Neutrophilic & Eosinophilic Dermatooses

UNTHSC/TCOM Dermatology Residency
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Bridget McIlwee, DO PGY4
Heather Reagin, DO PGY3
Michael Carletti, DO PGY3
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Neutrophil Biology & Neutrophilic Dermatoses
Neutrophil maturation and biology

- >5–10 × 10^{10} neutrophils produced daily in bone marrow
  - Differentiation from pluripotent stem cells requires 7–10 days
- Bone marrow upregulates neutrophil production in response to stress (e.g., infection)
- Mature neutrophils circulate in peripheral bloodstream for 3–12 hours
  - They then migrate into tissues, surviving 2–3 days further
Neutrophil biology

- Neutrophils are a crucial defense against microbes
  - Granulocytes: like eos, basophils
- Contain numerous granules—oxidative and non-oxidative
  - Enable destruction of target organisms

*Primary (azurophilic) granules*
- Acquired at promyelocyte stage
- Myeloperoxidase, lysozyme, neutrophil elastase, defensins, myeloblastin

*Secondary granules*
- Acquired at transition to myelocyte stage
- Lactoferrin, neutrophil collagenase, transcobalamin 1

*Tertiary granules*
- Acquired during later stages of maturation
- Neutrophil gelatinase
Neutrophil biology

- **Inflammatory factors** → neutrophil activation → $\beta_2$ ligand expression
- Binding to ICAM-1 (endothelial cells)
- **Diapedesis** = migration of neutrophils towards site of injury or inflammation

**Activation, adhesion, migration**
- Neutrophils "crawl" via use of lamellipodia
- Cells move along chemical gradient, responding to chemical factors (FMLP, C5a, PAF, LTB4)

**Tissue migration**
- Neutrophils activated at inflamed site → express surface receptors – e.g. TLR, for opsonins, CK
  - Activation →
    - degranulation
    - secretion of enzymes
    - oxidative burst
    - production of arachidonic acid metabolites
    - secretion of cytokines

**Activation**
- Neutrophils activated at inflamed site → express surface receptors – e.g. TLR, for opsonins, CK

**Phagocytosis**
- Opsonisation enhances recognition, attachment → targets particle for phagocytosis
  - Binding of particle to neutrophil receptors → engulfment
  - Particle fuses with lysosomal granule → phagolysosome
- Microbes killed by oxygen-dependent mechanisms → formation of ROS
  - Discharge of granule contents → degranulate neutrophil
  - Neutrophils then rapidly undergo apoptosis → ingested by macrophages

**Destruction of ingested material**
- Microbes killed by oxygen-dependent mechanisms → formation of ROS
  - Discharge of granule contents → degranulate neutrophil
  - Neutrophils then rapidly undergo apoptosis → ingested by macrophages
Neutrophilic pathophysiology

- Neutrophils move at up to 30\(\mu\)m/min – fastest cell in the body
  - Among first cells to arrive at sites of inflammation
- Neutrophils contain potent defense mechanisms
  - Destroy not only microbes and necrotic debris, but also normal tissue
- Release of lysosomal enzymes, ROS, prostaglandins and leukotrienes into the extracellular space → endothelial injury and tissue damage
- Neutrophils contribute to many acute and chronic diseases of skin, body
  - Varied diseases
  - Similar pathogenesis and histopathology → similar therapy
Neutrophilic dermatoses

- Sweet’s syndrome
- Pyoderma gangrenosum
- Behcet’s disease
- BADAS
- SAPHO syndrome
Sweet’s syndrome

- Acute febrile neutrophilic dermatosis
- Epidemiology
  - Occurs in all ages; average age of onset is 30-60 years
  - Female predominance (4:1)
    - Especially drug-induced
- Clinical presentation
  - Tender papules or nodules → coalesce into plaques
    - May have vesicular, bullous, or pustular appearance
  - Favor head, neck, UE
  - Oral ulcers
  - Exhibits pathergy

- Variants
  - Classical:
    - URI or GI infection
    - Inflammatory bowel disease
    - Pregnancy
    - Autoimmune disorders
  - Malignancy-associated:
    - AML
      - Vesiculobullous
  - Drug-induced:
    - G-CSF (granulocyte colony stimulating factor)
    - All-trans-retinoic acid
Sweet’s syndrome

**DIAGNOSTIC CRITERIA**

- **Major criteria** – *must demonstrate both*:
  1. Abrupt onset of cutaneous lesions consistent with typical Sweet’s syndrome
  2. Histopathology consistent with Sweet’s syndrome
- **PLUS 2 minor criteria**:
  - Preceded by associated systemic findings, such as infection, pregnancy, drugs, malignancy or other inflammatory conditions
  - Fever and constitutional symptoms
  - Leukocytosis
  - Excellent response to systemic corticosteroids

- Associated laboratory abnormalities:
  - Elevated white blood cell count
  - Elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)
Sweet’s syndrome

• Histopathology
  • Superficial dermal edema with diffuse neutrophilic infiltrate
  • Leukocytoclasia with minimal to no evidence of vasculitis

Treatment

• 30% will recur; 50% in patients with hematologic disorders

  • **First line therapy:**
    • Systemic corticosteroids for 4-6 weeks*
    • Intraleisonal or topical corticosteroids

  • **Second line therapy:**
    • Dapsone
    • Potassium iodide
    • Colchicine

  • Alternate therapies:
    • NSAIDs, clofazimine, cyclosporine, interferon-α, IVlg, thalidomide, TNF-α inhibitors, Anakinra
Pyoderma gangrenosum

• Epidemiology
  • Recurring, painful disease; unknown cause
  • Commonly affects women 20-50yo
  • 50% have underlying systemic disease
    • IBD, arthritis; hematologic disorders (IgA monoclonal gammopathy), other neutrophilic dermatosis
  • 25-50% of cases are idiopathic
  • 4% of cases occur in infants and children
  • Pathergy implicated in 20-30% of PG cases

• Clinical features
  • Classical: Tender papulopustule → fibrinous ulcer, violaceous induration, undermined
  • PAPA syndrome (AD): pyogenic sterile arthritis, pyoderma gangrenosum and acne
    • CD2 binding protein 1 gene mutation
  • 1. Classical/ulcerative
    • Pretibial areas; frequently seen in conjunction with IBD, RA
    • Resolves with cribiform scarring
  • 2. Atypical/bullous
    • Vesicles → bullae → superficial ulcers/erosions
    • Face and upper extremities, especially dorsal hands
    • Frequently occurs with AML, MDS, IgA gammopathy
  • 3. Vegetative – pyostomatitis vegetans
    • Sterile pyoderma +/- sinus tracts
    • Labial and buccal mucosa
    • Frequently occurs with IBD
  • 4. Pustular
    • Multiple pustules surrounded by erythematous halo
    • Extensor extremities and trunk; frequently occurs with IBD

Common variants

1. Classical/ulcerative
   • Pretibial areas; frequently seen in conjunction with IBD, RA
   • Resolves with cribiform scarring

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   • Multiple pustules surrounded by erythematous halo
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Sweet's syndrome • Pyoderma gangrenosum • Behcet's disease • BADAS • SAPHO syndrome
Pyoderma gangrenosum: *proposed* diagnostic criteria

*Currently a diagnosis of exclusion.*

- **Major criteria** (must have all 2)
  1. Rapid progression of painful, necrolytic ulcer with irregular, violaceous, undermined border
  2. Already excluded: other causes of cutaneous ulceration

- **Minor criteria** (must have ≥2)
  - History suggestive of pathergy or clinical finding of cribriform scar
  - History of systemic diseases associated w/PG
  - Histopathologic findings of PG
  - Rapid treatment response to systemic corticosteroids

Sweet’s syndrome  |  Pyoderma gangrenosum  |  Behcet’s disease  |  BADAS  |  SAPHO syndrome
Pyoderma gangrenosum

- **Histopathology**
  - **Early**: leukocytoclasia and sterile dermal neutrophilic infiltrate/abscess
  - **Advanced**: marked epidermal necrosis, leukocytoclasia, fibrosing inflammation at edge; thrombosis of vessels, extravasated RBCs

- **Treatments**
  - **None** show consistent efficacy
  - **Wound care**
    - Avoid debriding tissue
    - Hyperbaric oxygen, biologic dressings, grafts
  - **Corticosteroids**
    - Systemic, topical or IL corticosteroids
  - **TNF-α inhibitors**
    - Infliximab, adalimumab, etanercept
  - **Calcineurin inhibitors**
    - Cyclosporine, oral or topical tacrolimus, topical pimecrolimus
  - **Antimetabolites/cytotoxics**
    - Azathioprine, cyclophosphamide, mycophenolate mofetil
Behçet’s disease

• **Clinical features**
  • Recurrent **aphthous stomatitis** and **genital aphthae**
    • Aphthous stomatitis generally **first symptom**
  • **Erythema nodosum-like lesions**, superficial thrombophlebitis, palpable purpura
    • Favor legs, buttocks of women
  • **Other systems**
    • Ophtho: **Anterior/posterior uveitis**, vasculitis → blindness
    • MSK: **Arthritis, arthralgias** – non-erosive; occurs in **50%**
    • GI: pain and hemorrhage; **difficult to distinguish from IBD**
    • Neurologic: impaired memory, CN palsy, brainstem lesions
      • Occurs later in disease course – **portends poor prognosis**
    • Cardiac: **myocarditis**, coronary arteritis, aneurysms
    • Renal: **glomerulonephritis**

• **Epidemiology**
  • Rare, multisystem; unknown etiology; unpredictable relapses/remissions
  • **Triad: oral ulcers, genital ulcers, ocular inflammation**
  • Peak age of onset: 20-35 years
  • **HLA*B51** association (80% of Asian patients)
  • Common in Japan, Middle East (Turkey)

• **Related disorders**
  • **MAGIC** (mouth and genital ulcers with inflamed cartilage) syndrome
    • Features of Behcet’s and relapsing polychondritis
Behçet’s disease

**Diagnosis of Behcet’s requires score of 3 points**

<table>
<thead>
<tr>
<th>1 point</th>
<th>Oral aphthosis</th>
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</table>
| 1 point | Skin manifestations  
  • psuedofolliculitis  
  • skin aphthosis |
| 1 point | Vascular lesions  
  • phlebitis  
  • large vein thrombosis/aneurysm  
  • arterial thrombosis |
| 1 point | Positive pathergy test |
| 2 points | Genital aphthosis |
| 2 points | Ocular lesions |

**Simplified Diagnostic Criteria:**

- ≥3 episodes of **oral ulceration** in past **12mo**
- **PLUS 2** of the following:
  - Genital ulcers, eye lesions, skin lesions, positive pathergy test
Behçet’s disease

• Histopathology
  • Ulcerated epidermis or pustule
  • Angiocentric, neutrophilic infiltrates
  • Leukocytoclasia/LCV, RBC extravasation
  • +/- mural thrombosis and necrosis

Treatment

• Difficult secondary to variable nature and multi-organ involvement

  • Cutaneous lesions:
    • Topical, intralesional corticosteroids
    • Colchicine
    • Dapsone
    • Thalidomide
    • TNF-α inhibitors

  • Systemic Disease:
    • Prednisone
    • TNF-α inhibitors
    • Cyclophosphamide
    • Cyclosporine
    • Prednisone
    • Mycophenolate mofetil
Bowel-associated dermatosis-arthritis syndrome

- Characterized by **skin lesions, arthritis, and diarrhea** with **resultant malabsorption**

- Seen in patients who are **status-post Gl surgery** and with **blind loops of bowel**:
  - Gastric resection
  - Jejunoileal bypass
  - Biliopancreatic diversion

- Medical causes may include IBD, diverticulitis, peptic ulcer disease

- Occurs within **1-6 years** after the causative surgery

- Caused by **bacterial overgrowth** in a **blind loop of bowel**
  - Bacterial antigen → **immune complexes** → deposit in skin, synovium
  - Disappearance of the disease with antibiotic therapy or **surgical revision**
Bowel-associated dermatosis-arthritis syndrome

Signs and symptoms

• Constitutional signs and symptoms resemble serum sickness (fever, chills, arthralgia, myalgia)

• **Erythematous macules** → papules and purpuric vesicopustules within 48 hours
  • Lesions last for **2–4 weeks**
  • May **recur** at 4-6 week intervals
  • Favor proximal extremities and trunk
  • Also seen: **erythema nodosum** and/or **neutrophilic panniculitis**

Histopathology

• Variable dermal edema and necrosis
• Perivascular and interstitial neutrophilic infiltrate
• Abundant karyorrhexis – similar to acute febrile neutrophilic dermatosis (e.g., Sweet’s)
• Inflammation may involve subcutaneous
Bowel-associated dermatosis-arthritis syndrome

- **Extracutaneous manifestations**
  - Tenosynovitis
  - Polyarthritis – non-erosive, migratory
  - **Diarrhea → malabsorption**

- **Systemic complications**
  - Hepatic dysfunction or failure
  - Renal stones
  - Gallstones
  - Deficiencies: vitamin A, zinc
  - Hyperuricemia
  - Electrolyte imbalance

**Treatment**

- **Mild disease**
  - **Antimicrobials**
    - Tetracyclines, clindamycin, metronidazole
  - Anti-neutrophilic agents
    - Colchicine, dapsone, thalidomide

- **Severe disease**
  - **Surgical revision**
  - Systemic immunomodulators
    - Prednisone
    - Cyclosporine
    - Azathioprine
    - Mycophenolate mofetil
  - **TNF-α inhibitors:**
    - Infliximab
    - Etanercept
    - Adalimumab
SAPHO syndrome

- **Synovitis, acne conglobata, palmoplantar pustulosis, hyperostosis, osteitis**

- **Epidemiology**
  - Rare in the US
  - More prevalent in Japan, Scandinavian countries, Germany, and France
  - Affects children and young to middle aged adults

- **Pathophysiology**
  - SAPHO is classified as a **seronegative spondyloarthropathy**
    - Association with **HLA-B27**
    - Involvement of axial skeleton – e.g., sacroiliitis
SAPHO syndrome

Clinical presentation

- Characterized by **sterile osteoarticular lesions** and **pustular dermatoses**
- Dermatoses – *no timing association w/bone lesions*
  - Palmoplantar pustulosis
  - Pustular psoriasis
  - Severe acne
  - Other **neutrophilic dermatoses**
    - LABD, Behçets, Sweets
SAPHO syndrome

• Osteoarticular lesions – *remitting and relapsing*
  • Axial skeleton (HLA-B27), chest wall, long bones
  • **Recurrent, multifocal osteitis** and **osteomyelitis**, hyperostosis, synovitis, **aseptic osteomyelitis**
  • Pain, tenderness, edema over affected areas
  • Bone scintigraphy shows increased uptake, supporting **increased osteoblast activity** → hyperostosis, osteitis

• Treatment
  • **Bisphosphonates**: first line for bone lesions
  • NSAIDS
  • Immunomodulators: methotrexate, TNF inhibitors
  • Oral corticosteroids for skin and bone lesions

• *Isotretinoin has been reported to flare SAPHO*
Other conditions characterized by a prominent neutrophilic infiltrate
**Epidermal**
- Pustular psoriasis
- Keratoderma blennorrhagicum (reactive arthritis)
- Sneddon-Wilkinson disease
- Acute generalized exanthematous pustulosis (AGEP)
- IgA pemphigus
- Infantile acropustulosis
- Transient neonatal pustulosis

**Dermal**
- **No vasculitis**
  - Inflammatory bowel disease – skin findings
  - Neutrophilic eccrine hidradenitis
  - Rheumatoid neutrophilic dermatitis
  - Neutrophilic urticaria
  - Still’s disease
  - Erythema marginatum
  - Periodic fever syndromes
  - Majeed syndrome
  - Bullous dermatoses (DH, LABD, BSLE, iEBA)
- +/- vasculitis
  - Neutrophilic dermatosis of the dorsal hands
- **With vasculitis**
  - Small vessel vasculitis (LCV), including urticarial
  - Erythema elevatum diutinum (EED)
  - Medium vessel vasculitis

**DIRA syndrome:**
- DIRA = deficiency of the IL-1 receptor antagonist
- \( IR1RN \) mutation
EOSINOPHIL BIOLOGY
& EOSINOPHILIC DERMATOSES
**Eosinophil biology**

- Found in **tissues only during inflammatory responses**
  - **Exceptions**: GI tract, lymph, bone marrow
- Eosinophils guided into tissues by:
  1. Chemokines
     - Eotaxins 1-3
     - RANTES – regulated on activation, normal T-cell expressed and secreted
  2. Cytokines
  3. Surface adhesion molecules
     - VLA-4
     - Interacts with VCAM-1
     - CD11b/CD18 (MAC)
     - Critical for degranulation

**Eosinophil activation**: in order of potency
1. GM-CSF
2. IL-3
3. IL-5
4. TNF-α
5. IL-4
Eosinophilic granule contents

**CORE**
- **Major basic protein 1 (MBP-1)**
  - Damages helminths and mammalian cells
  - **Only** product that stimulates histamine release from basophils
  - Stimulates neutrophils, superoxide, lysozyme

**MATRIX**
- Eosinophil cationic protein (ECP, RNase3)
  - Potent parasite toxin
- Eosinophil-derived neurotoxin (EDN)
- Eosinophil peroxidase (EPO)
  - Kills microorganisms in presence of hydrogen peroxide
  - Stimulates mast cell secretion

Mechanism of active substance release from eosinophils:
1. Cytolytic degranulation
   - *Seen in atopic dermatitis, HES*
2. Piecemeal degranulation
3. Regulated secretion
Eosinophilic pathophysiology

- IL-5, other inflammatory cytokines
  - Allergic inflammation
- MBP-1
  - Damage to various mammalian cells
    - Exfoliation of bronchial cells
    - Toxic to tumor cells
- EPO and MBP-1
  - Potent platelet agonist → release of 5-hydroxytryptamine (serotonin); promotes clotting
- Eosinophil cationic protein, IL-1
  - Generates fibrosis
  - Act as APCs
  - Participate in innate and acquired immunity
Eosinophilic dermatoses

and other conditions characterized by a prominent eosinophilic infiltrate
Granuloma faciale

• **Etiology**: idiopathic inflammatory dermatosis

• **Epidemiology**: predominantly affects middle-aged white men

• **Pathophysiology**
  • Precise etiology remains unknown
  • Interferon-gamma and IL-5 have been suggested to play a role
Granuloma faciale

- **Treatment**
  - First-line therapy: intrallesional triamcinolone, 2.5-5mg/ml
  - Disease often resistant to treatment
  - Many other treatment options have been proposed
Papuloerythroderma of Ofuji

- **Etiology**: unknown
- **Epidemiology**:  
  - Approximately 100 cases reported  
  - Elderly Japanese men  
  - Male:female ratio of 7:1
- **Pathophysiology**: unknown
- **Presentation**: symmetric flat-topped, red-brown, pruritic papules  
  - Characteristically spare the skin folds → bands of uninvolved skin called "deck-chair sign"
Papuloerythroderma of Ofuji

- **Histology**: non-specific
- **Laboratory testing**
  - Majority of patients have *peripheral eosinophilia, lymphopenia, elevated serum IgE*
- **Treatment**
  - Systemic corticosteroids usually effective
  - PUVA alone or combined with systemic retinoids led to complete clearance in 2/3 of patients in one study
- **Associated diseases/medications**
  - *T-cell lymphoma, gastric carcinoma*
  - Leukemia, lung, colon, hepatocellular, prostate, renal, laryngeal carcinomas
  - **Infections**: HCV, HIV, dermatophytes, strongyloidiasis
  - **Drugs**: furosemide, ranitidine, aspirin, isoniazid, dideoxyinosine
Well's syndrome (eosinophilic cellulitis)

- **Etiology**: unknown
- **Epidemiology**
  - Over 100 cases have been reported to date
  - Affects newborns to elderly
- **Presentation**: recurrent edematous plaques on extremities; may resemble cellulitis
  - Lesions typically preceded by itching, burning
- **Pathophysiology**: exact pathogenesis unknown
  - Local hypersensitivity reaction has been suggested
  - Possible “triggers”: myeloproliferative disorders, drugs, insect bites, infections including dermatophytes, viruses, and *Toxocara canis.*
  - **Activated eosinophils** play a major role in the disease process.
Well's syndrome (eosinophilic cellulitis)

- **Histopathology**: extracellular eosinophilic granules are present in the dermis forming the characteristic **flame-figures**

- **Laboratory testing**
  - *Toxocara canis* infection proposed as trigger
  - If parasite suspected, lab testing includes:
    - stool studies, serum IgE levels, specific Ab assays

- **Treatment**
  - Oral corticosteroids → dramatic improvement
    - Tapering dose over 1 month – well-tolerated
    - Flares may be treated with repeat doses
  - For mild cases, potent topical steroids
Hypereosinophilic syndrome

- **Etiology**: myeloproliferative disorder characterized by persistent eosinophilia → end-organ damage.
  - L-HES (lymphocytic HES)
  - M-HES (myeloproliferative HES)

- **Epidemiology**:
  - Lymphocytic form has equal gender distribution
  - Myeloproliferative form typically affects males (90%)

- **Pathophysiology**: eosinophils are cause of end-organ damage
  - Lymphocytic HES: Clonal T-cells produce IL-5 → recruitment, activation of eosinophils
  - Myeloproliferative HES: FIP1L1-PDGFRA fusion gene → constitutively active tyrosine kinase
Hypereosinophilic syndrome

• **Clinical presentation**
  • Cutaneous lesions nonspecific; >50%
  • Pruritic erythematous macules, papules and nodules or urticaria, angioedema
  • **Extracutaneous**: heart, lungs, CNS/PNS, liver
• **Features of myeloproliferative HES**
  • Fever, weight loss, fatigue, increased serum vitamin B12 and tryptase
  • Endomyocardial fibrosis → restrictive cardiomyopathy
  • Oral, anogenital ulcers may occur

• **Histology**: non specific; eosinophils are *not* always present

**DIAGNOSTIC CRITERIA**
1. Peripheral blood eosinophil counts >1,500 cells/microliter for at least 6 months, or less than 6 months with evidence of organ damage
2. **Lack of evidence** for parasitic, allergic or other recognized causes of eosinophilia
3. Symptoms and signs of end-organ system involvement
**Hypereosinophilic syndrome**

- **Laboratory testing/safety monitoring**
  - Evaluate abnormal peripheral T-cell population:
    - flow cytometry, T-cell receptor gene rearrangement analysis
  - Screen for **FIP1L1-PDGFRA fusion gene**
  - Monitor for development of **cardiomyopathy** by periodic echocardiogram
  - Endomyocardial disease may worsen during first several days of imatinib therapy:
    - Serum troponin and NT-proBNP levels

- **Treatment**
  - **Lymphocytic HES**
    - Glucocorticoids +/- INF-alpha
    - Mepolizumab and reslizumab (Mab against IL-5) → decreased Th-2 cytokines in trials
  - **Myeloproliferative HES**
    - If **FIP1L1-PDGFRA** gene is present, **imatinib** (TK inhibitor) is drug of choice
      - Dose: 100mg weekly to 400mg daily
      - Maintenance therapy required to avoid relapse
    - If **FIP1L1-PDGFRA** gene rearrangement not present, first-line therapy is **prednisone** 1mg/kg/day

Granuloma faciale  Papuloerythroderma of Ofuji  Well's syndrome  Hypereosinophilic syndrome
Hypereosinophilic syndrome

• Associations
  • Lymphocytic-HES
    • Patients with clonal T-cells are at increased risk for developing lymphoma and should be closely monitored
  • Myeloproliferative-HES
    • Patients are at increased risk of endomyocardial fibrosis resulting in restrictive cardiomyopathy and should be monitored with echocardiograms

Granuloma faciale
Papuloerythroderma of Ofuji
Well's syndrome
Hypereosinophilic syndrome
Other conditions characterized by a prominent eosinophilic infiltrate
Eosinophilic folliculitis

- **Epidemiology:**
  1. AIDS-associated – low CD4 counts
  2. Eosinophilic pustular folliculitis (Ofuji’s)
  3. Eosinophilic pustular folliculitis of infancy

- **Clinical presentation:** pruritic follicular papules erupting on face, scalp, trunk

- **Treatment:** HAART (increase CD4 count), phototherapy, topical corticosteroids +/- oral antihistamine

- **Histology:** eosinophils around follicles; exocytosis of eosinophils and lymphocytes into follicular epithelium
Angiolymphoid hyperplasia with eosinophils

- **Etiology**: unknown
- **Epidemiology**: young to middle-aged adults; no gender predilection
- **Clinical presentation**: red, pink, or brown papules/nodules, **classically periauricular** or on the scalp/forehead; may be painful
- **Histology**: vascular proliferation with “hobnail” endothelial cells, surrounding eosinophils
- **Treatment**: surgical excision; >30% recur
Kimura’s disease

- **Etiology**: unknown; benign condition
  - Suspected: allergic reaction or alteration of immune regulation
  - Associated with other atopic conditions
- **Clinical presentation**: painless LAD/mass of head and neck
- **Histopathology**: abnormal proliferation vascular endothelium with lymphoid follicles; eosinophilic infiltrate
- **Treatment**: seldom curative; recurrence common
  - Observation
  - Intraleisional or oral steroids
  - Surgical excision
Episodic angioedema associated with eosinophils (Gleich syndrome)

• **Diagnosis requires triad of:**
  1. Hypereosinophilia
  2. Recurrent angioedema
  3. Good response to systemic glucocorticoids

• **Prognosis:** good
  • No organ involvement

• **Treatment:** systemic glucocorticoids to control flares
Eosinophilic fasciitis

• Clinical presentation
  • History of **strenuous physical activity** preceded clinical findings in 30% of cases
  • Classic presentation is symmetric, severe induration and edema of skin, subcutaneous
    • Spares the hands, feet and face
  • Edema and pain → fibrosis, activity limitation
  • The "**groove sign**" refers to linear depressions where veins appear sunken in indurated skin

• Histology
  • Fascia thickened 10-50x normal; dermal fibrosis
  • +/- eosinophils; lymphocytes and plasma cells
Eosinophilic fasciitis

- **Laboratory**: hypergammaglobulinemia, elevated ESR, peripheral eosinophilia

- **Associated diseases**: Chronic GVHD, pancytopenia, anemia, thrombocytopenia, myeloproliferative disorders

- **Associated malignancies**: Hematological malignancies reported
  - Unexplained anemia → BM biopsy

- **Treatment**: prompt; to preserve function
  - First line: oral steroids; dose tapered 6-24mo
  - Improvement may take several months
Toxic oil syndrome

• 1981 – affected more than 25,000 individuals in Spain
• 600 died; 300 others left permanently disabled
• Aniline-processed rapeseed oil $\rightarrow$ systemic inflammatory response
• Genetically-susceptible individuals
• Signs and symptoms
  • Morbilliform eruption $\rightarrow$ LP, morpheaform, or sclerodermoid presentation
  • Flu-like – fever and headache $\rightarrow$ inflammation in CNS, lungs, salivary glands
Eosinophilia-myalgia syndrome

- 1989 – contaminated batches of L-tryptophan in the United States
- >1500 individuals affected; 30 died
- Clinical presentation
  - Severe myalgias, fever, dyspnea
  - Edema
  - Macular exanthem
  - Peripheral eosinophilia
- Chronic phase
  - Diffuse, deep sclerodermoid induration of extremities
  - Progressive peripheral neuropathy, myopathy
Other categories of disease featuring prominent eosinophils

- Drug reactions
- Arthropod assault
- Bullous dermatoses (bullous pemphigoid)
- Urticaria
- Eosinophilic vasculitis (Churg-Strauss)
References

Thank you!