Figurate Erythemas and Purpuras

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Disclosures

• None
Figurate Erythemas
Objectives

• Discuss the following figurate erythemas and treatments
  - Erythema Annulare Centrifugum
  - Erythema Marginatum
  - Erythema Migrans
  - Erythema Gyratum Repens
• Discuss the different types of purpuras and their etiologies
• Review basic methods of coagulation
• Review specific purpuric syndromes
• Discuss treatment modalities
Erythema Annulare Centrifugum

• Introduction
  • Superficial and deep forms.
  • More common in adults.
  • Peak incidence in 5\textsuperscript{th} decade of life.
  • Duration: days to months, often self-limiting
  • Most commonly idiopathic, but can be related to infection or other exposures.
  • Reaction pattern or “hypersensitivity” reaction to one of many antigens
Pathogenesis

- Infectious causes:
  - Dermatophytes (Tinea Pedis)
  - Fungal: Candida, Penicillium in blue cheese.
  - Viruses (e.g. poxvirus, EBV, varicella-zoster virus, HIV)
  - Parasites and Ectoparasites (e.g. Phthirus pubis).

- Drug induced: diuretics, NSAIDs, antimalarials, gold, finasteride, amitriptyline, etizolam

- Other: Pregnancy, certain foods, autoimmune endocrinopathies, hyper-eosinophilic syndrome and occasionally, lymphomas and leukemia.
Clinical Features

• Initial lesions begin as firm pink papules that expand centrifugally and then develop central clearing.
• Can enlarge to greater than 6 cm.
• Favors upper legs, hips and trunk.
• In the superficial form, lesions are minimally elevated, and there is desquamation at the inner margin, i.e. “trailing scale.” +/- pruritus.
• In deep gyrate erythema, the advancing edges are indurated and raised, and there is usually no scale. Non-pruritic.
• As lesions resolve, PIH is common.
A) Superficial EAC
B) Deep Gyrate Erythema
Pathology

- Superficial lesions: mild spongiosis, focal parakeratosis, superficial perivascular lymphohistiocytic infiltrate
- Fairly tight aggregates around vessels, the so-called “coat sleeve” anomaly.
- Rarely eosinophils. Edema in the papillary dermis.

- Deep lesions: lymphoctic infiltrate with a sharply demarcated perivascular arrangement is present primarily within the mid and lower dermis.
Differential Diagnosis

- Tinea Corporis
- Annular Psoriasis
- Annular Urticaria
- Erythema Marginatum
- Allergic Urticarial Eruption
- Autoimmune disorders, including linear IgA bullous dermatosis, Sjögren’s syndrome and lupus erythematosus, can also have erythematous annular, arciform and polycyclic lesions.
Treatment

• If EAC is due to an underlying disorder, the skin lesions will usually resolve once the disease has been successfully treated

• Usually self-limited.

• Topical corticosteroids.

• Topical anti-pruritics and sedating antihistamines for pruritus.

• Systemic corticosteroids, however recurrence is common after discontinuation.

• Case Reports: Empiric use of antibiotics, anti-fungal agents, topical tacrolimus, topical calcipotriene, oral metronidazole, subcutaneous etanercept and subcutaneous interferon-alpha
Erythema Marginatum

- Cutaneous manifestation of Rheumatic Fever
- ~ 3% of patients with untreated group A β-hemolytic Streptococcal infections can develop acute rheumatic fever
- Latency period of 2-5 weeks before development of rheumatic fever
- Rash occurs in less than 10% of patients with acute rheumatic fever.
- Higher incidence in children, peak age 5-15 years.
- Associated findings: Jones Criteria: Carditis, Migratory Polyarthritis, Sydenham’s chorea, fever and subcutaneous nodules.
Clinical Features

- Lesions begin as erythematous macules that spread peripherally and become patches or plaques, can be polycyclic, with NO scale.

- Usually asymptomatic.

- Migrates over a period of 12 hours (by 2–12 mm).

- Lasts from a few hours to a few days – usually transient. Can recur over a few weeks.

- Most commonly on the trunk, axillae and proximal extremities, spares face.
Erythema Marginatum
Differential Diagnosis

• Annular urticaria
• Annular erythema of infancy
• Neutrophilic figurate erythema of infancy
• EAC
• Erythema Gyratum Repens
• Hereditary periodic fever syndromes (particularly TNF receptor-associated periodic syndrome [TRAPS])
• Kawasaki disease
Treatment

• Treat underlying rheumatic fever disease.
• No specific treatment for the rash.
• Lesions usually resolve spontaneously.
• Treatment of rheumatic fever does not usually affect the rash.
Erythema Migrans

- Initial cutaneous presentation of Lyme disease in 60-90% of cases

- Lyme disease infection is caused by the spirochete *Borrelia burgdorferi* and transmitted by species of the *Ixodes* tick

- Lyme disease is most prevalent in US and in Europe (Scandinavia and central Europe)
Clinical Features

• Typically 1-2 weeks after tick detachment

• Erythematous annular plaque with light-colored central area of a bull’s eye appearance

• Favors trunk, axilla, groin and popliteal fossa

• Untreated, usually last four weeks

• Disseminated EM – EM and satellite oval-shaped widespread patches due to spirochetemia
Erythema Migrans
Stages and Major Organ Manifestations of Lyme Disease

• Early Localized disease – EM, flu like symptoms, regional lymphadenopathy

• Early Disseminated disease – neural involvement (facial nerve common), migratory joint pain, carditis, conjunctivitis

• Chronic Disease – acrodermatitis chronica atrophicans, persistent neurologic and rheumatologic symptoms
Diagnosis

- Clinical presentation AND either history of exposure or laboratory evidence of infection
- PCR, culture, serological evidence
- Borrelia antibodies detection in serum might not be specific as peak specific IgM response is 3-6 weeks into infection
- Serologic tests will stay positive for months to years
Pathology

- Superficial and deep perivascular and interstitial infiltrate of lymphocytes, sometimes with abundant plasma cells and eosinophils

- Warthin-Starry stain is positive in 50% showing spirochetes
Differential Diagnosis

- Arthropod assault
- Erysipelas
- Cellulitis
- Non-pigmented fixed drug eruption
- Allergic contact dermatitis
## Treatment

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Antibiotic</th>
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</thead>
<tbody>
<tr>
<td>Early localized disease</td>
<td><strong>First choice for adults and children ≥8 years</strong></td>
</tr>
<tr>
<td>Early disseminated disease or chronic disease, mild</td>
<td>Doxycycline 100 mg (2 mg/kg) po q12h, 14–21 days†</td>
</tr>
<tr>
<td>Cranial nerve palsy, 1st or 2nd degree heart block</td>
<td>Amoxicillin 500 mg po q8h (50 mg/kg po per day divided q8h), 14–21 days§</td>
</tr>
<tr>
<td></td>
<td>Cefuroxime axetil 500 mg (15 mg/kg) po q12h, 14–21 days</td>
</tr>
<tr>
<td>Early disseminated disease or chronic disease, severe</td>
<td><strong>First choice</strong></td>
</tr>
<tr>
<td>Meningitis, radiculopathy, 3rd degree heart block</td>
<td>Ceftriaxone 2 g (75–100 mg/kg) iv once daily, 14–28 days</td>
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<tr>
<td></td>
<td>Cefotaxime 2 g (50–70 mg/kg) iv q8h, 14–28 days</td>
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<tr>
<td></td>
<td>Penicillin G 18–24 million units (200 000–400 000 units/kg) iv per day divided q4h, 14–28 days</td>
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*†§ Alternative choice*
Erythema Gyratum Repens

- Rare, males=females, Caucasians
- Gyrate polycyclic rapidly growing erythematous plaques with a trailing scale
- Migrates up to 1cm/day
- Wood grain resemblance due to “rings within rings” pattern
- Can be pruritic
- Additional findings: acquired ichthyosis, palmoplantar keratoderma and hypereosinophilia
Erythema Gyratum Repens
Erythema Gyratum Repens

- Unknown etiology, malignancy association >80% cases, i.e. the most specific paraneoplastic syndrome
- 1/3 patients = lung cancer, 8% esophageal cancer, 6% breast cancer
- The figurative eruption can precede, occur concurrently or appear after the diagnosis of the neoplasm
- Non-paraneoplastic cases: TB, CREST syndrome, pregnancy, bullous dermatosis
Differential Diagnosis

- Erythema annulare centrifugum
- Erythema migrans
- Resolving pityriasis rubra pilaris
- Erythrokeratoderma variablis
Erythema Gyratum Repens

- Treatment: identify and treat underlying malignancy
Purpuras
Definition

• Visible hemorrhage into the skin or mucous membranes.

• Divided into 6 subsets;
  
  • Petechiae
  
  • Macular Purpura
  
  • Macular ecchymoses
  
  • Palpable purpura
  
  • Non-inflammatory retiform purpura
  
  • Inflammatory retiform purpura
• **Petechiae** (<4 mm red-purple hemorrhagic macules):
  - Seen in: ITP, TTP, DIC, Platelet function defects, Aspirin/NSAID use, trauma, valsalva-manueaver, etc.

• **Macular Purpura** (5-9 mm red-purple hemorrhagic macules that don’t blanch):
  - Seen in: Hypergammaglobulinenima of Waldenstrom, thrombocytopenia

• **Macular Ecchymoses** (>1 cm red-purple-green patch due to bleeding in skin):
  - Seen in: Anticoagulant use, hepatic insufficiency, Vitamin K deficiency, DIC, Actinic purpura, steroid use, Vitamin C deficiency, Ehlers-Danlos disease, platelet function diseases, etc.
- Macular purpuras are all due to hemorrhage, with mild inflammation and extravasated red blue cells causing what is seen in the patient.
• **Palpable Purpura**: (raised, non-blanching inflammatory purpura with erythema)
  
  • Seen in: Idiopathic, infection IgG/IgA/IgM complexes, Hypergammaglobulinemic purpura of Waldenstrom, Urticarial vasculitis, Mixed cryoglobulinimia, Rheumatic vasculitis, ANCA associated diseases, etc.

• **Non-inflammatory retiform purpura** (mottled lace-like livedo reticularis pattern causing a purple-ish discoloration):
  
  • Seen in: Heparin necrosis, thrombocytosis, TTP, cryoglobulinimia, ecchyma gangrenosum, Protein C/S deficiency, warfarin necrosis, livedoid vasculopathy, cholesterol emboli, etc.

• **Inflammatory retiform purpura** (visible hemorrhage into skin or mucous membranes in the livedo reticularis pattern):
  
  • Seen in: IgA vasculitis, mixed cryoglobulinimia, polyarteritis nodosa, chillblains, wegener’s granulomatosis, livedoid vasculopathy, etc
Livedo Reticularis

- Seen due to blood flow regulation in dermal and subcutaneous vessels and shows a net-like pattern.

Retiform Purpura

- Retiform purpura is due to occlusion of vessels that cause the livedo reticularis; distinguish the 2 by presence or absence of purpura.
Coagulation
Coagulation

• Primary hemostasis consists of the formation of a platelet plug that is sufficient for minor injuries to the microvascular system.
• If the size of the vessel or injury is too large, secondary hemostasis with clot formation is necessary.
• Too little clotting → death by hemorrhage.
• Too much clotting → thrombosis, embolus, necrosis.
• Requires extensive regulation and balance between procoagulant, anticoagulant, and fibrinolytic pathways.
Coagulation Related Pathways

Platelet Plug (Primary Hemostasis)

http://www.sharinginhealth.ca/multimedia/images/hemostasis_Kathryn_Dorman.jpg
Thrombin (factor II)

- Generated in small amounts from primary clot
- Activates platelets, leads to binding of procoagulant factors
- Also stimulates release of factor V from platelet granules
- Activates tissue factor VIIa
- Activates Factor IX to IXa and Factor X to Xa
Anticoagulant pathway

- Initiation phase of clotting is down-regulated by tissue factor pathway inhibitor (TFPI) and antithrombin III (ATIII)
- Both bound to heparin sulfate molecules on endothelial cells
- Capture activated clotting factors and prevent them from leaving the vicinity
- TFPI can inactivate factor Xa; ATIII can neutralize thrombin, factor IXa, Xa, XIIa
- Thrombomodulin/protein C/protein S
- Important in large vessels
- Thrombin from clot bind to thrombomodulin, and thus loses its ability to cause procoagulatory effects
- Activates protein C $\rightarrow$ inactivates Factor Va, VIIIa
Tests for Coagulation

• Thorough history and physical exam
• Labs: Platelet count, PT, and APTT
• If PT or APTT prolonged, can repeat testing using 1:1 mixture of pt plasma and normal plasma ->if time normalizes then there is a factor deficiency
• Prolonged PT + normal APTT: factor VII deficiency or use of PO anticoagulant
• Prolonged APTT + normal PT: use of Heparin, lupus anticoagulant, acquired factor VIII deficiency, or von Willebrand Disease
• Prolonged PT + APTT: fibrinogen deficiency, prothrombin, factor V or Factor X deficiency
Pigmented Purpuric Eruptions

- Diseases characterized by petechial hemorrhage likely due to capillaritis
- Minimal inflammation and hemorrhage of superficial papillary dermal vessels
- Source of inflammation unknown and no coagulation abnormalities
- Several variants
Schamberg's Disease

- Yellow-brown patches with an oval to irregular outline, pinpoint petechiae within patches (cayenne pepper)
- Most common form, peak frequency in middle aged to older men
- Usually involves lower extremities
- Stasis purpura clinically has more hemosiderin and less
Purpura annularis telangiectodes of Majocchi

- Uncommon, adolescents, young adults, especially women
- 1-3 cm annular plaques that slowly expand, punctate telangiectasias and petechiae within border, possible yellow center
- Trunk, proximal lower extremities

Bologna, “Dermatology”, figure 22.6
Rare Variants

- Pigmented purpuric lichenoid dermatitis of Gougerot and Blum: Schamberg like- purpuric red-brown lichenoid papules

- Eczematid-like purpura of Doucas and Kapetanakies: Scaly petechial or purpuric macs, paps and patches, usually pruritic

- Lichen aureus: solitary patch, color varies from golden to rust to purple brown
Lichen Aureus

Lichen Aureus

http://www.cortesedermatology.com/dermatitis-images.html
Histology

- Red cell extravasation, endothelial swelling, perivascular lymphs, and hemosiderin containing macrophages

- Lichen aureus and Gougerot-Blum variants are characterized by lichenoid infiltrate

- Eczematid like purpura of Doucas and Kapetanakis often has spongiosis, patchy parakeratosis
Treatment

- Topical steroids especially if pruritic
- PUVA, NBUVB
- Ascorbic acid 500 mg BID with Rutoside 50 mg BID
- Cyclosporine
Hypergammaglobulinemic Purpura of Waldenstrom

- Associated with a hypergammaglobulinemia
- Presence of small circulating immune complexes containing IgG or IgA rheumatoid factor
- IgG and IgA rheumatoid factors are highly soluble, which may explain the speed with which lesions appear and resolve
- Can be primary or secondary
- In younger patients, it is usually primary, but eventually patients may develop an autoimmune connective tissue disease (usually Sjogren’s)
- Complications include the development of a monoclonal gammopathy, lymphoma, or multiple myeloma
- Differential Dx: classic cutaneous small vessel vasculitis syndromes
Hypergammaglobulinemic Purpura of Waldenstrom

- Usually affects women
- Mild pruritus, tingling, or burning may precede the presence of purpura
- Symptoms are exacerbated by prolonged standing, tight fitting garments, and heat
- Petechiae or larger purpuric macules on lower extremities is the most common presentation
- Labs: Polyclonal hypergammaglobulinemia, elevated ESR, anti-Ro and anti-La Abs are usually present and may predict a higher likelihood of developing autoimmune connective tissue disease
  - Standard RF assays will only detect IgM, therefore they will not detect IgG or IgA
Pathology

- Histopathology may show hemorrhage, a mild perivascular infiltrate, or a leukocytoclastic vasculitis
- Image shows dilated superficial capillaries, extravasation of red blood cells, and sparse mononuclear infiltrate without evidence of vasculitis
Treatment

• Limited treatment options
• Aspirin
• Support stockings
• Avoidance of triggers such as alcohol, prolonged standing
Mondors Disease:

- First described in 1939 by Henri Mondor
- Superficial thrombosis (SVT)
- Self limited
- Most commonly seen in patients aged 30-60 year old
- Female > male; 3:1
Clinical Presentation

- Predisposing factors include:
  - Increased coagulation state
  - Thoracic surgical procedures
  - Breast surgery
  - Tight clothes
  - Mammary infections
  - Pendulous breast
  - Chronic inflammatory disease states
- Presents as a fibrous painful cord, with or without skin retraction, and with or without local inflammation.
- Can present on the chest well, involving other venous areas, and following breast disease
Work up

- Complete history and physical
- Ultrasonographic to confirm
- Mammography if suspicion of breast cancer
• Most cases are idiopathic
• In a pool analysis of the four largest and most recent series:
  • Idiopathic (32.5%)
  • Breast Cancer (6.3%)
  • Iatrogenic (11.9%)
  • Inflammation (4.8%)
  • Trauma (32.5%)
    • Including: injury, muscular, heavy load, tight support, thrombophilia, hormone therapy
Treatment

• Mondor’s on chest wall: Spontaneous resolution in 2-8 weeks
• Other locations: less known, can consider anticoagulation and etiologic management if known. Surgery in persistent cases
• Mondor’s after breast surgery: This is not a thrombotic process. Reports suggest that manual rupture of the fibrous bands ensures immediate functional recovery and pain relief.
• Penile Mondor’s: conservative treatment.
• There is approximately 13% recurrence
Conclusion

• Reviewed the four “classic” figurate erythemas: erythema annulare centrifugum, erythema marginatum, erythema migrans, and erythema gyratum repens

• Reviewed specific purpuric syndromes and treatment modalities

• Provided practical applications for these dermatological conditions
References

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Thank You