HIV and the Skin

Charles A. Gropper, M.D.
Chief of Dermatology
St. Barnabas Hospital, Bronx, NY
Arthur Ave
Kasich Tastes New York Values on Arthur Avenue in the Bronx

By Jillian Jorgensen • 04/07/16 2:51pm
New York Botanical Garden
Bronx Zoo
Yankee stadium

http://modmyi.com/images/Messany/yankee-stadium.jpg
Wave Hill
Invasion
History of HIV

• July 1981
  – 26 initial cases of young men with unusual presentation of dermatologic findings reported by NYU
    • KS: not classical type
    • Oral Candidiasis
    • Chronic HSV
  – Now more likely to present with other STD such as syphilis
HIV Facts and Figures

- More than 60 million people infected with HIV and more than half have died since epidemic began
Number of people living with HIV and accessing treatment globally

<table>
<thead>
<tr>
<th>Year</th>
<th>People living with HIV</th>
<th>People receiving treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>28.9 million</td>
<td>770,000</td>
</tr>
<tr>
<td>2005</td>
<td>31.8 million</td>
<td>2.2 million</td>
</tr>
<tr>
<td>2010</td>
<td>33.3 million</td>
<td>7.5 million</td>
</tr>
<tr>
<td>2011</td>
<td>33.9 million</td>
<td>9.1 million</td>
</tr>
<tr>
<td>2012</td>
<td>34.5 million</td>
<td>11 million</td>
</tr>
<tr>
<td>2013</td>
<td>35.2 million</td>
<td>13 million</td>
</tr>
<tr>
<td>2014</td>
<td>35.9 million</td>
<td>15 million</td>
</tr>
<tr>
<td>2015</td>
<td>36.7 million</td>
<td>17 million</td>
</tr>
</tbody>
</table>

Source: UNAIDS 2016

AVERT.org
People living with HIV (all ages)

Source: UNAIDS Estimates 2016
AIDS-related deaths (all ages)
HIV Facts and Figures

• Annual number of new HIV infections has remained stable

• New infections remain high: Estimated 56,300 Americans get infected each year

• More than 18000 people with HIV die each year in the US

HIV: Still a Problem

GLOBAL
- Living with HIV $37 \times 10^6$
- Incidence: $2 \times 10^6$
- Cumulative AIDS mortality $36 \times 10^6$
- Once diagnosed only 43% engage in care

USA
- Living with HIV $1.2 \times 10^6$
- Incidence 50,000
- Cumulative AIDS mortality 658,000
- Once diagnosed only 40% engage in care

http://www.cdc.gov/hiv/statistics/overview/ataglance.html
Federal health officials are reporting a sharp increase in unprotected sex among gay American men, a development that makes it harder to fight the AIDS epidemic.

The same trend has recently been documented among gay men in Canada, Britain, the Netherlands, France and Australia, heightening concerns among public health officials worldwide.

According to the Centers for Disease Control and Prevention, the number of men who told federal health investigators that they had had unprotected anal sex in the last year rose nearly 20 percent from 2005 to 2011. In the 2011 survey, unprotected sex was more than twice as common among men who said they did not know whether they were infected with H.I.V.

Being tested even once for H.I.V. is associated with men taking fewer risks, whether the test is positive or negative,

- 20% Rise in Unprotected Sex from 2005-2011
- People are “sero-sorting”
- Better treatment and bad economy lead to risky behavior
- New infections still about 50,000/year
- Government goal to decrease to 30,000/year
Travel and STDs

- 5-50% short-term travelers engage in casual sex
- At least half do not practice safe sex (e.g. condom)
- Problem accentuated in travelers 18-30 years old
cART should be initiated among all adults with HIV regardless of WHO clinical stage and at any CD4 cell count.

cART should be initiated in all pregnant and breastfeeding women living with HIV regardless of WHO clinical stage and at any CD4 cell count and continued lifelong.

cART should be initiated among all infants, children and adolescents living with HIV regardless of WHO clinical stage and at any CD4 cell count.
On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection

Jean-Michel Molina, M.D., Catherine Capitant, M.D., Bruno Spire, M.D., Gilles Pialoux, M.D., Laurent Cotte, M.D., Isabelle Charreau, M.D., Cécile Tremblay, M.D., Jean-Marie Le Gall, Ph.D., Eric Cua, M.D., Armelle Pasquet, M.D., François Raffi, M.D., Claire Pintado, M.D., Christian Chiodo, M.D., Julie Chas, M.D., Pierre Charbonneau, M.D., Constance Delaugerre, Pharm.D., Ph.D., Marie Suzan-Monti, Ph.D., Benoît Loze, B.S., Julien Fonsart, Pharm.D., Gilles Peytavin, Pharm.D., Antoine Cheret, M.D., Ph.D., Julie Timsit, M.D., Gabriel Girard, Ph.D., Nicolas Lorente, Ph.D., Marie Préau, Ph.D., James F. Rooney, M.D., Mark A. Wainberg, Ph.D., David Thompson, B.C.L., LL.B., Willy Rozenbaum, M.D., Veronique Doré, Ph.D., Lucie Marchand, B.S., Marie-Christine Simon, B.S., Nicolas Etien, B.S., Jean-Pierre Aboulker, M.D., Laurence Meyer, M.D., Ph.D., and Jean-François Delafraissey, M.D. for the ANRS IPERGAY Study Group


Abstract - Article - References - Citing Articles (1)


Tenofovir disoproxil fumarate and emtricitabine
Pre-exposure Prophylaxis

- Used in those with “high risk” of HIV
- Typical is to take preventative drugs DAILY
- Study: 400 gay/bisexual men divided into those who took medication 2-24 hours before and 24 & 48 hours after unprotected sex versus placebo at same interval
- Nine months: use “on demand” PrEP reduced HIV acquisition by 86%
- Side effect: GI upset (14% vrs placebo 5%)
- Message: persons at high risk of HIV can take PrEP on an on-demand basis, and still be relatively protected

Vaginal Ring ART Effective Prophylaxis!

- Monthly use of vaginal ring vrs PBO
- Contains ART 25mg dapivirine
  - NNRTI
- ASPIRE trial: 2629 women, age 18-45, Malawi, Uganda, Zimbabwe, and South Africa; half used, half did not
- Regular use decreased HIV 50-75%

N Engl J Med 2016;Feb 22 e-pub
PLoS One 2016; March 10;11(3): 014773
HIV Transmission: Variable Laws

- **California** – Felony punishable by up to 8 years in prison

- **Missouri** – Class B felony to expose a person to HIV. If complainant becomes infected, the charge is a class A felony. The use of a condom is not a defense

- **New York** – Reckless endangerment in the first degree for engaging in conduct which creates a grave risk of death to another person

- **Texas** – Aggravated assault laws whereby a person “intentionally, knowingly, or recklessly… uses or exhibits a deadly weapon as part of an assault”. Saliva of an HIV infected person is considered a deadly weapon
HIV Discrimination

Most recent data as of 2015

- 60.6+%
- 49.3 - 60.6%
- 28 - 49.3%
- < 28%
## Primary vs Secondary HIV Skin Conditions

### Table 1 Classification of HIV-1-related skin pathology

<table>
<thead>
<tr>
<th>Primary Manifestations</th>
<th>Infectious</th>
<th>Secondary Manifestations</th>
<th>Neoplastic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Herpes simplex</td>
<td>Kaposi's sarcoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Varicella-Zoster</td>
<td>T cell lymphoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HPV infection</td>
<td>Basal cell carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Molluscum contagiosum</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. Aureus infections</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Folliculitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Bullous impetigo</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Ecthyma</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mycobacterial cutaneous</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bacillary angiomatosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>P. Aeruginosa cutaneous</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Candidiasis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dermatophyte infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Histoplasmosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Criptococosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pneumocystis</td>
<td></td>
</tr>
</tbody>
</table>

HIV AND THE SKIN

• Prevalence of cutaneous abnormalities approaches 100% in patients with HIV

• Some cutaneous conditions are unique and pathognomonic for HIV
  – Example: Kaposi’s Sarcoma

• Skin findings may be marker of disease stage
  – Example: EPF usually occurs in pts with T Cell Count <200
HIV and the Skin

KEY POINT:

DERMATOLOGISTS SHOULD STILL CONSIDER HIV INFECTION IN PATIENTS PRESENTING WITH BOTH COMMON AND RARE SKIN ABNORMALITIES
<table>
<thead>
<tr>
<th>Table 1</th>
<th>Skin conditions frequently observed in HIV-infected patients</th>
</tr>
</thead>
</table>

**AIDS-defining mucocutaneous conditions**
- Ulcerating herpes simplex virus infection (duration > 1 month)
- Kaposi’s sarcoma
- Cryptococcosis of the skin (usually in the context of disseminated infection)
- Histoplasmosis of the skin (usually in the context of disseminated infection)

**Non-AIDS-defining mucocutaneous conditions indicative for HIV-1-associated immunodeficiency**
- Oral candidiasis
- Herpes zoster infection exceeding one dermatome or generalized
Oral hairy leukoplakia
Bacillary angiomatosis
Mollusca contagiosa—extensive or large lesions in adults
Eosinophilic folliculitis
Papular pruritic eruptions
Other mucocutaneous conditions frequently found in HIV-infected patients
Seborrheic dermatitis
Xerosis cutis
Proximal subungual onychomycosis
Crusted scabies
Anal intraepithelial neoplasia
### Correlation of CD4 Count with HIV-Associated Dermatologic Disorders

<table>
<thead>
<tr>
<th>&gt;500 CD4+ cells/mm³</th>
<th>&lt;500 CD4+ cells/mm³</th>
<th>&lt;250 CD4+ cells/mm³</th>
<th>&lt;50 CD4+ cells/mm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Acute retroviral syndrome</td>
<td>• Oropharyngeal candidiasis (Thrush)</td>
<td>• Eosinophilic folliculitis</td>
<td>• Large, non-healing mucocutaneous HSV</td>
</tr>
<tr>
<td>• Oral hairy leukoplakia</td>
<td>• Herpes Zoster</td>
<td>• Seborrheic dermatitis, refractory</td>
<td>• Papular pruritic eruption</td>
</tr>
<tr>
<td>• Vaginal candidiasis</td>
<td>• Psoriasis, severe or refractory</td>
<td>• Mollusca, extensive</td>
<td>• Giant mollusca</td>
</tr>
<tr>
<td>• Seborrheic dermatitis</td>
<td>• Eruptive atypical melanocytic nevi and melanoma</td>
<td>• Bacillary angiomatosis</td>
<td>• Perianal ulcers 2/2 CMV</td>
</tr>
<tr>
<td></td>
<td>• Kaposi’s sarcoma</td>
<td>• Miliary/extrapulm TB</td>
<td>• Aspergillosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• HSV, diss.</td>
<td>• Acquired ichthyosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cryptococcosis, diss.</td>
<td>• MAC infections</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Histoplasmosis, diss.</td>
<td>• Major aphthae</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Coccidioidomycosis, diss.</td>
<td></td>
</tr>
</tbody>
</table>
CATEGORIES OF SKIN PROBLEMS IN HIV

- INFECTIOUS
- INFLAMMATORY
- NEOPLASTIC
Viral Infections with HIV

- Acute HIV Morbilliform Rash
- Herpes Simplex
- Syphilis
- Varicella/Zoster
- HPV
- Oral Hairy Leukoplakia
INFECTIOUS

- HERPES SIMPLEX VIRUS
  - CDC Defined Index Infection in making AIDS.
  - Dx
  - Clinical findings similar to non HIV patients if immune system relatively intact
  - Once immunosuppressed, HIV patients often develop chronic painful ulcer
    - Perianal, perioral, periungual
Treatment of HSV in HIV patients

- Acyclovir, Famciclovir, Valacyclovir
- Acyclovir-Resistant HSV Infection
  - Thymidine-kinase-negative, acyclovir resistant HSV-2
  - IV: foscarnet and cidofovir
  - Topical: trifluridine, cidofovir, and imiquimod
HSV in HIV
Syphilis

Concurrent Primary + Secondary Lues = HIV+

Clin Infect Dis. 2015;61:281-7

Courtesy Ted Rosen, MD
HZV in HIV

• Herpes Zoster often precedes thrush and oral hairy leukoplakia
  – May be early sign of HIV
  – Duration, pain and amount of scarring may be more severe in HIV patients
  – Recurrences in up to 25%
  – Dissemination with widespread ulcers or hyperkeratotic, verrucuous lesions may occur
Disseminated HZV
HPV

• HPV infection more common in immunocompromised patients
• Cervical dysplasia is common in HIV infected women
• Increased risk of anal warts and anal carcinoma in homosexual men
HPV

http://bayloraids.org/atlas/images/22.jpg
Anal HPV
Acute HIV Exanthem and Enanthem

- Maculopapular rash which sometimes resembles P. rosea
- Upper trunk, proximal limbs, palms, and soles
- Oral erythema or erosions may be present
- Usually resolves in 1-2 weeks
- Patients may seronegative and most infectious at time of rash
HIV Acute Rash

http://depts.washington.edu/hivaids/images/arvae/arvae_c1_q01.gif
ORAL HAIRY LEUKOPLAKIA

• Develops in about 25% of infected individuals
• Predictor of rapid decline and AIDS progression
• White plaques with hair-like progressions
• No malignant potential
• May regress with antiretrovirals therapy
Oral Hairy Leukoplakia

http://www.lib.uiowa.edu/hardin/md/pictures22/cdc/6061_lores.jpg
Molluscum Contagiosum

Extragenital molluscum contagiosum occurs almost exclusively in HIV-infected or immunocompromised patients.

The following infections resemble molluscum-like lesions:
- Coccidioidomycosis
- Cryptococcus
- Histoplasmosis
- Aspergillosis
Deep Fungal Infections

- **Cryptococcus**
  - Presents with meningitis
  - May present as molluscum like lesions on the face and neck
Deep Fungal Infections

• Histoplasmosis
  – May represent reactivation of previous infection
  – Cases seen in NYC mostly in patients who lived previously in an endemic area
  – Variable skin lesions: pustules, acneform, ulcerations and plaques
  – May be fatal syndrome with sepsis, DIC, and pulmonary, CNS and renal failure
HISTOPLASMOSIS

Mucocutaneous histoplasmosis in HIV with an atypical ecthyma like presentation
Vandana Mehta, Abhishek De, C Balachandran, Puja Monga
Dermatology Online Journal 15 (4): 10
A 55-year-old white woman presented to the emergency department reporting a rash of 5 weeks' duration, severe fatigue, and a fever.

A rapid HIV test was positive with an absolute CD4+ count of 3 cells/µL.

Histoplasmosis, the most common endemic mycosis in AIDS patients, is caused by the dimorphic fungus *H. capsulatum*, a primary pathogen that can cause opportunistic infections in immunocompromised hosts.

In the United States, it is prevalent in the Mississippi and Ohio River valleys. Worldwide it is endemic in areas of Mexico, Central and South America, Africa, and Asia.

Histoplasma antigen detection
- Performed on samples of urine, serum, cerebrospinal fluid, bronchoalveolar lavage fluid.
- Most sensitive method of diagnosing disseminated disease.
Disseminated cutaneous histoplasmosis in newly diagnosed HIV
Deep Fungal Infections

• Sporotrichosis
  – Asymptomatic pulmonary infection that spreads to the skin
  – Widespread ulcers and SQ nodules
Sporotrichosis in HIV

http://medicalimages.allrefer.com/large/sporotrichosis-on-the-forearm.jpg
Deep Fungal Infections

- Aspergillus
  - May be primary or secondary
  - Primary from local skin injury
  - Red plaques with pustules and ulcers or molluscum like lesions
  - Treatment with amphotericin B or itraconazole
Aspergillus
INFECTIOUS

• BACILLARY ANGIOMATOSIS
  – Bartonella henselae or B. quintana
  – Differential Dx: Kaposi’s Sarcoma
Bacillary Angiomatosis

http://www.scielo.cl/fbpe/img/rci/v24n2/img12-01.jpg
BACILLARY ANGIOMATOSIS

http://www.skincareguide.com/images/glossary/bacillary_angiomatosis.jpg
Onychomycosis in HIV

• 4 Types of Onychomycosis
  – Distal and Lateral Superficial (DLSO)
    • T rubrum and T mentagrophytes most common
  – Proximal Subungual (PSO)
    • Marker of HIV
  – Superficial White (SWO)
    • T mentagrophytes
  – Total Dystrophic (TDO)
Proximal Subungual Onychomycosis
INFLAMMATORY

- Xerosis/Ichthyosis
- Seborrheic dermatitis
- Psoriasis
- Reiter’s Syndrome
- Papular Pruritic Eruption of AIDS
- Eosinophilic Folliculitis
- Erythema Elevatum Diutinum
- Photosensitivity
XEROSIS AND ICHTHYOSIS

• Xerosis most prominent on lower legs
• HIV pts often have refractory pruritus
• Similar to astageotatic eczema seen in elderly
• Worse in patients with atopic diathesis
• Acquired ichthyosis is seen in advanced HIV (CD4+ <50)
• Treatment with moisturizers and topical steroids
  – Often unsatisfactory
SEBORRHEIC DERMATITIS

- Affects ~5% of Non-HIV population
- Most common skin disorder to affect HIV pts, up to 85% incidence
- Usually affects the scalp and central face
- With HIV, can be widespread or inverse
- If exaggerated, sudden onset, or acute worsening, consider HIV infection
PSORIASIS and HIV

- Overall incidence **not** increased with HIV
- Similar clinical features with or without HIV
- With HIV, may have increased intertriginous involvement and more dramatic presentation
- Significant nail dystrophy and arthritis may be seen
- Not uncommon to develop psoriatic erythroderma
- Worsens with declining immune status

http://www.dominapharm.com/Images/Psoriasis%20pictures/Inverse_psoriasis.jpg
REITER’S SYNDROME

• All pts with newly diagnosed Reiter’s should have HIV testing
• Commonly occurs in HIV pts with HLA-B27 after GU or GI infection
• Palms and soles develop pustules and form keratotic papules.
  – coalesce until soles are thickened and scaled = keratoderma blennorrhagicum
• Nails, groin & axilla, and oral (erosions, geographic tongue) & genital (circinate balanitis) regions often affected
• Histo is identical to psoriasis and same Tx for both diseases
PAPULAR PRURITIC ERUPTION (PPE)

- Marked pruritus
- Symmetrical, non-follicular papules, with secondary changes
- May be secondary to peripheral eosinophilia, hyperreactive mast cells, or neural irritation from direct HIV infection
- May be on spectrum which includes eosinophilic folliculitis or response to arthropod Ag’s

http://www.rihes.cmu.ac.th/Ped_HIV/06-cli_present/s2_02/01-PPE.jpg
Patient with itchy Rash

• 40 YO Hispanic Man with 2 week h/o itchy bumps on his face, chest, back
• PMH: HIV/AIDS: CD4 31
• Recent stay at hotel with “bed bugs”
Eosinophilic Pustular Folliculitis

- Treatment with Betamethasone Valerate cream, erythromycin 2% solution, and ketoconazole cream
- Much improved at 2 week followup
Eosinophilic Pustular Folliculitis

- Highly pruritic, follicular papulopustular eruption of the face, neck, trunk, and extremities
- Cultures are negative
- Peripheral eosinophilia may be present
- CD4+ usually <200
- One of most characteristic pruritic dermatosis associated with HIV
- May be exaggerated reaction to *Malassezia* yeast
Eosinophilic Pustular Folliculitis

- Treatment with Betamethasone Valerate cream, erythromycin 2% solution, and ketoconazole cream
- Much improved at 2 week followup
EED in HIV

- Chronic form of cutaneous LCV
- CD4+ count <200
- Necrotising vasculitis with firm red - brown papules, plaques, or nodules, symmetrically on extensor surfaces
- Asymptomatic or painful itching/burning (worse after exposure to cold)
- Tx: Dapsone

Patient with spots on the back

- 34 year old female
- Spots on back for one month
- CD 4 4
- On HAART, bactrim
Photosensitivity

- May be symptom of HIV or drug side effect
  - In some reported cases, photosensitivity was the first clinical sign of HIV
  - Occurs in 5.4% in sero-positive patients
  - More common in individuals of African descent

- Most HIV patients are UVB sensitive
  - The most severely affected individuals are both UVB and UVA sensitive
Photosensitivity

- Reported cases of photodermatitis with subsequent Vitiligo-like Leukoderma

Theories:
- HIV triggers immune dysregulation leading to autoimmunity against the skin
- Viral-mediated melanocyte destruction
- Koebner phenomenon induced by photodermatitis in susceptible people.
KAPOSI’ S SARCOMA
KAPOSI’S SARCOMA

- Neoplasm of endothelial cells
- Closely associated with HHV-8 infection
- Predominantly seen in MSM
- Initially red-brown macules. Small violaceous papules, large plaques, ulcerated nodules also seen
- Internal involvement in 72%, usually in GI tract and lymphatics → secondary lymphedema
- Poor prognosis, avg survival time of 18 months
• 23 cases of KS in HIV infected persons
• 7/23 had CD4>300
• 5/23 had never had any prior treatment with HAART
• These cases can not be directly attributed to immune re-constitution syndrome
• Conclusion: All patients with HIV should be screened for KS
LYMPHOMAS

• CD4+ counts <200
• Pink – violaceous papules, often ulcerate
• In patients with HIV:
  – Most are non-Hodgkin B-cell type
  – Younger age of onset
  – Extranodal (esp. CNS) involvement at presentation
• HIV+ children ↑ incidence of MALT lymphomas
• Decreased incidence lymphomas with HAART
Lymphoma of Skin
LIPODYSTROPHY aka Fat Redistribution Syndrome

- HIV patients treated with HAART may have lipohypertrophy, lipoatrophy or a mix of both
- Commonly have hypertriglyceridemia and insulin resistance
- Lipoatrophy associated with:
  - Duration of tx with thymidine analogues
Lipodystrophy

- HIV patients being treated with antiretrovirals may have
  - Lipohypertrophy
  - Lipoatrophy
  - Mix of both
LIPOHYPERTROPHY

- Enlarged dorsocervical fat pad
- Circumferential expansion of the neck
- Breast Enlargement
- Abdominal Visceral Fat Accumulation
LIPOHYPERTROPHY

- Enlarged dorsocervical fat pad
- Circumferential expansion of the neck
- Breast Enlargement
- Abdominal Visceral Fat Accumulation

LIPOATROPHY

• LIPOATROPHY IN HIV
  – Peripheral fat wasting with loss of SQ tissue in face, arms, legs and buttocks
  – Face involvement is most common
    • May have social stigma
LIPOATROPHY

- Peripheral fat wasting with loss of SQ tissue in face, arms, legs and buttocks
- Face involvement is most common - especially cheeks & temples
  - May have social stigma
- Stavudine (NRTI) a/w higher risk
- Substituting non-thymidine analogue for stavudine → gradual improvement
- Tx: Pravastatin, pioglitazone for peripheral lipoatrophy; cosmetic sx

http://ias.umn.edu/images/EventsS10/Lipoatrophy.jpg
LIPOATROPHY
**LIPOATROPHY GRADING SCALE**

Table I. **Facial Lipoatrophy Grading Scale based on the final consensus of the Facial Lipoatrophy Panel**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No facial lipoatrophy.</td>
</tr>
<tr>
<td>1</td>
<td>Mild flattening or shadowing of one or more facial regions. No prominent bony landmarks. No visibility of underlying musculature.</td>
</tr>
<tr>
<td>2</td>
<td>Intermediate point between grade 1 and grade 3.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate concavity of one or more facial regions. Prominence of bony landmarks. May have visibility of underlying musculature.</td>
</tr>
<tr>
<td>4</td>
<td>Intermediate point between grade 3 and grade 5.</td>
</tr>
<tr>
<td>5</td>
<td>Severe indentation of one or more facial regions. Severe prominence of bony landmarks. Clear visibility of underlying musculature.</td>
</tr>
</tbody>
</table>

Immune Reconstitution Inflammatory Syndrome (IRIS)

- Occurs with sudden increased CD4 count or decreased viral load
- Flare of skin conditions with improved immune function
- Often follows start of HIV medications.
- Skin Conditions which flare: EPF, KS, HSV, HZV
Immune Reconstitution Inflammatory Syndrome (IRIS)

- The initiation of antiretroviral treatment for individuals with HIV may be accompanied by
  - a paradoxical flare of underlying inflammatory diseases
  - the recurrence of dormant infections
  - worsening of prior treated opportunistic infections
Pyoderma Gangrenosum: IRIS
Medication Reactions

- Patients with HIV have an increased incidence of cutaneous drug eruptions
- Risk for TEN is 1000x greater in AIDS patients

Two weeks after receiving Bactrim for PCP prophylaxis
Drug-Induced Hyperpigmentation

- Azidothymidine (zidovudine, AZT)
  - Causes hyperpigmentation of mucous membranes and nails in 10%
  - Typically occurs after 4-6 weeks of therapy
  - Increase in melanin in basal layer and dermal melanophages
  - Fades after discontinuation
Eruptive Dermatofibroma

• Common benign fibrous nodule that often arises on the lower legs

• Multiple eruptive DF is rare but frequently associated with underlying immunocompromising disease
• **Chief Complaint:**
  – Numerous mildly itchy nodules x6 months

• **HPI:**
  – 28 year old African-American woman with PMH of AIDS and hypercholesterolemia who presents with a 6 month history of pruritic hyperpigmented papules and nodules on the trunk and extremities
  – Lesions are not painful
  – Occurred rapidly over the course of a few months while off antiretroviral therapy (ART)
    • Has recently restarted ART
  – No prior treatment
• **PMH:**
  – AIDS, diagnosed 2011, 2/2 blood transfusion, CD4 16 at presentation, now 61
  – Homozygous familial hypercholesterolemia
  – HPV with low grade squamous intraepithelial lesion (LSIL)
  – Chronic anemia of unclear etiology, multiple transfusions as child
  – Hepatic leiomyoma, s/p bx, benign but with elevated LFTs
• **PSH:**
  – MRSA lung abscess s/p thoracotomy and numerous blood transfusions in 2014

• **Allergies:**
  – Bacitracin (anaphylaxis); cephalosporins (angioedema)

• **Medications:**
  – Emtricitabine/tenofovir disoproxil (Truvada)
  – Dolutegravir (Tivicay)
  – Dapsone
  – Atorvastatin (Lipitor)
  – Exetimibe (Zetia)
  – Mipomersen (Kynamro)
• **Family Hx:**
  – No cancer, skin or autoimmune diseases
  – Strong family history of early coronary artery disease

• **Social Hx:**
  – Single, 2 children
  – Denies smoking, drinking, drug use
  – Not currently sexually active

• **Review of Systems:**
  – Denies fever, chills, cough, weight loss, recent travel outside the country
• **Labs**
  – CBC shows mild pancytopenia
    • Hb 9.1, WBC 4.2, Plt 134
  – CMP unremarkable except AST 39
  – Total Cholesterol 299, LDL 251, Triglycerides 45
  – CD4 61, Viral Load undetectable
  – RPR negative
  – Quantifieron gold negative
  – Hepatitis B SAb, SAg, CAb, Hepatitis C Ab all negative
  – TSH 1.15
Physical Exam
Physical Exam
Physical Exam
Differential Diagnosis

- Epidermal inclusion cyst
- Melanocytic or blue nevus
- Nodular melanoma
- BCC, esp pigmented
- Prurigo nodules
- Keloid or hypertrophic scar
- Schwannoma
- Pilomatrixoma
- Cold abscess
- Neurofibroma
- Kaposi sarcoma
- Cutaneous metastasis
- Dermatofibrosarcoma protuberans
- Dermatofibroma
- Dermatomyofibroma
- Leiomyoma
- Sarcoidosis
Dermatopathology
Patient PW

Specimen Source:
A. Right Upper Arm; Skin biopsy:
Factor13a (+)

CD34 (-)
A. Right Upper Arm; Skin biopsy:

- CELLULAR FIBROUS HISTIOCYTOMA (CELLULAR DERMATOFIBROMA), EXTENDING TO ALL MARGINS.

Comment: The tumor cells are positive for Factor XIIa and negative for CD34, HHV8, and ERG. There is entrapment of fat by tumor cells within the superficial subcutis, which is an unusual finding. Although these tumors typically follow an indolent clinical course, there is an increased risk for local recurrence. Re-excision is recommended. Multiple levels have been examined.
Cellular Dermatofibroma

• Introduction
  – Dermatofibroma – 2nd most common fibrohistiocytic tumor of the skin
  – First described in 1994, one of many subtypes of DF
  – Considered to be locally aggressive and have potential for metastasis

• Epidemiology
  – Rare, ~5% of all DF
  – Occur in young to middle age adults, male predominance
  – Overall rate of metastasis is unknown but thought to be very rare
  – No reported cases in HIV or AIDS patients

Cellular Dermatofibroma

• Pathogenesis
  – Unknown, possibly trauma however newer literature debates this reactive origin
    • Eruptive DF associated with immunosuppression
    • Potential for recurrence and metastasis
    • Association with multiple chromosome abnormalities
  – DF of all types known to be eruptive in:
    autoimmune disorders, atopic dermatitis, immunosuppression (esp HIV)
    • No reports of eruptive cellular DF in HIV or AIDS patients

Examined 4 aggressive or metastatic cellular DF along with mixed type DFs
All showed marked chromosomal abnormalities
Recurrence occurred between 8 months and 9 years
Metastasis occurred between 3 months and 8 years after diagnosis
2 patients died of their disease
Examined 5 metastatic cellular DF using array based comparative genomic hybridization analysis

Compared above to 5 non-metastatic cellular DF and normal DNA

Showed that increased chromosomal abnormalities associated with metastatic potential

- Acknowledge that chromosome analysis is currently too costly to perform on all cellular DF

Recommend cautious management of patients with large cellular DF
Cellular Dermatofibroma

• Clinical Features
  – Appear clinically similar to benign DF
  – Occur in upper extremities and non-classical locations – face, ears, hands and feet
  – Diagnosis made by biopsy
  – Per published case series, most are larger (3+ cm)

Cellular Dermatofibroma

• Pathology:
  – High cellularity, minimal intracellular collagen, abundant mitosis, extension into the subcutis and no cellular atypia or nuclear pleomorphism
    • Central necrosis or infarction has been reported.
  – Variable expression of smooth muscle actin, seen much more frequently than in ordinary dermatofibroma.
  – Positive for factor XIIIa, negative for CD34
    • Focal, peripheral expression of CD34 and desmin reported

Cellular Dermatofibroma

- **Treatment:**
  - All literature recommends complete excision, no consensus on margins
    - 1 publication reported 0.5 mm margin with fatal outcome
  - Recurrence rate of 26-64% depending on source
  - Rare reports of metastasis to lymph nodes, lungs, soft tissue, brain
  - No consensus on treatment of metastatic disease beyond complete excision if possible
  - Metastatic disease fatal in 32% of reported cases (7/22)

Published in American Journal of Dermatopathology 2014

Recommend complete excision and careful surveillance especially for local recurrence
  – Multiple local recurrence associated with metastasis

If large primary or local recurrence recommend chest X-ray and ultrasound lymph node exam
  – Repeat CXR if any pulmonary symptoms develop

Follow Up and Treatment Options

• Patient has 2 large biopsy proven cellular DF
• Next step is to remove these 2 lesions
• As our patient’s CD4 count increased and her viral load decreased many of her previously nodular lesions have become macular
  – Should these be biopsied?
• With >10 lesions, 2 biopsy proven cellular DF, is biopsy and excision of all lesions feasible without causing extensive disfigurement?
Conclusion

• Many skin findings are associated with HIV
• The prevalence of HIV is still high even as the incidence has waned
• Dermatologists should be aware of HIV associated skin conditions and consider HIV testing when there is suspicion of infection
THE END: THANK YOU!
THE END

• THANK YOU!