbidities, presented from an outside dermatologist with biopsy-proven atypical fibroxanthoma (AFX) of the left parietal scalp. The lesion was treated with Mohs micrographic surgery and the tumor was cleared after two stages. The final defect measured 4.0 x 3.5 cm, and it was left to heal by secondary intention (Figure 3).

Wound check six months after Mohs micrographic surgery revealed a new firm nodule. Re-biopsy was consistent with a hypertrophic scar with scattered atypical epithelioid cells, present on the margins, concerning for AFX. He returned for a second Mohs micrographic surgery, and the surgery was stopped after two stages given AFX extension into bone. The defect at this point measured 5.5 x 5.0 cm. The patient was sent to ENT for evaluation. The patient underwent radical resection of the outer cortex of the scalp and the defect was repaired with a perstring closure, as well as a full-thickness skin graft from the left supraclavicular fossa. The patient followed-up with ENT one month after surgery, with a 3.0 x 4.0 cm new growth at the surgical site. Repeat biopsy was consistent with AFX recurrence. The preliminary plan is resection and radiation therapy.

**Physical Examination**

Initial clinical visit revealed a well-appearing Caucasian male with an approximately 2.5 x 2.5 cm ulcerated red nodule and surrounding indurated erythematosus plaque of the left parietal scalp.

**Radiology**

CT of the head without contrast at initial ENT consultation revealed a subacute or chronic left subdural hematoma with mild midline shift but no mass effect. Follow-up CT of the head without contrast approximately one month later, after discovery of second recurrence, showed diffuse volume loss and periventricular white matter changes consistent with age-related atrophy and no evidence of hemorrhage.

**Histology**

Figures 2A-D. Immunohistochemical stains as noted. Stains not pictured: CD31-, CD10+, SMA-.

AFX is an uncommon fibrohistiocytic tumor, regarded as a less aggressive, superficial variant of undifferentiated pleomorphic sarcoma (UPS). Clinically, AFX presents as a pink/red firm, asymptomatic papule/nodule with ulceration, typically less than two centimeters in diameter on the sun-exposed areas, especially the head and neck of older males. AFX of the extremities is usually larger, slower-growing, and with less well-defined borders. The pathogenesis of AFX remains largely unknown with contributing etiologies including ultraviolet radiation, p53 mutations, cyclobutane pyrimidine dimers, prior radiation therapy, and immunodeficiency. There is considerable controversy regarding the differentiation between UPS and AFX. Some authors suggest that tumors larger than two centimeters in diameter, involving the fascia or muscle, exhibiting necrosis, vascular invasion, or metastasis should be regarded as UPS, given its more aggressive nature.

Immunohistochemistry plays an important role in differentiating AFX from its histological differential, including spindle cell squamous cell carcinoma (SCC), desmoplastic melanoma, and UPS. Cytokeratin markers and S-100 are negative in AFX but positive in spindle cell SCC and desmoplastic melanoma, respectively. CD10 is a cell-surface glycoprotein that is strongly positive in AFX and much weaker and focal in both desmoplastic melanoma and spindle cell SCC. (Figures 2A-D) LN-2 is a promising marker in delineating the difference between UPS and AFX. Studies show that 90% of UPSs stain strongly for it and 90% of AFXs have weak or no staining.

Treatment with Mohs micrographic surgery has a lower recurrence rate than excision. Radiation may be used as an adjunctive treatment for recurrent or metastatic disease. Induration, ulceration, or poor wound healing predict recurrence, which typically occurs within one to three years of treatment. Depending on modality of treatment, recurrence has been reported in up to 16% of cases, and it often foreshadows metastasis. Metastasis to lymph nodes, liver, lung, and subcutaneous tissue has been described in up to four percent of patients. While AFX has been noted in unusual sites such as the ethmoid sinus, eyelid, and cornea, this is the first case of parietal bone involvement to our knowledge.

**Clinical Images**

Figures 3A-B. AFX prior to Mohs micrographic surgery (A) and after two layers (B).

**References**


Epidermolysis Bullosa Aquisita: A case presentation

Kiran Mian, DO and Navid Nami, DO
Western University/Chino Valley Medical Center

Case Presentation

Chief Complaint: Sores on my body

History of Present Illness: Patient is a 54 year old thin Hispanic male who presents to clinic with complaints of sores on his body of a two year onset. These sores start off spontaneously as blisters on his chest, arms, and feet, and are somewhat painful. He denies any other systemic symptoms, and is otherwise healthy. His major concern is not being able to work due to the painful sores on his feet.

Past Medical History: None

Medications: None

Family History: Noncontributory

Social History: Lives at home with family, works in a factory, although has been unable to work since onset of this condition. Denies alcohol/tobacco/illicit drug use

Allergies: NKDA

Physical Exam: Multiple areas of sclerotic plaques in various stages of healing on forehead, chest, posterior upper extremities, dorsal feet, and bilateral toes, with some plaques exhibiting central ulceration and others with hyperkeratotic crust. No mucosal or fingernail changes noted.

Laboratory tests: CBC, CMP, ANA, HIV screen within normal limits

Histology:

H&E: ulcer with inflamed fibrosing granulation tissue

DIF: Subepidermal bulla with linear IgG and C3 along DEJ

IIF: IgG on dermal side of DEJ

Patient Course/Treatment: Considering laboratory, histologic, and clinical findings, the patient was diagnosed with Epidermolysis Bullosa Aquisita, inflammatory type. He was prescribed trimacimolone 0.1% ointment for active lesions as well as a tapered course of oral prednisone, and referred to a tertiary center for further management.

Discussion

Epidermolysis bullosa acquisita (EBA) is an autoimmune mucocutaneous blistering disease which usually occurs in adults. The disease is characterized by the production of IgG autoantibodies which target type VII collagen, the primary collagen found in anchoring fibrils of the lamina densa (1,2). Anchoring fibrils serve to attach the epidermal basement membrane to the dermis (3), and the buildup of IgG creates tissue fragility by mechanically disrupting this normal architecture. Most commonly, this disease presents with tense vesicles and bullae on a noninflammatory base, most pronounced at sites of repetitive minor trauma such as the feet, hands, knees and elbows. The resulting erosion lead with scarring and milia. A subset of EBA can manifest via an alternative inflammatory process, in which collagen VII autoantibodies attack anchoring fibrils triggering an inflammatory cascade and activating complement. This leads to destruction of essential matrix proteins in the DEJ and causes the BP-like inflammatory EBA variant. Our patient correlates with this subtype of EBA, with lesions in a distribution beyond the characteristic sites of trauma. Most noninflammatory EBA patients also have mucosal involvement, and severe cases may be complicated by alopecia, nail dystrophy, or hand-foot deformities - the so-called mitten deformity (4). Our patient did not have mucosal involvement, further aligning with inflammatory EBA.

The evaluation of EBA begins with a thorough history and exam of suspicious lesions and is confirmed with biopsy. A biopsy taken from lesional skin can reveal the subepidermal site of separation, with a cell poor infiltrate. The BP-like EBA displays a more robust inflammatory infiltrate, as consistent with our case. A biopsy taken from perilesional skin can be used for direct immunofluorescence, which will reveal deposition in the dermal-epidermal junction (DEJ) primarily of IgG as well as possibly complement, IgA, IgM, Factor B and properdin (2,4).

Additionally, indirect immunofluorescence may be performed on salivary split skin separated at the lamina lucida of the basement membrane zone. In EBA, antibody deposition is seen most prominently on the dermal surface. This is in contrast with bullous pemphigoid or linear IgA bullous dermatosis, which contain antibodies primarily on the epidermal surface (2,4).

The treatment for EBA currently relies on pharmacotherapy, with variable results. Treatment should begin with agents that can be tolerated for chronic use with minimal side-effects. Colchicine is frequently used as a first-line therapy. Dapsone can also be used either alone or in conjunction with other drugs such as colchicine or corticosteroids. Prednisone (0.5 to 1.5 mg/kg per day) has frequently been used, though its side-effect profile and lack of efficacy limits its use to second-line or in combination with other therapies (4,5).

Immunosuppressive medications have been used in refractory disease, including rituximab, azathioprine, cyclophosphamide, mycophenolate mofetil and cyclosporine. These are often used in conjunction with steroids or other anti-inflammatory medications such as those described above (6). IVIG has been used for widespread or refractory disease, either alone or combined with other agents (7-9).

As with many chronic and relapsing dermatologic conditions, patient education is first and foremost in the management of EBA. Patients should be counseled to take precautions against minor trauma. They should cleanse their skin gently, avoid scratching, and seek medical treatment early should infection be suspected.

References


Figure 1-3: Clustered erythematous, scarred plaques with crust on the forehead, and metatarsal digits. Figure 4: IIF showing a subepidermal bulla with thick band of IgG deposition along dermal surface
Multiple Mastocytomas: A Case Report and Discussion

Kevin Miller, DO¹
¹PGY-3, Affiliated Dermatology, Scottsdale, AZ, USA

Background
Mastocytosis is a clonal proliferation of mast cells in various tissues of the body with skin being the most common.

Case Report
An otherwise healthy 8-month female presented with brown lesion on the face, chest, and bilateral upper and lower extremities that had become larger and more numerous since their onset five months prior. Physical exam revealed numerous 0.5-3.0 cm brown papules and plaques that urticate when gently stroked (Darier’s sign). Shave biopsy of a representative lesion was performed and revealed a nodular aggregate of mast cells in the epidermis. Serum tryptase level was normal.

Discussion
Mastocytosis is a proliferation of mast cells that affects patients of all ages and several organ systems, with the skin being the most common. Cutaneous mastocytosis has classically been categorized into three clinical presentations: mastocytomas, maculopapular cutaneous mastocytosis (AKA urticaria pigmentosa) and diffuse cutaneous mastocytosis. More than 50% of mastocytosis cases have an onset of symptoms before the age of 2.¹ Pediatric patients are more likely to have mild cutaneous lesions that often resolve by puberty while adults tend to have systemic manifestations that are chronic and can cause multisystem complications such as anaphylaxis.²,³

Although mast cells proliferate throughout the body, their abundance in the skin leads to a high proportion of cutaneous symptoms. Since no cure exists for cutaneous mastocytosis, treatments focus on avoidance of triggers in addition to various symptomatic treatments. Mast cell degranulation triggers include: physical stimuli such as heat and friction; stress and anxiety; numerous medications including NSAIDs, opioids, and radiocontrast; and venomous stings. Medical management options for pediatric patients include: topical and intralesional steroids, topical calcineurin inhibitors, 1st and 2nd generation H1 antihistamines, H2 blockers, and leukotriene antagonists.⁴

References

Disclosures
There are no financial or other relevant relationships to disclose.

Conclusion
Mastocytosis is a proliferation of mast cells in various organs of the body that manifests quite differently in pediatric and adult patients. Most pediatric cases begin before age 2 and are characterized by mild cutaneous symptoms that often resolve by puberty, whereas adult-onset mastocytosis is more likely to have systemic manifestations with an increased risk of serious complications. Current management is targeted at the avoidance of mast cell degranulation triggers and utilization of various symptomatic treatments.
INTRODUCTION

- Neutrophilic eccrine hidradenitis (NEH) is an uncommon neutrophilic dermatosis of the eccrine sweat glands. NEH was most often reported in adult patients receiving induction chemotherapy, notably, cytarabine for acute myeloid leukemia (AML), characterized by self-limited eruption of erythematous papules and plaques.  
- NEH has since been described in association with other malignancies, infections, and following the ingestion of related immunomodulators and acitretin. 
- Featured is a case of NEH presenting as a persistent polymorphous eruption in a child receiving intensification chemotherapy for an even rarer, underlying Philadelphia-chromosome positive acute lymphoblastic leukemia.

PRESENTATION

- An 8-year-old Hispanic male with Ph+ ALL presented to the emergency department with a two-day history of fever and rash on the extremities, arms, cheeks, lower trunk, and legs which began within two hours of leucostein infusion, nearly 2 days following administration of methotrexate and cytarabine. 
- Additional history included sulfas-induced urticarial eruption, seizure disorder, recurrent pneumonia and otitis media, asthma, and anemia requiring multiple transfusions. 
- Some medications included dasatinib, levofloxacin, and acitretin.
- Physical examination revealed symmetric, non-tender, blanchable, edematous, erythematous, follicular papules and pustules of the cheeks, extremities, and abdomen (Figure 4), superficial erosions with hemorrhagic crusts of the lower lip and a pink velvety dorsal tongue were also noted. Scalp alopecia prominent. Palms and soles were spared. 
- Histology showed hyperkeratosis, clefting below the granular layer, vacuolar interface dermatitis, follicular penetration by dermal neutrophils, and granulomatous perivascular infiltrates of the superficial and mid-dermis around eccrine ducts and eccrine glands. 
- Laboratory tests revealed leukopenia with neutropenia, lymphocytosis, mild monocytosis, anemia, thrombocytosis, elevated transaminases, hypogammaglobulinemia, and hyposplenism. 
- Renal function tests, CRP, coagulation profile, cultures, and chest radiograph were unremarkable. 
- Serology negative for anti-streptolysin O, human immunodeficiency virus-1/-2, hepatitis B and C virus, Mycoplasma pneumoniae IgM, parvovirus B19, Epstein-Barr virus. 
- PCR negative for parvovirus, adenovirus, cytomegalovirus, human herpes virus-1/2/6/7, and enterovirus. 
- Bone marrow aspiration revealed minimal residual disease with erythroid and granulocytic hyperplasia. 
- Findings were consistent with NEH, and in all likelihood, the result of cytarabine. However, methotrexate as the offending agent could not be excluded. Further, dasatinib has been reported to cause follicular papular and pustular eruptions, similar to the acneiform and keratosis pilaris-like eruption seen in our patient. 
- Treatment included empiric antibiotics and antifungals pending negative cultures and topical corticosteroids. 
- One month later, the patient presented to the dermatology clinic with minimal improvement of the eruption and was started on oral prednisolone to further facilitate recovery.

DISCUSSION

- NEH is a neutrophilic dermatosis of the eccrine glands. 
- To date, adults receiving chemotherapy (most commonly cytarabine) seen in our patient for AML remains the most common presentation reported in literature. 
- Of note, neutrophils may be absent on histology in chemotherapy-induced neutropenic patients termed “chemotherapy-induced eccrine hidradenitis.” NEH may rarely occur in patients with no previous treatment or following methotrexate (potential etiology in our case), granulocyte colony stimulating factor, acitretin, azathioprine, bexarotene, cytarabine, cyclophosphamide, vincristine, imatinib-misplt, or upon initiation of imidazolone.
- Infrequently, NEH has been reported in association with other hematological malignancies, solid tumors, Behçet’s disease, hemolytic-uremic syndrome, and systemic infection with HIV, Streptococcus, Serratia, Staphylococcus, and Staphylococcus aureus.
- Clinically, NEH most often presents in febrile adults as a self-limited eruption of non-tender, erythematous papules and plaques of the face, trunk, and extremities on an average of 9.7 days following drug exposure. Less frequently, as a polymorphous eruption of papules, nodules, purpura, urticaria, or as pustules mimicking cellulitis which may make it difficult to distinguish from other neutrophilic dermatoses such as Sweet’s syndrome and pyoderma gangrenosum. 
- Rarely, an oligoclonal variant of NEH presents in children with lesions limited to the palms and soles referred to as “palmarplantar eccrine hidradenitis”, thought to be the result of mechanical and/or thermal trauma in healthy children.
- Regardless of etiology, the eccrine glands and coalesc vast as the ultimate target of destruction, usually a result of drug-induced neutrophilic chemotaxis following stimulation by inflammatory mediators such as tumor necrosis factor-alpha, resulting in damage and necrosis of eccrine epithelium. 
- Alternatively, NEH may be considered along the neutrophilic dermatoses spectrum rather than a distinct entity, a paraneoplastic phenomenon, or in healthy individuals suggesting underlying sweat gland abnormalities. 
- Diagnosis is confirmed by skin biopsy showing an infiltration of neutrophils, and possibly necrosis around and within the eccrine glands and ducts, often with edema and extravasation of red blood cells in the dermis. 
- Exclusion of infection is paramount in the prevention of life-threatening complications and unnecessary administration of antibiotics or changes in chemotherapy regimens. 
- NEH tends to be self-limited, although relapse may occur upon re-exposure to an offending agent. 
- Treatment is supportive with topical or systemic corticosteroids and antihistamines as needed. 

REFERENCES

HISTOLOGY/IMMUNOHISTOLOGY

Histologic findings in STS include proliferating vascular channels that dissect dermal collagen. The tumor endothelial cells that line the vascular channels are hyperchromatic and pleomorphic, usually undergoing mitotic changes. The endothelial cells are round to oval and often project into the lumen of the vessel, with erythrocytes found inside the channels.4

Immunohistochemistry plays an important role and may be necessary for diagnosis. Angiosarcomas demonstrate positive staining for laminin, collagen IV, vimentin, CD31, CD34 and factor VIII-related antigen.4 Additionally, lymphatic-associated antibodies have been developed that stain angiosarcomas: podoplanin (D2-40), lymphatic vessel endothelial hyaluronan receptor-1, prospero homeobox protein 1 and vascular endothelial growth factor receptor 3 (VEG-F-3). These were all found to be expressed in STS and angiosarcoma induced by radiotherapy, demonstrating lymphatic differentiation.7

DISCUSSION

STS has a poor prognosis. Medical management with chemotherapy and/or radiation therapy is adjacent to surgery. Early amputation or wide local excision gives the best chance of long-term survival, though even in cases of early surgical treatment, there remains a high rate of local recurrence and metastasis.8 The mean survival after tumor onset is approximately 20 months.9 Due to breast conservation therapy, improvement of surgical and radiation therapy techniques, and the development of new chemotherapeutic agents, the incidence of STS has significantly decreased.10 Most radiotherapists no longer irradiate the axillae after lymphadenectomy, which has decreased the incidence of chronic lymphedema after breast cancer therapy from 40% to 4%.12

REFERENCES

CASE PRESENTATION

Sheena Nguyen, DO and Navid Nami, DO
Western University of Health Sciences/Chino Valley Medical Center

Chief Complaint: White spots all over body

Signs and symptoms: Patient is an eight-year-old girl who presented to clinic with a three-year history of asymptomatic, hypopigmented macules spread diffusely throughout her body. She denied any preceding illnesses, or systemic symptoms.

Past Medical History: None

Medications: None

Family History: Non-contributory

Social History: Lives at home with parents, attends elementary school, denies alcohol/tobacco/illicit drug use, denies recent travel

Surgical History: None

Allergies: N/D

Previous Treatment: Patient’s mother reported having been prescribed and using Tramcicline 0.1% ointment on affected areas twice daily for the patient for one month without improvement.

Physical Exam: Patient is a well-nourished, well-appearing female who presented in no acute distress. She had a diffuse eruption of scattered hypopigmented macules without other surface changes ranging in size from 2mm - 12mm throughout her face and body. There was no oral involvement.

Laboratory Tests: Complete blood count and blood chemistries within normal limits.

Quantitative T-cell subset and T-cell receptor rearrangement in blood are negative.

Quantitative immunoglobulins are normal.

Dermatohistopathology: A shave biopsy was performed on the left upper back that demonstrated mild perivascular hyperplasia of the epidermis with a paucicellular atypical epidermotropic lymphoid infiltrate. Rare focal demonstrating "lining up" of atypical lymphoid cells along the dermoepidermal junction and haphazardly infiltrating the epidermis. In addition, there is superficial perivascular lymphohistocytic inflammatory infiltrate with abundant intercellular melanin pigment. PAS stain is negative for fungal organisms.

Immunohistochemistry performed reveals a predominance of CD3+ T-cells in the atypical lymphoid cells. The CD6:CD4 ratio appears markedly increased, although the total number of atypical cells is small. There is some loss of staining with pan T-cell marker CD3. Both CD20 and CD30 immunostains highlight rare lymphoid cells. Mart-1 demonstrates a normal distribution and number of melanocytes arguing against vitiligo and most cases of pityriasis alba.

Patient Course/Treatment: Once the diagnosis of hypopigmented mycosis fungoides was made, patient was referred to oncology for close follow-up and started on a regimen NB-UVB therapy.

DISCUSSION

Mycosis fungoides (MF) is the most common primary cutaneous T-cell lymphoma that usually presents in the stages of patches, plaques, tumor, or erythroderma [1-4]. There are several distinct variants of MF that have their own clinical behaviour and outcome. They include plaque-type, bullous, papular, follicular, erythrodermic, verrucous, unilocular, invasive, granulomatous, hypopigmented, and hypopigmented mycosis fungoides (HMF) [2, 5].

HMF is an indolent cutaneous T-cell lymphoma that represents a rare clinical variant of the early patch stage of MF [1, 3, 6, 7]. It is most commonly seen in dark skinned and Asian individuals, it has infrequently been reported in Caucasians as well [1-3]. The average age of onset is usually seen between the first and third decades as compared to classic MF, which manifests around the sixth decade [1, 2, 6, 7, 9].

Patients will most commonly present with multiple, ill-defined, hypopigmented patches of varying sizes on the trunk, back and proximal extremities [2, 4-8]. Cutaneous sensation will be intact with a variable degree of scaling, atrophy, infiltration, and pruritus [2, 4-8].

The differential diagnosis for HMF includes all possible etiologies for hypopigmented patches on the skin, such as vitiligo, leprosy, progressive macular hypomelanosis, seborrheic keratosis, linear Ta-T cell lymphoma, lichenoid keratosis, and poikiloderma. A study of clinicopathologic profile of 15 cases of hypopigmented mycosis fungoides (HMF) presented a significant number of cases that had a negative T-cell receptor gene rearrangement, blood tests, and diagnostic imaging.

The diagnosis is usually rendered by clinicopathological correlation of the histological appearance of the involved skin using immunohistochemical staining with pan T-cell marker CD3. HMF is defined as MF with a low CD4+/CD8+ ratio, unlike classic MF that presents with a CD4+/CD8+ predominant infiltrate [1-9].

Proposed mechanisms for the cutaneous hyperpigmentation include the systemic effect of CD8+ T cells on CD3+ causing dysregulation and/or loss of melanocytes, a deficit in the transfer of melanomatos from melanocytes to keratinocytes, and a nonspecific result of inflammation [1, 3, 4, 9].

The presence of a T-cell receptor gene arrangement is seen in a large percentage of patients with HMF; however, the absence of clonality does not rule out the disease [1, 6-9]. Initial evaluation may include CBC with differential, quantification of T and B cell lymphocytes using flow cytometry, physical exam of the peripheral lymph nodes, and diagnostic imaging if suspecting any systemic involvement [2, 7].

Psoralen + UVA (PUVA) or a narrow band UVB with topical steroids is the mainstay of treatment [1-10]. Topical nitrogen mustard, topical and intralesional corticosteroids, and phototherapy can be utilized. However, the effectiveness is variable. Most patients require repetitive cycles of phototherapy or maintenance therapy due to the high recurrence rates associated with HMF [2, 5].

HMF has an indolent course with an overall survival of 98% at 20 years, significantly better prognosis than classic MF [1, 3, 5]. However, it has been reported that the progression cases of MF+ T cells, and MF presents the evolution of HMF lesions to MF plaque and tumors by participating in the protective Th1 response [2, 3, 9]. Hypopigmentation may be considered as a marker of good prognosis.

The diagnosis is usually rendered by a clinical and histopathological correlation supplemented by immunohistochemistry and ancillary studies such as TCR-gene rearrangement, blood tests, and diagnostic imaging. Occasionally, you may need several skin biopsies to confirm the disease.

Due to the increasing frequency of HMF it is important to be aware of this entity and perform a skin biopsy especially in patients with persisting or progressing hypopigmentation despite therapy. HMF is a malignant neoplastic disease with a lethal potential and should be treated as such with proper work-up and mandatory follow-up.

REFERENCES

Introduction

Rowell Syndrome was originally described in 1963 as an association or overlap between cutaneous lupus erythematosus and erythema multiforme in the same individual with associated serum immunologic abnormalities. Since its initial description, the syndrome has been controversial as source quintet whether it is truly a unique entity or simply part of the spectrum of clinical manifestations of cutaneous lupus erythematosus. We report a case of new-onset SCLE presenting with EM-like and SJS/TEN-like lesions, an entity some describe as Rowell Syndrome.

Case

A 48-year-old female with no significant past medical history presented to our facility in August of 2013 complaining of a rash of 5-6 weeks duration. She reported the rash started on bilateral thighs and subsequently spread to her back, arms, chest and face. She had visited the ER before coming to our facility and was told to follow up with her outpatient dermatologist. He then referred her to our center for further workup and treatment.

Upon arrival the patient exhibited multiple scattered erythematous annular macules and patches with collarette of scale and areas of denudation on bilateral upper and lower extremities as well as abdomen and back (Fig 1). Her chest and face revealed extensive areas of desquamation, her lips were scaly and crusted (Fig 2). She did not display any intraoral or ocular involvement; she did not have any other mucosal lesions. The lesions were painful (7/10 on pain scale) particularly in areas of denudation. On review of systems, she admitted to decreased appetite, cyclic fevers (Tmax 102), and chills.

Clinical Photos

Fig 1. Extensive area of demodum seen on the back

Fig 2. Lips and neck exhibiting areas of desquamation and crusting

Antibody work-up revealed positive ANA (homogenous pattern, 1:1280), positive dsDNA, negative hls-70, negative antinuclearas, decreased total complement C3/C4, anti-Smith, and SS-Ro/La negative. Three punch biopsy specimens were obtained; two were submitted for immunofluorescence and one for routine H&E.

Pathology

Frozen sections revealed full thickness epidermal necrosis consistent with cutaneous lupus erythematosus with a toxic epidermal necrolysis like clinical presentation.

Direct Immunofluorescence was positive for IgG colloid bodies and C3 granular deposition consistent with lupus erythematosus.

Discussion

Many cases of Rowell Syndrome have been reported since Rowell’s original work in 1963. In reviewing the literature, it is evident that a single set of diagnostic criteria does not exist and, moreover, Rowell’s original criteria are not well preserved.

In 2012 Torchia et al. conducted an extensive literature review and suggested new major and minor criteria. Major criteria: chronic cutaneous lupus, EM-like lesions, at least one positivity among speckled ANA, anti-Ro/La antibodies, and negative IIF on EM-like lesions. Minor criteria: absence of triggers, absence of typical EM location, and presence of at least one additional ARA criterion for diagnosis of SLE. They require all 4 major and at least one minor criterion for the diagnosis of Rowell syndrome.

Currently no therapeutic standard for Rowell Syndrome exists. Most patients are treated with therapies directed at their underlying LE. These treatments include corticosteroids, methotrexate, dapsone, hydroxychloroquine, and azathioprine. While our patient did not meet the proposed diagnostic criteria, we believe this to be a unique and interesting presentation of SCLE that serves to further the discussion regarding the pathogenesis and significance of Rowell’s.

References

Systemic Nickel Allergy Syndrome
Jessica Perkins, DO, PGY-III
Nova Southeastern University, Largo Medical Center
Largo, FL

Introduction
Nickel hypersensitivity is the leading cause of contact dermatitis and has recently been recognized as a potentially common culprit in systemic contact dermatitis. Dietary nickel has also been found to be a considerable cause in chronic allergic dermatitis. Some authors also recognize systemic nickel allergy syndrome (SNAS) if associated with extra-cutaneous symptoms ranging from gastrointestinal to respiratory or even neurologic findings. Furthermore, there are case reports of hypersensitivity to exogenous nickel used in implants, prosthesis and other surgical ware.

Case Presentation
We present a case of systemic contact dermatitis in a 58 year old male. The patient presented to the hospital with diffuse eczematous dermatitis ongoing for almost 2 years with recent worsening. Pt had undergone patch testing in the past revealing an allergy to Nickel. Medical history was significant for cardiovascular disease requiring stents, Chron’s disease and follicular thyroid carcinoma. Pt states the rash started after cardiac stent placement. On physical exam, the patient had diffuse erythematous plaques with overlying scale and excoriations covering majority of the extremities and trunk. The dermatitis was refractory to topical steroids, oral steroids and light therapy.

Histology and Lab Results
Outpatient biopsy showed spongiotic dermatitis and negative DIF. Previous patch testing revealed a positive nickel allergy. Lab evaluation revealed an IgE level greater than 10 times normal range. ESR mildly elevated at 30.

Discussion
Nickel is a major allergen associated with contact and systemic allergic dermatitis. Case reports have noted reaction to intrametal, pelvic coils and other implanted nickel (4, 6). Several studies have also demonstrated diet containing nickel to be a culprit in systemic allergic contact dermatitis (1, 3). More recently, a syndrome entitled, systemic nickel allergy syndrome, has been described. This Syndrome is defined by systemic reactions to nickel, most commonly skin and gastrointestinal. Patients with this entity have positive patch testing reactions to nickel. Skin manifestations include a diffuse eczematous dermatitis consistent with allergic contact dermatitis (2, 7, 8). Gastrointestinal symptoms include diarrhea, nausea, vomiting, recurrent aphthosis, abdominal pain, bloating, and constipation (7, 8). Diagnosis can be made by positive patch test reaction as well as exacerbation by nickel oral challenge and/or improvement on nickel restricted diet. Lab findings that have been found in patients with systemic contact dermatitis may include eosinophilia or elevated IgE levels (5). Foods with high nickel content include chocolate, soy, oatmeal, nuts and legumes. In addition, patient should avoid drinks and vitamin supplements with nickel as well as canned food (9).

Conclusion
Given the findings and history, we suggest the skin and gastrointestinal findings could be consistent with SNAS. SNAS may represent an underdiagnosed entity with implications in our chronic systemic contact dermatitis patients. The diet could represent an exacerbating factor in these patients once sensitized to nickel. Foods to avoid are listed in the chart above (7). Consideration should be given to SNAS patients with systemic allergic contact dermatitis, GI findings and positive patch testing to Nickel. A diet trial may help with diagnosis and aid in resolution of these systemic symptoms for the patient.

Foods to AVOID

<table>
<thead>
<tr>
<th>Vegetables</th>
<th>Asparagus, Broccoli, Artichokes, Carrots, Cabbage, Cauliflower, Onions, Fennel, Mushrooms, Lettuce, Tomatoes, Celery, Brussel Sprouts, Spinach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruit</td>
<td>Apricots, Avocado, Cherries, Figs, Kiwi, Pears, Pineapples, Watermelon, Grapes, Plums, Berries</td>
</tr>
<tr>
<td>Herbs and Dicings</td>
<td>Bay leaves, Basil, Marjoram, Parsley</td>
</tr>
<tr>
<td>Cereals</td>
<td>Ketchup, Seed oil, Mustard</td>
</tr>
<tr>
<td>Legumes</td>
<td>Lentils, Peas, Beans, Green Beans</td>
</tr>
<tr>
<td>Seafood</td>
<td>Cod, Shellfish, Salmon, Octopus, Squid</td>
</tr>
<tr>
<td>Chocolate</td>
<td>All</td>
</tr>
<tr>
<td>Nuts</td>
<td>All</td>
</tr>
<tr>
<td>Drinks</td>
<td>Tea</td>
</tr>
</tbody>
</table>

References
Cytokeratin AE1/AE3 a more sensitive Merkel cell carcinoma marker: a retrospective case series

Nicolas E. Poulos, DO*, Evangelos G. Poulos, MD**, Stanley E. Skopit, DO, MSE***

* 2nd year resident, Larkin Community Hospital/NSU-COM-Dermatology Residency Training Program, Miami, FL** Global Pathology Laboratory, Miami Lakes, FL***Program Director, Larkin Community Hospital/NSU-COM -Dermatology Residency Training Program, Miami, FL; Advanced Dermatology & Cosmetic Surgery, Margate, FL

**Background**

Introduction: Merkel cell carcinoma (MCC) is an aggressive cancer of neuroendocrine origin. First described by Toker, the Merkel cell was named after its resemblance to the normal Merkel cell. The Merkel cell is a specialized cell related to touch that is located in the basal layer of the epidermis (1,7). Although the cells of MCC and the normal Merkel cell share some commonalities, the link has not been explored (1). Consequently, many synonyms exist: trabecular carcinoma, primary small cell carcinoma, carcinoid epidermal and primary neuroendocrine carcinoma. However, the term Merkel cell carcinoma is still widely prevalent.

Trabecular carcinoma, primary small cell carcinoma, carcinoid epidermal and primary neuroendocrine carcinoma are synonyms of Merkel cell carcinoma. However, the term merkel cell carcinoma is still widely prevalent. 

Currently, various histological stains are paramount to confirm the suspected diagnosis of MCC. Cytokeratin, especially Cytokeratin 20 (ck20), are considered paramount in the immunohistochemical differentiation of this malignancy. Ck20 is positive in a large majority of MCC cases (3) with a specific perinuclear dot or globular pattern. Ck20 is considered the benchmark stain for MCC, however, in several studies it has not been 100% sensitive, which is why other stains have been explored in a panel.

Other stains in the MCC panel include AE1/AE3 (a monoclonal antibody that highlights monofilaments of intermediate weight in human skin (6). TTF-1 is used to differentiate MCC from other pulmonary and extra pulmonary neuroendocrine tumors (10). In MCC, TTF-1 should be negative to rule the possibility of metastatic cancer (especially lung). S100 is also negative.

Because of the varying diagnosis of a series of other MCC markers, we sought to undertake a study using another cytokeratin marker, AE1/AE3, that may improve diagnostic accuracy and speed of MCC. Cytokeratin AE1/AE3 has been previously highlighted in characteristics of intermediate weight in human skin (11). To date, no description of the AE1/AE3 in the staining of a significant number of cases of MCC has been described. We suggest AE1/AE3 be used in addition to or in lieu of other cytokeratin in the identification of MCC.

**Results**

A total of 19 cases were reviewed. Ck 20: 16 of 19 positive. AE1/AE3: 19 of 19 positive. Cd56: 18 of 19 positive. Synaptophysin: 19 of 19 positive. Neurofilament: 8 of 19 positive. Ck20 is considered the benchmark stain for MCC, however, in several studies it has not been 100% sensitive, which is why other stains have been explored in a panel.

**Conclusion**

We suggest AE1/AE3 be used in addition to or in lieu of other cytokeratin in the identification of MCC.

**Background**

Background:

Merkel cell carcinoma (MCC) is the only tumor to stain positive for cytokeratin 20 (ck 20).

Objective:

To find a more sensitive cytokeratin marker for Merkel cell carcinoma.

Methods:

To date, no description of the AE1/AE3 in the staining of a significant number of cases of MCC has been described. We suggest AE1/AE3 be used in addition to or in lieu of other cytokeratin in the identification of MCC.

Results:

A total of 19 cases were reviewed. Ck 20: 16 of 19 positive. AE1/AE3: 19 of 19 positive. Cd56: 18 of 19 positive. Synaptophysin: 19 of 19 positive. Neurofilament: 8 of 19 positive. Ck20 is considered the benchmark stain for MCC, however, in several studies it has not been 100% sensitive, which is why other stains have been explored in a panel.

Limitations:

This study did not control for the positivity of AE1/AE3 in other basaloid or blue cell tumors and neuroendocrine proliferations. Further study should be conducted to determine staining characteristics for the aforementioned pathological processes. This study is an observational chart review and is subject to selection bias.

Conclusion:

We suggest AE1/AE3 be used in addition to or in lieu of other cytokeratin in the identification of MCC.

**Abstract**

We suggest AE1/AE3 be used in addition to or in lieu of other cytokeratin in the identification of MCC.

**Bibliography**

CASE REPORT
An obese, 14-year-old, Native American male, presented to his pediatrician complaining of a mildly itchy rash that started on his upper extremities. Over the next 10 days it migrated onto his torso and legs. Parents admitted to starting a new laundry detergent but denied being exposed to any other new products - including foods, medications, or lotions prior to the rash.

The patient applied an OTC topical corticosteroid cream for several days without any improvement. During the review of systems poorly controlled diabetes mellitus (DM) and obesity were noted. The patient was otherwise well and thriving. Family history was remarkable for obesity, hyperlipidemia, and DM was present on both sides of the family.

On physical examination the patient had multiple crops of 1-3 mm non-umbilicated, yellow to red papules on his arms, legs, and torso (Figure 1). Labs were ordered and serum triglyceride levels were 2,100 mg/dL (normal <150 mg/dL), fasting serum glucose levels were 250 mg/dl (normal <199 mg/dl) with a hemoglobin A1c of 13.4 (normal <5.7)."
Extensive Locally Invasive Cutaneous Tumors

Kelly Quinn, DO, Nektarios Lountzis, MD, and Stephen M. Purcell, DO
Lehigh Valley Health Network, Allentown, Pennsylvania

Case One

Patient: 76-year-old Caucasian female.

History of Present Illness: Our patient presented to the emergency department with a 2 week history of generalized weakness. She was noted to have a large fungating mass on the left parietal scalp. She reported a chronic wound secondary to injury in this region for 7 years, but noted rapid growth of the mass during the previous 2 months with significant oozing. An incidental biopsy of the scalp including skin and subcutaneous tissue revealed a sarcomatoid basal cell carcinoma (BCC). Further workup for metastatic disease was negative.

The patient was started on vandetanib prior to surgical intervention. She was managed on this for 1 month but was re-admitted to the hospital with progression of the tumor. The tumor had eroded away a significant amount of calvarium leaving dead exposed bone. Her surgery date was advanced and she had completed craniotomy and resection of 13 x 15 cm scalp mass which reconfirmed sarcomatoid BCC. The patient was discharged on vandetanib and did well until a fall at home secondary to weakness 5 months later. She was admitted and imaging showed rapid regrowth of the previously-resected mass for which she again underwent left parietal craniectomy for gross total resection of recurrent disease. Follow-up imaging disclosed no new nodules or enhancing mass. She has since been followed by radiation oncology, including lately radiated local radiotherapy and has had restoration of daily activities of daily living.

Medical/Surgical History: Yes

Family History: No family history of skin cancer

Physical Examination: There is a large, multilobulated, red, fungating mass on the left parietal scalp which is fungating tumor with central necrosis on the right crown of the scalp. The lesion is indurated with fixation to the underlying structures. The tumor periphery is friable with hemorrhage.

Imaging Studies: CT scan with and without contrast: 19 x 100 x 20 mm ulcerated, enhancing mass involving the underlying right frontal and parietal bones.

Histopathology: A large ulcerative mass involving the left frontal and parietal scalp. There is a large area of underlying and adjacent dermal and subcutaneous tissue involving the left frontal and parietal calvarium.

Histopathology: Skin, ulcerating scalp: “Squamous cell carcinoma, moderately differentiated, 31mm in depth with perineural invasion and regression.” Skull, frontal right parietal: “Invasive squamous cell carcinoma, invading through full thickness of bone into the dura.”

Previous Treatments:

Family History/Social History: Brother with SCC and BCC

Medical/Surgical History:

Discussion:

The locally invasive potential of the two most commonly encountered skin cancers, basal cell carcinoma and squamous cell carcinoma, have been well described. Although the mechanisms regarding local invasion are proposed to be different, they can be equally as destructive and fatal.

Basal cell carcinoma (BCC), the most common cutaneous malignancy, accounting for up to 70% of all malignant diseases of the skin, often presents at an early stage that is amenable to diagnostic biopsy and subsequent treatment. However, if left to proliferate for an extended period of time, these tumors may become not only strikingly large but also difficult to treat. The particular subset of basal cell carcinoma histopathologically can often predict the aggressiveness of the tumor. An uncommonly described variant of BCC known as a sarcomatoid basal cell carcinoma (formerly carcinosarcoma in the literature) has a particular preponderance for invasion. The primary characteristics of this variant necessitate that the tumor displays both an epithelial and mesenchymal component and that both populations are malignant. A review of the literature identifies over 40 individual cases of this type of malignancy. Though there is variability among individual case reports, a meta-analysis performed on 42 cases did show that this type of tumor is an aggressive form of non-melanoma skin cancer (MMSC). Findings from this analysis additionally revealed that certain clinical characteristics predict worse prognosis for patients with sarcomatoid BCC, which include recent growth, large tumor size, regional lymph node metastasis, and longstanding pre-existing skin tumor.

Squamous cell carcinoma (SCC), the second most common form of skin cancer in Caucasians, has a known tendency not only for local invasion but also metastasis. These tumors have a known tendency for recurrences and metastasis based on features including but not limited to deep invasion, poor differentiation and perineural invasion. Clinical factors that correspond to an increase in mortality include lesion diameter of greater than or equal to 4 cm, histopathological evidence of perineural invasion, and deep invasion beyond subcutaneous structures. The presence of any one of these risk factors reduces the 3 year survival rate from 100% to 70%.

The purpose of this presentation is to further emphasize the importance of early discovery and intervention in commonly encountered skin cancers. While their locally invasive nature is well known to the field of dermatology, their true potential for destruction or ultimate fatality should not be underestimated.

References:


NEVUS LIPOMATOSUS CUTANEOUS SUPERFICIALIS

Heather Reagin DO,1 Joseph Susa DO2

1University of North Texas Health Science Center, Fort Worth, TX
2Cockerell Dermatopathology, Division of Dermatopathology, Dallas, TX

Introduction

Nevus lipomatosus cutaneous superficialis (NLCS) is a rare adipose tissue hamartoma. Two distinct subtypes have been reported. The solitary subtype is more common and presents as a single, pedunculated skin colored nodule.1 The classic subtype of NLCS is rare and characteristically occurs in a segmental or zosteriform distribution most commonly on the posterior surface of the trunk or thigh.2,3 We present a case of classic NLCS.

References


Discussion

Nevus lipomatosus cutaneous superficialis (NLCS) is a rare adipose tissue hamartoma. Two distinct subtypes have been reported including a solitary form and a classic form.2 The classic subtype is often in a segmental or zosteriform distribution and it is typically unilateral, as seen in our patient.2,3 It often presents at birth or within the first two decades of life.3,4 Clinically it appears as multiple asymptomatic, soft papules and nodules that coalesce into a plaque that may have a smooth or cerebriform surface.3,4 The classic subtype most commonly forms on the lower back, gluteal area or posterior thighs.3 The histologic differential diagnosis includes focal dermal hypoplasia (Goltz syndrome), a rare X-linked dominant disorder, which is invariably present from birth in affected females. While the histologic appearance on H&E can be identical, on special staining, the elastic fibers may be counterintuitively increased or thickened in NLCS. NLCS is benign and typically asymptomatic. However, patients may elect for treatment to optimize cosmesis. Surgical excision is a well recognized treatment approach but is invasive. CO2 laser has been reported to be successful in a localized lesion and may be more appealing to patients due to the less invasive nature of the procedure.6

Case Presentation

A 50-year-old Caucasian female presented with a complaint of a rash on her left leg. The lesion had been present for ten years and had never been previously treated. At the time of presentation, the patient reported it had recently grown in size. The patient was otherwise in good health. Physical examination revealed soft, fleshy papules and nodules coalescing into a 22 cm x 10 cm plaque with cerebriform appearance and various shades of yellow and pink. The lesion was in a segmental distribution on her posterior thigh and leg (Fig 1). Biopsy was obtained and sections demonstrated an admixture of mature adipose tissue lobules within the collagen of the reticular dermis (Fig. 2). A Verhoeff Van Gieson (VVG) stain demonstrated preserved elastic fibers in a normal pattern (Fig. 3). A diagnosis of nevus lipomatosus cutaneous superficialis was made. The pathology was reviewed with the patient. For cosmetic reasons, the patient was interested in treatment. She was referred to plastic surgery where she was offered full thickness skin grafting or excision with tissue expansion and primary closure. However, the patient elected to defer treatment and was lost to follow up.

Fig.1 Fleshy papules coalescing into 22cm x 10cm plaque on posterior thigh and leg.

Fig. 2 H&E demonstrating mature adipocytes in the dermis.

Fig. 3 VVG Elastin Stain
Artery Secondary to Systemic and Topical Absorption of Colloidal Silver Through Natural Mineral Supplementation

Veronica Rutt, DO, Josh Levin, MD, and Stephen M. Purcell, DO
Lehigh Valley Health Network, Allentown, Pennsylvania

Case Presentation:

Patient: 69 year-old Caucasian female.

History of Present Illness: The patient presents with a six year history of skin dysesthesia and complaint of a substances extruding through the skin. She was noted to have a distinct blue-gray discoloration of the skin on her face and hands. She is self-medicating with an over-the-counter silver supplement called “NutraSilver.” The patient has been ingesting the liquid supplement and putting it in her eyes, nose, and ears intermittently for two years. She uses approximately 2-10 drops orally per day.

Medical History/Surgical History: Hypertension, hyperlipidemia, chronic headaches, cholelithiasis, coronary artery disease with coronary artery bypass graft and angioplasty

Social History: Retired office receptionist, married with children, denies current use or history of tobacco, alcohol, or illicit substances

Medications: NutraSilver micro-particle silver water (contains 3600 PPM colloidal silver), amiodipine, propranolol/hydrochlorothiazide, atorvastatin, aspirin, amitriptyline, probiotic supplement

Physical Examination: Examination reveals slate-gray to blue discoloration of the skin most prominent on the forehead, cheeks, and nose with sparing of the periorbital and perinasal skin (Figure 1). The conjunctiva and oral mucosa appear discolored and lunulae have a faint blue hue (Figure 2). Her hair does not have a silver tinge.

Laboratory Data: BPAg 180, CBC, and CMP were all WNL or negative.


Discussion:

Argyria is a well-documented condition due to chronic exposure to products that contain silver. It is characterized by slate-gray or blue dyspigmentation of the skin, conjunctiva, lunulae, hair, and oral mucosa. The most pronounced discoloration occurs in photodistributed areas. The differential diagnosis for argyria is large and includes cyanosis, Addison disease, Wilson disease, hemochromatosis, and methemoglobinemia. Histopathologically, argyria is characterized by multiple dark brown-black granules deposited in a band-like fashion in the basement membrane of the sweat glands. The granules are also found in elastic fibers in the papillary dermis, connective tissue sheaths around pilosebaceous follicles, in the arrector pili muscles, and in arterial walls. There is usually an increase in melanin pigment in the basal layer and increased melanophages in the papillary dermis. Extracellular clusters of granules deposited between collagen fibers have been demonstrated on electron microscopy.

Historically, silver has been used in medicine to treat mental illness, infections, and epilepsy as far back as the eighth century. It is still used today as a cauterizing agent, and an antimicrobial in the treatment of burns. Today the most likely cause of argyria is through ingestion of dietary supplements. Although the Food and Drug Administration banned the use of colloidal silver and silver salts in over-the-counter products in 1999, this ban did not apply to products that are marketed as dietary supplements. The advent of the internet in combination with its accessibility and lack of regulation allowed silver to be marketed as an “alternative health” and cure-all for the treatment of cancer, Lyme disease, HIV, arthritis, and Morgellon disease.

It has been shown that at least six grams of silver ingested orally, or one gram of intravenous silver, is required to produce clinically apparent argyria. The mechanism by which the gray-blue cutaneous discoloration occurs is still up for debate. One theory suggests that it is the result of sunlight enhancing the direct stimulation of silver deposits on melanocytes to increase melanin production. Alternatively, some suggest sunlight acts as a catalyst for the reduction of silver within the dermis. Silver can also deposit into other organs such as the eyes, brain, spinal cord, stomach, liver, kidneys, adrenal glands, spleen, and testes. Adverse effects depend on the dose, duration, form, and route of exposure. Silver salts are more toxic than silver proteins and consumption of large doses can result in hemolysis, renal failure, pleural edema, seizures, and coma. Reports of physiologic derangement or organ damage are extremely rare in cases of tissue deposition. The discoloration of argyria may fade with time if ingestion is ceased, but rarely shows significant improvement. Chelation therapy with British anti-Lewisite (BAL) and D-penicillamine, intravenous therapy with sodium thiosulfate and potassium ferrocyanide, and topical therapy with hydroquinone and dermabrasion have all been tried with little to no success. Q-switched frequency doubled Nd-Yag laser has been shown to be successful in a case report. It is important to always recommend sun avoidance and sunscreens to prevent further pigmentary change.

References:

An Unusual Presentation of a Congenital Myofibroma: A Case Report

Pamela Sheridan, D.O.1 Sergey Arutyunyan, M.S.2

1. Broward Health Medical Center, Fort Lauderdale, FL.  2. Nova Southeastern University College of Osteopathic Medicine, Fort Lauderdale - Davie, FL.

INTRODUCTION

Infantile Myofibroma (IM) is a rare benign mesenchymal soft tissue tumor manifested by a solitary nodular lesion involving the skin, subcutaneous tissues, muscles, bone or viscera. These lesions are composed of contractile myofibroblastic cells arranged around thin-walled blood vessels and primarily occur in neonates or infants, with few reports of adult onset. IM presents as firm, flesh- or purple-colored solitary or multiple nodules that can be sporadic, congenital, or familial, with most lesions occurring in the head and neck region. Treatment is almost always successful with complete excision of the lesion. Although the prognosis for solitary IM lesions is excellent and recurrence is unusual, these tumors, when involving the viscera, are associated with poor prognosis and can even be fatal when involving the gastrointestinal or cardiorespiratory systems. It is important to consider together the clinical, histological and immunohistochemical features to make an accurate diagnosis and proceed with the proper treatment.

CASE DESCRIPTION

History of Present Illness: This is a 1 day old biracial (Asian/Caucasian) male who presented with a soft well-circumscribed flesh-colored left cheek mass with a prominent network of blood vessels at birth. On day 2, the lesion began to form a central area of necrosis. From Day 2 to 7, the central area of necrosis continued to enlarge and the mass became more firm. On Day 7, the mass was biopsied and because of the extensive necrosis, the lesion was completely excised.

Past Medical History: Mother, 32-year old, gravid 2, para 2 at 39 weeks gestation. Delivered via cesarean section and with an unremarkable pregnancy. Weight, 8 lb 10 oz and Appgar scores of 9 and 10 at 1 and 5 minutes respectively.

Family History: Noncontributory.

Physical Exam: A 3.0 x 3.0 cm solitary, firm, dome shaped, well circumscribed, flesh-pink-colored dermal/subcutaneous nodule on the left zygomatic arch with a rich network of blood vessels and a central area necrosis. No facial asymmetry or structural facial defects were appreciated and no other lesions of the skin or deeper tissues were noted.

Imaging: Brain MRI without contrast revealed a well circumscribed mass in the subcutaneous soft tissues of the left zygomatic region measuring 1.5 cm transverse x 2.4 cm anteroposteriorly x 2.0 cm craniocaudal. The mass was slightly heterogeneous but predominantly T1 and T2 hypointense. No feeding vessels leading to the mass were noted. The mass appeared to be separated from the left orbit, and no intracranial extensions of the mass were noted. A small cystic structure within the temporal horn of the left lateral ventricle was noted. Otherwise, the ventricular system was normal in size, shape and configuration. No intracranial mass lesions or midline shift were noted. The visualized major intracranial vessels appeared patent. No abnormality was seen in visualized portions of the orbits. The middle ear cavities, mastoid air cells and paranasal sinuses were clear.

Figure 1. Infantile Solitary Myofibroma (A) at the time of delivery, (B) at 2 days old, and (C) at 6 days old.

Tender to palpation and are red-brown in color

DISCUSSION

The purpose of this case report is to present a unique clinical vignette and progression of the solitary form of infantile myofibroma.

HISTOPATHOLOGY AND IMMUNOHISTOCHEMISTRY

Histopathology: Sections showed normal skin with an underlying dermal and subcutaneous lesion demonstrating a peripheral rim of viable tissue with a necrotic center. The viable cells had oval nuclei with small, non-prominent nuclei. They were associated with a rich network of vessels, some demonstrating a branching "hemangiopericytoma-like" pattern. Scattered mitotic figures were also noted.

Figure 2. (A) Hemangiopericytoma-like pattern in the dermis. (B) Viable tissue with necrotic center.

Immunohistochemistry: Cells stained positive for smooth muscle actin (SMA). CD31 staining highlighted the numerous vessels with their focal branching pattern.

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Vimentin</th>
<th>SMA</th>
<th>S-100</th>
<th>Desmin</th>
<th>CD34</th>
<th>Pan-cytokeratin</th>
<th>Ki-67</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

Table 1. Immunohistochemical Profile

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>FEATURES</th>
</tr>
</thead>
</table>
| Infantile Hemangiomata | • Most common tumor of infancy  
| | • Typically appear between 1 and 4 weeks  
| | • Benign vascular neoplasm |
| Infantile Fibrosarcoma | • Mesenchymal cell tumor that is composed of malignant fibroblasts in a collagen background  
| | • Presents in the first 2 years of life  
| | • Actin is variable, no specific markers |
| Rhabdomyosarcoma | • Most common soft tissue sarcoma in children  
| | • Arise from primitive muscle cells  
| | • Can present with spindled & leiomyomatous cell pattern  
| | • Desmin (+) |
| Leiomyoma | • Presents as smooth, firm papules or nodules < 2cm  
| | • Tense to palpation and are red-brown in color  
| | • Can develop anywhere smooth muscle is present  
| | • Desmin (+) |

Table 2. Differential

REFERENCES

A CHALLENGING CASE OF PYODERMA GANGRENOsum
Christine Sickles, DO; Gary Gross, MD; Daniel Hurd, DO.
Edward Via College of Osteopathic Medicine, Blacksburg, VA; LewisGale Medical Center, Salem, VA;

Introduction:
Pyoderma gangrenosum (PG) is an uncommon, ulcerative disease characterized by neutrophilic infiltrates on histology.1 Bruns et al first described PG as a purulent skin infection caused by microorganisms such as Streptococcus and Staphylococcus. Today, although the pathogenesis remains largely unknown, it is widely accepted that PG does not have an infectious etiology.2 PG typically affects women during the second to fifth decades of life and is seen in only 3-10 patients per million per year.3 Fifty percent of cases have an associated disease or condition which may emerge either before, during, or after PG is evident on the skin. The most common associations with PG are inflammatory bowel disease (Crohn’s disease, ulcerative colitis), arthritis (seronegative arthritis, rheumatoid arthritis), or lymphoproliferative diseases (acute and chronic myelogenous leukemia, myelodysplasia, monoclonal gammopathy).1, 3 Classically, PG appears as a rapidly enlarging, painful ulceration with irregular, undermined borders however, variants such as vesiculobullous, pustular, superficial granulomatous, and pyostomatitis vegetans exist.1, 3

Case Report:
A 63 year old Caucasian female presented to her primary care physician for evaluation of two new onset erythematous cutaneous plaques located on the bilateral dorsal hands. The lesions began as erythematous crusted papules, which progressed to nodules and plaques. An oral antibiotic was prescribed for a suspected infectious etiology and she was referred to wound care for further management. The wound care physician recommended a shave biopsy of one of the lesions. The pathology was read as a squamous cell carcinoma and she was referred to dermatology for a Mohs micrographic surgery. The surgery was performed on both areas and the defects were repaired with skin grafts. The patient returned for follow up visits because the skin grafts were not healing as expected. The lesions became erythematous, edematous, pustular and very painful. She completed multiple courses of oral antibiotics without improvement and was then admitted to the hospital for intravenous antibiotics. During her hospitalization, the diagnosis of pyoderma gangrenosum was suspected and she was started on oral prednisone. The lesions on her hands were noted to have rapid improvement, however, the patient did not receive a confirmed diagnosis of pyoderma gangrenosum. After being discharged, the patient continued to take prednisone and her condition was stable. She sought a second opinion at a tertiary medical center, where the diagnosis of pyoderma gangrenosum was confirmed. She was advised to follow up with a local dermatologist and primary care physician for further evaluation and management.

The patient was subsequently referred to a rheumatologist, where she was started on azathioprine 100 mg daily and prednisone 40 mg daily. She was worked up for underlying malignancies and inflammatory bowel disease. The results of this were unremarkable. The patient discontinued the azathioprine after two months of therapy due to side effects, but continued the prednisone. After six months of taking oral prednisone for control of her disease, the patient was advised to discontinue the medication without a taper. She became ill, experiencing anorexia, confusion and flaring of the PG on her hands. She started on lorazepam 0.5 mg twice daily for symptom control. She was then referred to psychiatry for evaluation of suspected lorazepam abuse. The patient follow up with a different local dermatologist where the diagnosis of vesiculobullous pyoderma gangrenosum was made. She is currently maintained on azathioprine 50 mg daily and prednisone 5 mg daily without clinical activity of PG.

Discussion
Pyoderma gangrenosum is a rare, neutrophilic dermatosis with an incidence of 3-10 cases per million each year. It is predominately seen in women who are in their second through fifth decade of life.4 Although PG can be idiopathic, a recent review found the most common PG association is inflammatory bowel disease (65.2%), followed by arthritis (16.1%), and lastly, hematologic disorders such as paraproteinemias and malignancies.5 The classic form of PG is ulcerative, but variants exist such as vegetative, crusted, and vesiculobullous.6 Trauma, or pathergy, evoke further lesional neutrophil recruitment and therefore, potentiate PG. Toklachyov et al found that 90% of patients with post-operative PG were initially treated with antibiotics and 73% of patients with PG underwent at least one surgical debridement.5 Mismanagement post-operatively is likely secondary to PG initially being diagnosed as necrotizing fasciitis, which leads to further morbidity and increases the length of time before an accurate diagnosis is elucidated.7 The patient presented in this case report was initially diagnosed with squamous cell carcinoma (SCC) secondary to a biopsy showing pseudopitheliomatous hyperplasia (PEH), which is a benign histological finding characterized by epithelial proliferation into the dermis. PEH can be seen secondary to trauma, ulceration, infection, and/or neoplasms of the skin and often is misdiagnosed as SCC.8, 9 However, PEH is differentiated from SCC by two main findings: the absence of nuclear atypia and mitoses, and positive immunohistochemical nuclear staining for Ki67 and ps3 in the basal epithelial layer only (versus positive staining throughout the full-thickness of the epithelium in SCC).10 PG is a diagnosis of exclusion and there are no pathognomonic histological findings, although skin biopsy should be performed to rule out other potential differentials. Differential diagnoses to exclude include: bacterial, parasitic or deep fungal infections, spirochetes, melanoma, pigmented spindle cell nevus of Reed, pemphigus vegetans, lichen sclerosis in the setting of severe scratching, granular cell tumors, necrotizing fasciitis, vasculitis, and other neutrophilic dermatoses.11 Su et al developed a list of criteria to diagnose PG including two major criteria of a rapidly progressive ulcer with irregular, undermined borders and exclusion of other ulcerative etiologies.10 Other minor criteria include: history of pathergy, associated systemic disease, histopathologic findings of dermal neutrophilia ± lymphocytic vasculitis, and rapid response to systemic steroid treatment.12, 13 Unfortunately due to the complicated nature and various underlying diseases, there is no gold standard treatment of PG. One treatment approach is wound management with moisture-retentive dressings showing superiority over drying gauzes in promoting collagen and vascular growth and facilitating natural debridement.14 Topical calcineurin inhibitors and corticosteroids have had success in individual cases and smaller case studies, but unfortunately, there is limited evidence at a large case study level.15 Prednisone is often used to quickly induce remission in patients with the classic variant of PG however, in some patients more time in necessary in response and therefore, steroid-sparing systemic agents are utilized such as: cyclosporine, methotrexate, and thalidomide.13 Biologics, particularly TNF-α blocking agents, have more recently been studied for their role in the treatment of PG. However, infliximab is the only biologic proven in a randomized, double-blind study to show efficacy over placebo (46% vs. 6%).14

Conclusion
Pyoderma gangrenosum is a challenging diagnosis to make due to limited knowledge regarding pathophysiology and histology, and its varying clinical presentation. Unfortunately, this uncertainty ultimately often leads to misdiagnosis and mismanagement causing significant morbidity and grief for patients.
INTRODUCTION
Linear and whorled nevoid hypermelanosis (LWNH) is a rare disorder of hyperpigmentation that typically presents within a few weeks of birth. It was first described as a distinct disease by Kalter in 1988. The pigmentation occurs along Blaschko’s lines with a streaky or swirl-like pattern and is not preceded by other skin lesions. It is also referred to as pigmented mosaicism. Approximately one quarter of patients may have associated extracutaneous findings, which can involve the CNS, musculoskeletal, ocular systems and rarely heart. Histology is non-specific which can involve the CNS, associated extracutaneous findings, and approximately 25% of patients have associated systemic manifestations.

ABSTRACT
Linear and whorled nevoid hypermelanosis is a rare entity characterized by whorls and linear hyperpigmented macules and patches along Blaschko’s lines. 45 cases have been described to date and approximately 25% of patients have associated extracutaneous findings. One quarter of patients may have associated systemic manifestations.

CASE SUMMARY
An 11-year-old male presented for evaluation of a “dark rash” present on his neck, trunk, and upper extremities within the first 2-3 years of life. The extent of hyperpigmentation increases during the first 2-3 years prior to stabilizing. Di Lernia (2007) in a retrospective case series of 16 unrelated children with LWNH reported that 10/16 cases were unilateral like ours. The unilateral cases did not have any associated abnormalities, while 1/6 of the bilateral cases had associated abnormalities. Clinical findings include reticulate hyperpigmented macules and patches that coalesce to form streaks and whorls along Blaschko lines. An S-shaped or whorled pattern presents over the anterior and lateral aspects of the trunk, a V-shaped pattern is noted over the spine and a linear arrangement over the extremities and genitalia. These patterns were also observed in our patient. Palmoplantar skin, mucosa and hair are typically spared. Most cases appear to be sporadic, due to mosaicism. Mosaic trisomy 7, 14, 18, 20 and X chromosomal mosaicism have been reported. However, familial cases have been described.

DISCUSSION
LWNH is a rare skin condition. 45 cases have been reported to date. Typically lesions present within a few weeks of birth. The extent of hyperpigmentation increases during the first 2-3 years prior to stabilizing. Di Lernia (2007) in a retrospective case series of 16 unrelated children with LWNH reported that 10/16 cases were unilateral like ours. The unilateral cases did not have any associated abnormalities, while 1/6 of the bilateral cases had associated abnormalities. Clinical findings include reticulate hyperpigmented macules and patches that coalesce to form streaks and whorls along Blaschko lines. An S-shaped or whorled pattern presents over the anterior and lateral aspects of the trunk, a V-shaped pattern is noted over the spine and a linear arrangement over the extremities and genitalia. These patterns were also observed in our patient. Palmoplantar skin, mucosa and hair are typically spared. Most cases appear to be sporadic, due to mosaicism. Mosaic trisomy 7, 14, 18, 20 and X chromosomal mosaicism have been reported. However, familial cases have been described.

REFERENCES
Introduction

Melanoma is the most common cancer in 25-29 year olds
Risk factors: sun exposure, >50 moles, atypical moles, family
and/or personal history, skin type, immunosuppression
90% of all recurrences occur during the first 5 years following
primary diagnosis, with greatest risk in the first 2 years
Metastatic melanoma (MM) has a 15-20% 5-year survival rate

Case Report

45-year-old female with past medical history of melanoma on
right triceps treated with Mohs, skin graft and one year
interferon therapy in 2005 presented with an enlarging right
upper quadrant cutaneous nodule that appeared one month
prior
Physical Exam: 5x5x2cm bullous, violaceous nodule
Imaging: CT scan of abdomen showed 5.8x6.2cm lesion with
well-defined and enhancing rims in skin and subcutaneous fat
of upper right abdominal wall, appearing to minimally
infiltrate underlying rectus abdominus musculature without
intrapertoneal communication (Figure A)
Surgical excision was performed and patient was discharged
with outpatient follow-up instructions, however returned ~3
months after surgical excision due to recurring, fast growing
mass (Figure B, Figure C)
Histopathology: Preliminary pathological findings were
consistent with invasive high grade undifferentiated
malignant neoplasm (Figure D)
Immunohistochemical (IHC) stains: (+) SOX-10, vimentin, EMa, Ki-67; (-) Mart1, HMB45, pancytokeratin, desmin, SMA,
CD31, CD34, CD33, ERG, tyrosinase
Given the clinical history, the morphologic and
immunophenotypic findings were found consistent with
malignant melanoma of metastatic origin
Further testing revealed positivity for BRAF VE1 and BRAF
V600E, further confirming the diagnosis

Discussion

Clinical presentation and histopathology of metastatic
melanoma vary and may make diagnosis difficult
A variety of IHC markers that help characterize metastatic
melanoma now exist: S100, SOX10, HMB-45, Melan A/Mart-
1, tyrosinase, Ki-67/Mib-1, MITF, Vimentin among others
SOX10 is a transcription factor involved in differentiation of
neural crest cells to melanocytes, and is suggested to be
superior in regards to sensitivity, specificity, staining intensity
and ease of interpretation compared to S100 and others

Conclusion

This case is a unique presentation of MM that appeared 10
years after the primary lesion was treated with Mohs and interferon
Although the lesion appeared vascular in nature, both clinically
and surgically, the positivity for the SOX-10 marker and the
clinical history helped hone the diagnosis of malignant
melanoma of metastatic origin

References

1) Vrotsos Alexis. Can SOX-10 or KBA.62 Replace S100 Protein in IHC Evaluation of SLN for MM?
3) Jennings and Kim. Identification of Nodal Metastases in Melanoma Using Sox-10. Am J
   Dermatopathol. 2011;33: 477-482.
5) Willis et al. SOX10: a useful marker for identifying MM in SLNs. Appl Immunohistochem Mol
6) Ordonez. Value of Melanocytic-Associated IHC Markers in the Diagnosis of Malignant
Patient Presentation and History

A 95 year old male presented to our clinic for follow up on a previously diagnosed with solitary Merkel Cell Carcinoma three years ago. His medical history includes diabetes mellitus type 2, GERD, glaucoma, hypothyroidism for which he takes appropriate medications. He also has a history of numerous non-melanoma skin cancers on the face and upper extremities in the past. The initial MCC was located on the patient’s forehead, and was treated with wide local excision. After the excision, patient was referred to Oncology for further surveillance. Follow up PET CT showed metastatic lesions in mediastinum, lungs, and colon. These were presumed to be metastatic MCC although a workup for a second primary tumor was completed. The patient then underwent treatment with radiation and etoposide with improvement in metastatic lesions. He was followed by Oncology with PET CT scans. He presented to our clinic with new nodular lesions as pictured in Figure 1 and Figure 2.

Histopathology

The histopathology of Merkel Cell Carcinoma is composed of scant cytoplasm and small round blue cells. The nuclei are atypical in appearance and tightly packed. The cells may form sheets or a trabecular array. These features are shown in Figure 3 and Figure 4. In addition, apoptotic cells, mitoses, and nuclear molding may also be seen. To differentiate among other tumors of small blue cells, special stains and immunostains can point to a diagnosis of MCC. CK20 is typically positive in MCC in a paranuclear pattern and will usually be negative in small cell lung carcinoma. In addition, MCC should also be considered in the differential of MCC, however it is usually S-100 positive and MCC is S-100 negative. Lymphoma will have positive hematopoietic markers, which are negative in MCC. Other markers of MCC include synaptophysin, chromogranin, and neuron-specific enolase.

Discussion

Merkel Cell Carcinoma (MCC) is a cutaneous neuroendocrine carcinoma, and has both epithelial and neuroendocrine differentiation. This aggressive tumor occurs most commonly on the head and neck of elderly patients in sun exposed areas. Concurrent overlying actinic keratosis or squamous cell carcinomas are frequently found on histopathology due to the occurrence chronic sun exposure areas. MCC can also occur less frequently on the extremities or trunk. MCC presents as an asymptomatic solitary nodule, which is rapidly growing.

MCC is usually a pink, blue, or red cutaneous or subcutaneous nodule. Regional lymphadenopathy may be present. MCC is more common in immunosuppressed patients and erythema ab igne sites, and may also associated with sun exposure and polyoma virus. Recurrence and metastatic rates of MCC are high despite treatment and has a 30-50% mortality rate at 2 years. The mnemonic "AEIOU" may be helpful in remembering the characteristic features of MCC.

Recently it is reported in the literature that 20% of MCCs are not caused by MCPyV (polyoma virus), and virus-negative MCC represent a more aggressive subtype which warrants a closer clinical follow-up after initial treatment. There are also new treatments emerging for MCC. Immune checkpoint blockade with anti-programmed death receptor 1 (PD-1) antibody for treatment of a patient with metastatic MCC (pembrolizumab) after the disease had progressed during therapy with oral etoposide.

References


Intervally Collected Granular Safety Data Throughout Treatment with Polypodium leucotomos Extract for 56 days in 40 Adult Patients

Richard R Winkelmann, DO*, David E Cohen, MD, PhD**, Brian Berman, MD, PhD ***, Mark S Nestor, MD, PhD****

*OhioHealth Dermatology Resident Physician; ** Professor of Dermatology, New York University School of Medicine; *** Professor Emeritus of Dermatology, University of Miami Miller School of Medicine and Co-Director, Center for Clinical and Cosmetic Research; **** Voluntary Associate Professor of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine and Director, Center for Clinical and Cosmetic Research.

**Polypodium leucotomos** (PLE) is a fern native to Central and South America that is widely available today as an extract (PLE) with versatile photoprotective and antioxidant properties. Historically, PLE has been studied for its use in treating psoriasis, atopic dermatitis, vitiligo, melanoma, and polymorphic light eruption. Basic science studies have demonstrated the antioxidant, immunomodulatory, antimutagenic, and photoprotective effects of PLE but a knowledge gap regarding its safety profile is evident without prospective trials assessing its clinical and/or serological adverse events in human subjects over time.

A 2015 retrospective review outlined 19 human and 6 basic science studies in which oral PLE was administered at 120-1080 mg daily doses. No adverse effects were reported from laboratory studies. In humans, mild-moderate side effects including gastrointestinal complaints and pruritus were found in a small composite number of patients (16/1016 [2%]). Overall, authors determined PLE was well tolerated and associated with a negligible risk of side effects. Recent Ames, murine, and clinical studies provide further evidence supporting the lack of treatment related adverse outcomes from PLE administration.

A previously published randomized trial evaluating the photoprotective effects of PLE alluded to the clinical safety profile observed during the study. The purpose of this article is to further expand upon granular safety data collected during the trial in which patients treated with PLE were monitored intervallically for serological and clinical adverse events.

**Methods**

40 healthy adult men and women between the ages of 18 and 65 years old with Fitzpatrick skin types I-IV were enrolled in the randomized prospective study. Subjects were excluded if they had an identified medical condition or were on a medication known to interfere with the primary objective of the study. Participants agreed to forego any skin procedures or treatments and women of childbearing potential used an effective form of birth control throughout the duration of treatment. Forty patients qualified and were randomized to receive 240 mg capsules of PLE twice daily (480 mg daily) for 56 days and were compared to placebo (n=20) twice daily for two months.

Vital signs, hematometry, comprehensive metabolic panel, partial thromboplastin time (PTT), and prothrombin time (PT) were analyzed every 2 weeks. Baseline and days 14, 28, and 56 of the trial. Statistical significance (defined as p<0.05) was measured using repeated measures NOVA methods for analyzing group difference of study outcomes over time. Additional subset analysis was performed in clusters grouped by age, gender, and skin type.

**Clinical Adverse Events**

Patient #4-Control described one episode of sunburn. Two patients (Patient #10-Active and Patient #12-Control) reported symptoms of fatigue. Patient #28-Active and Patient #41-Active recounted mild GI discomfort/bloating symptoms. Patient #43-Active reported one episode of transient headache.

**Vital Signs**

Non-statistically significant weight change of 29 pounds from baseline was noticiable in three patients. Patient #7-Active and Patient #24-Active reported a weight gain of 10 pounds and weight loss of 9 pounds, respectively. Patient #5-Control lost a total of 51 pounds over the 56-day period.

**Hematologic Studies**

White blood cell (WBC) counts (normal: 4,500-10,000 WBCs/ml) from Patient #1-Control were elevated at baseline (12,000 WBCs/ml), normalized to 5,600 WBCs/ml on day 14, fell below the normal reference range to 2,400 WBCs/ml on day 28, and subsequently normalized again to 6,100 WBCs/ml at day 56. Patient #25-Active had transiently elevated WBC counts of 11,600 WBCs/ml on day 14 which increased from a baseline of 7,000 WBCs/ml.

This abnormal WBC level in Patient #25-Active was not statistically significant and was not considered to be associated with treatment. All other reported abnormal laboratory values were in hematologic, PT, and INR parameters were not associated with clinical symptoms and were considered to be unrelated to PLE administration.

We report that PLE demonstrated a favorable safety profile in the doses studied for 20 adult treatment group subjects throughout 56 days of daily 480 mg PLE therapy. Most non-statistically significant differences in clinical laboratory parameters observed between test and control subjects were marginal in comparison to historical control ranges and were not considered to be associated with the treatment. Statistical analysis of granular serological data collected throughout the trial provides additional support for claims that PLE has a negligible risk of side effects. More studies may be required to better understand if there are any potential long-term clinical and serological effects of PLE therapy.

**Metabolic Studies**

Two patients in the PLE experimental arm began the study with elevated liver enzymes prior to PLE therapy. Patient #8-Active had AST and ALT levels of 45 U/L and 67 U/L at baseline that fell to 18 U/L and 23 U/L, respectively, by the end of the study on day 56. Patient #24-Active had AST and ALT levels of 46 U/L and 73 U/L at baseline, respectively, normalizing to 16 U/L and 11 U/L by day 56.

Patient #13-Active had the highest overall baseline weight (257 pounds) in the treatment group. Patient #13-Active began with normal liver enzymes on baseline and ALT on day 14, and day 28 which became elevated on day 56. Baseline levels of AST and ALT in Patient #13-Active were 21 U/L and 20 U/L, respectively, completing the study with markedly elevated levels of 45 U/L and 54 U/L on day 56 despite values within normal limits on days 14 and 28. Patient #39-Control had abnormal liver enzymes as well and had the highest baseline weight of control group patients (255 pounds at baseline). Patient #39-Control’s liver enzymes increased from 23 U/L and 25 U/L at baseline, 21 U/L and 27 U/L on day 14, 52 U/L and 83 U/L at day 28, to 94 U/L and 90 U/L on day 56 for AST and ALT, respectively.

**Conclusions**

Over the course of the trial, no statistically significant variance in laboratory values was evident in serological studies commonly used by dermatologists to monitor for drug adverse events from test and control groups (all p>0.05). Additional subset analysis by age, gender, and skin type did not reveal statistically significant variance among groups over 56 days of PLE therapy (all p>0.05). Clinical side effects in the treatment group were mild, transient, and limited to bloating (n=2), headaches (n=1), and fatigue (n=1), all of which resolved by the end of the trial. No subjects withdrew from the study due to serious adverse events.

Mildly abnormal liver enzyme laboratory values were observed in one patient from the PLE treatment group and one study control subject and were not considered to be associated with treatment. All other reported abnormal laboratory values in hematologic, PT, and INR parameters were not associated with clinical symptoms and were considered to be unrelated to PLE administration.

**References**


Introduction

The first case of granuloma annulare (GA) was described by Calcott in 1895.2 Today, the cause of this dermal inflammatory process is still not well understood.3

GA has been associated with some medications, trauma, diabetes mellitus, thyroid diseases, tuberculosis, borreliosis, and malignancies. It is also believed that there is some association between GA and some infectious agents, e.g., hepatitis C virus, human immunodeficiency virus, and Epstein-Barr virus.1,4

It exists in several forms. Localized GA is the most common, it presents on the distal extremity as an erythematous, non-scaly, annular plaque. Generalized GA, which makes up less than 25% of total cases presents as scattered erythematous papules and plaques on the trunk and extremities.1,5 While localized GA is typically self-limiting and more of a cosmetic concern, generalized GA rarely resolves spontaneously and can be recalcitrant to treatment.6 Though more than 30 treatments have been described in the literature no well-established treatment protocols exist.7,8 This article will focus on the use of adalimumab as a successful treatment option for generalized GA.

Cutaneous examination revealed a Fitzpatrick type 3 patient with scattered erythematous to violaceous annular plaques and papules on her bilateral lower legs. There was no overlying scale or ulceration and the remainder of the skin exam was unremarkable. It was noted that she had a generalized granuloma annulare and agreed to a confirmatory punch biopsy. This revealed necrobiotic centers of granulation tissue with a granulomatous infiltrate.

Because GA can often present as well defined annular papules or plaques on arms, legs, hands, or feet.1,2 Subtypes exist including subcutaneous, perforating, and patch. Localized GA typically presents as well defined annular plaques or plaques on arms, legs, hands, or feet.1,2,5,6 Though more than 30 treatments have been described in the literature, no well-established treatment protocols exist.7,8 This article will focus on the use of adalimumab as a successful treatment option for generalized GA.

Case Report

A 45 year old female presented to the office with a 9 month history of erythematous to violaceous annular plaques and papules on her bilateral lower legs. There was no overlying scale or ulceration and the remainder of the skin exam was unremarkable. It was noted that she had a generalized granuloma annulare and agreed to a confirmatory punch biopsy. This revealed necrobiotic centers of granulation tissue with a granulomatous infiltrate.

There have been numerous treatments for generalized granuloma annulare all with varying limited success. This case supports the recent article of 7 patients who had similarly impressive clearance with adalimumab in GA.4 Our case further illustrates successful re-challenging of adalimumab after disease recurrence.

Granuloma annulare can exist in many forms but is most commonly a self-limited, benign cutaneous disease that classically presents as annular plaques located on the extremities of young people.6 While benign, these lesions can cause significant cosmetic distress to the patient and cause social withdrawal. The cause of GA is unknown but insect bite reactions, sun exposure, trauma, tuberculin skin testing, PUVA therapy, and viral infections have all been proposed as the initiating factor.4 Localized GA is the most common form followed by generalized but other subtypes exist including subcutaneous, perforating, and path. Localized GA typically presents as well defined annular plaques or plaques on arms, legs, hands, or feet.1,2,5,6 Though more than 30 treatments have been described in the literature, no well-established treatment protocols exist.7,8 This article will focus on the use of adalimumab as a successful treatment option for generalized GA.

There have been numerous treatments for generalized granuloma annulare all with varying limited success. This case supports the recent article of 7 patients who had similarly impressive clearance with adalimumab in GA.4 Our case further illustrates successful re-challenging of adalimumab after disease recurrence.

Granuloma annulare can exist in many forms but is most commonly a self-limited, benign cutaneous disease that classically presents as annular plaques located on the extremities of young people.6 While benign, these lesions can cause significant cosmetic distress to the patient and cause social withdrawal. The cause of GA is unknown but insect bite reactions, sun exposure, trauma, tuberculin skin testing, PUVA therapy, and viral infections have all been proposed as the initiating factor.4 Localized GA is the most common form followed by generalized but other subtypes exist including subcutaneous, perforating, and path. Localized GA typically presents as well defined annular plaques or plaques on arms, legs, hands, or feet.1,2,5,6 Though more than 30 treatments have been described in the literature, no well-established treatment protocols exist.7,8 This article will focus on the use of adalimumab as a successful treatment option for generalized GA.

Clinical Photographs

Figures 1 and 2: Clinical photographs taken on initial presentation

Discussion

There have been numerous treatments for generalized granuloma annulare all with varying limited success. This case supports the recent article of 7 patients who had similarly impressive clearance with adalimumab in GA.4 Our case further illustrates successful re-challenging of adalimumab after disease recurrence.

Granuloma annulare can exist in many forms but is most commonly a self-limited, benign cutaneous disease that classically presents as annular plaques located on the extremities of young people.6 While benign, these lesions can cause significant cosmetic distress to the patient and cause social withdrawal. The cause of GA is unknown but insect bite reactions, sun exposure, trauma, tuberculin skin testing, PUVA therapy, and viral infections have all been proposed as the initiating factor.4 Localized GA is the most common form followed by generalized but other subtypes exist including subcutaneous, perforating, and path. Localized GA typically presents as well defined annular plaques or plaques on arms, legs, hands, or feet.1,2,5,6 Though more than 30 treatments have been described in the literature, no well-established treatment protocols exist.7,8 This article will focus on the use of adalimumab as a successful treatment option for generalized GA.

Conclusion

Treatment of GA with adalimumab has been reported several times in the literature,9,10,11 the importance of this case study is showing its tremendous efficacy when treating the patient after complete cessation of the medication. Further studies are needed to elucidate effective treatment protocols including dosing and length of taper. If further studies continue to show similar dramatic resolution of GA, we suspect that adalimumab will rapidly rise towards first line therapy of generalized GA. Practically, cost and insurance will be large barriers towards faster adoption. Although a benign condition, it can have devastating psychosocial and cosmetic effects on patients and for this reason treatment options need further exploration.

Bibliography

Upcoming Meetings:

2017 AOCD Fall Meeting
Intercontinental New Orleans
New Orleans, LA
October 25 - October 28, 2017

2018 AOCD Spring Meeting
Hilton
West Palm Beach, FL
March 21 - March 24, 2018

2018 AOCD Fall Meeting
Westin San Diego - Gaslamp Quarter
San Diego, CA
October 9 - October 13, 2018