

# NEUTROPHILIC DERMATOSES

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# OBJECTIVES

- A case...
- Describe some neutrophilic dermatoses
- Nauseate the room with photographs 😊
- Treat the case...

# A CASE...

- 49F with T1N2 breast cancer
- Had chemo with taxotere causing neutropenia
- Received G-CSF (Neupogen) during neutropenic state
- Developed progressive bullous, necrotic soft tissue lesion at site of i.v. trauma
- Initially thought to be aggressive cellulitis
- Cultures negative, not antibiotic responsive
- Worsened post-debridement

# Neutrophilic Dermatoses

- Sweet's Syndrome (1964 – Dr. Sweet)
- Pyoderma Gangrenosum (1930 – Dr. Brunsting)
- Erythema Elevatum Diutinum
- Neutrophilic Dermatoses of the Dorsal Hands
- Rheumatoid Neutrophilic Dermatoses
- Subcorneal Pustular Dermatoses
- Neutrophilic Eccrine Hidradenitis

# A SPECTRUM

- **Some people present with overlapping presentations of these conditions**
- **E.g., Sweet's and Pyoderma Gangrenosum**
- **E.g., Pyoderma Gangrenosum and Subcorneal Pustular Dermatitis**

# Commonalities

- Pustules, nodules, plaques, or ulcers
- Neutrophilic infiltrate – can affect all skin layers
- General malaise, fever
- Multi-system: Joint, kidney, lung, eye, etc.
- Cutaneous manifestations of systemic disease

# **SWEET'S SYNDROME**

- **Classical**
- **Idiopathic**
- **Malignancy-associated (20%)**
- **Drug-Induced**

# CLASSICAL

- **Pregnancy (1<sup>st</sup> and 2<sup>nd</sup> trimester)**
- **Inflammatory bowel disease**
- **Post-streptococcal**
- **Upper respiratory tract infection**
- **Yersinia, toxoplasmosis, histoplasmosis, salmonella, tuberculosis**
- **Tonsillitis**
- **Vulvo-vaginal infections**

# MALIGNANCY-ASSOCIATED

- Non-lymphocytic leukemia (AML, CML)
- Lymphoma
- Polycythemias
- Solid tumors: GU, GI, Breast
  
- May pre-date heme malignancy by 3 months to 6 years

# DRUG-INDUCED

- **G-CSF, GM-CSF: at site of infusion or distant sites; even in neutropenic states**
- **Birth control pills**
- **Trimethoprim-sulfamethoxazole**
- **Minocycline**
- **All-trans-retinoic acid (promyelocytic leukemia)**

# SWEET'S DIAGNOSTIC CRITERIA

## Major Criteria

- Abrupt onset of characteristic lesions
- Diffuse neutrophilic infiltration + dermal edema

## Minor Criteria

- Preceded by or associated with described clinical conditions
- Malaise and fever
- ESR >20, CRP +, peripheral leukocytosis, left shift
- Excellent response to systemic corticosteroids
- Both major + 2 minor criteria = diagnosis

# SKIN LESIONS

- Acute, tender, red
- Plaques, nodules, pseudovesicles, blisters, annular/arciform
- Occur on head, neck, legs, arms, dorsum hands/fingers, less frequent on trunk
- No pathergy

# SWEET'S SYNDROME











# CLINICAL PRESENTATION

- **Fever (50%)**
- **Myalgia/Arthralgia/Arthritis (62%)**
- **Eye involvement (38%)**
- **Oral aphthous ulcers (13%)**
  
- **A recurrent condition**

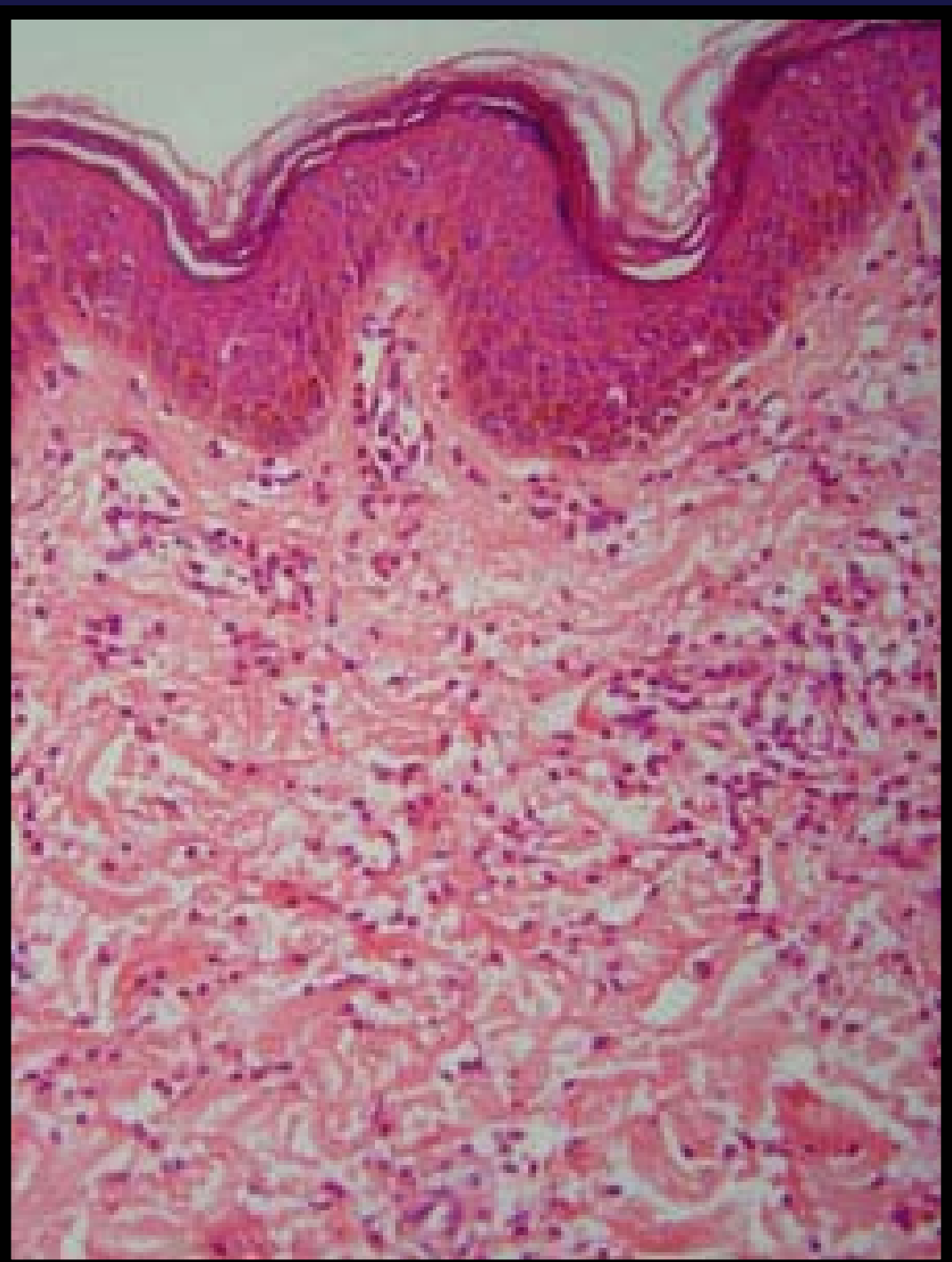
# LABS

- **Moderate leukocytosis**
- **Elevated ESR**
- **Slightly elevated ALP**
- **ANCA positive in some**

# SKIN BIOPSY

- **Papillary and mid dermal edema**
- **Neutrophilic infiltrate with nuclear fragmentation**
- **No vasculitis in early lesions, but can occur**

# SWEET'S SYNDROME



# SECONDARY CAUSE

- Age > 50
- Anemia
- Thrombocytopenia
- Bullous or necrotic lesions

# TREATMENT

- Underlying cause
- Prednisone 1mg/kg/d x 2-6 weeks
- Topical/Intralesional a possibility
- Fever, leukocytosis, new skin lesions should subside within 72 hours
- Skin lesions clear in 3 to 9 days with residual milia or scar
- Alternates: Potassium iodide, colchicine, indomethacin, dapsone, CsA

# PYODERMA GANGRENOSUM

## Inflammatory Associations

- IBD (UC & Crohn's), Sarcoid, RA, Chronic/active hepatitis (HCV), Takayasu, HIV, SLE, PAPA syndrome (Pyogenic arthritis, PG and acne)

## Pregnancy

## Malignancy

- Non-lymphocytic leukemias (AML, CML), Polycythemias, Myeloid metaplasia, IgA monoclonal **gammopathy**

## Drug

- G-CSF, GM-CSF, IFN, anti-psychotics

## Idiopathic (50%)

# SKIN LESIONS

- Tender, red
- Macule, papule, pustule, nodule, bullae
- Usually start as papulopustules (not plaques like Sweet's). Pustular especially in IBD.
- Surrounding halo
- Necrotizing extends peripherally to form necrotic ulcer with purulent base and purple margin and surrounding erythema
- Small lesions may fuse together
- Usually <10cm but may increase with pathergy
- Also heal with scar
- Can be confused with Erythema Nodosum and Sweet's early on

# ERYTHEMA NODOSUM



# PYODERMA GANGRENOSUM



















# CLINICAL PRESENTATION

- **Post-trauma (pathergy)**
- **Recurrent lesions (30%)**
- **Seronegative large joint arthritis (40%)**
- **Distal legs most common, but can be anywhere**
- **In IBD usually appears 5-10 years into disease course**

# DIFFERENTIAL DIAGNOSIS

- Vasculitis
- Venous disease
- Factitial
- Spider bite
- Infections: deep fungal, mycobacteria, syphilis, gangrene, amebiasis
- “ulcerating lesions”

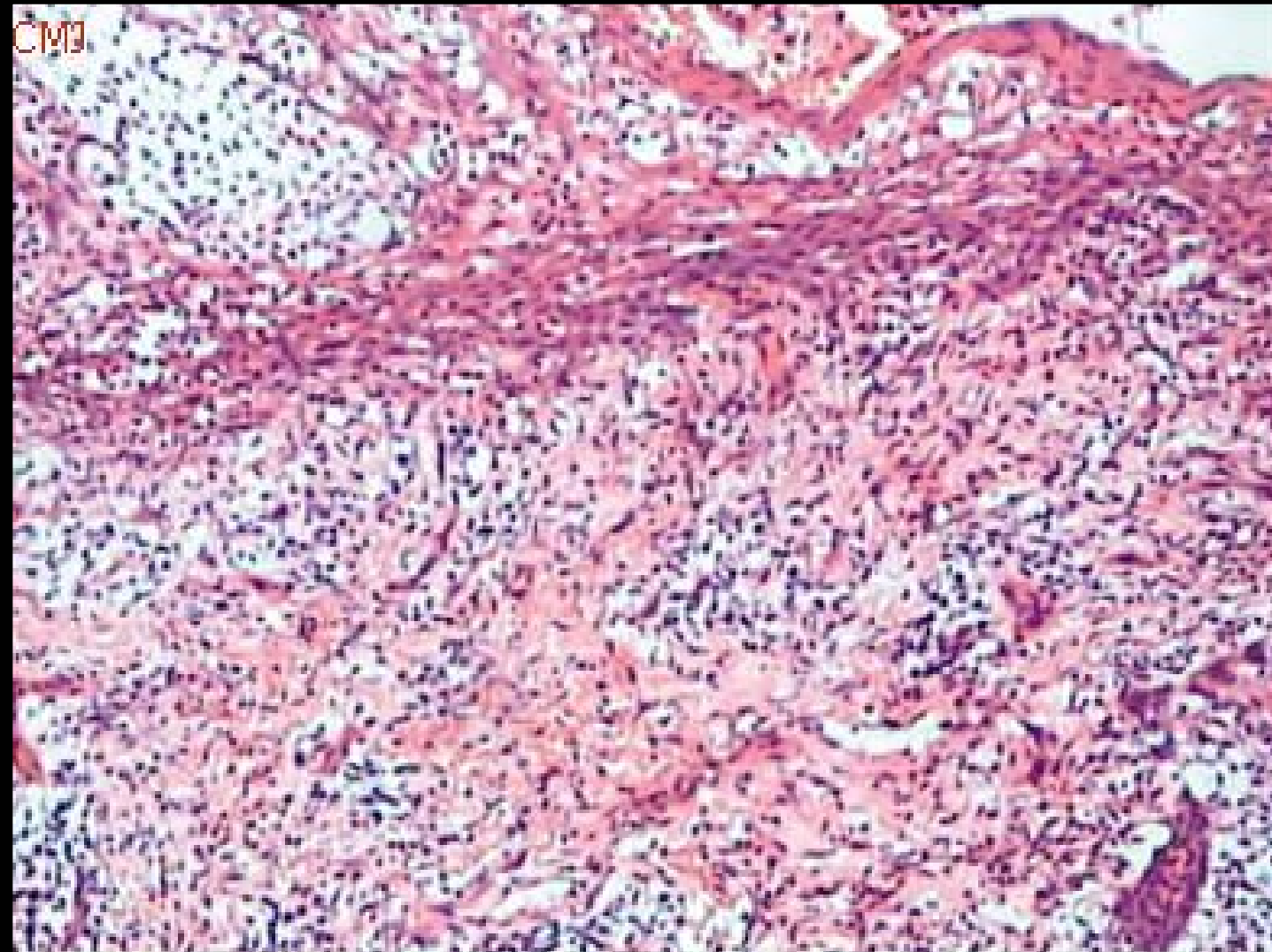
# LABS

- Not very helpful
- Less systemic symptoms than Sweet's
- SPEP etc. if suspect monoclonal gammopathy
- ANCA negative
  
- Historically, overlapped with “Malignant Pyoderma” which is C-ANCA positive—later considered to be cutaneous Wegener's Granulomatosis

# SKIN BIOPSY

- Evolves from suppurative folliculitis to form sterile abscess
- Dermal edema
- May involve subcutaneous fat
- +/- leukocytoclastic vasculitis (late)
- Suppurative granulomatous dermatitis
- Findings are not diagnostic. Need to rule out infectious etiology.

# PYODERMA GANGRENOSUM



# TREATMENT

- Underlying cause
- Avoid trauma
- Topical/Intralesional steroid to abort early lesions
- Corticosteroids (1 mg/kg/d) x 3-4 weeks, plus CsA (if steroids ineffective) are first-line agents
- Infliximab first-line in IBD
- Reports of azathioprine, MMF, cyclophosphamide, IVIG, chlorambucil
- Thalidomide (in overlap with Behcet's)

# TREATMENT

- Drug effect is independent of underlying cause
- Occlusive dressings to avoid infections
- No role for surgery

# EXTRACUTANEOUS PYODERMA GANGRENOSUM

- Joints
- Lungs (patchy infiltrates, interstitial pneumonitis)
- Heart
- GI, oropharyngeal
- Spleen
- Liver
- Eye
- Glans penis

# BACK TO THE CASE...

- **Diagnosis: Pyoderma Gangrenosum**
- **Secondary to skin trauma (pathergy) and G-CSF therapy**
- **Treatment: Prednisone 1 mg/kg/d x 4 weeks, then taper by 5mg q week**
- **Lesion began to regress within 24 hours**

# SUMMARY

- Neutrophilic dermatoses are a spectrum of disorders with overlapping disease associations and pathological features.
- One must consider pyoderma gangrenosum in the case of a spreading 'sterile' ulcer.
- Look at the big picture. What drugs was the patient on?
- Consult dermatology/plastics early to look for characteristic morphology before attempting debridement etc.
- Typically responsive to corticosteroids, but must search for underlying cause.

# REFERENCES

- Reichrath et al. Treatment recommendations for pyoderma gangrenosum: An evidence-based review of the literature based on more than 350 patients. *JAAD* 2005; 53: 273.
- Andrews et al. *Diseases of the Skin. Clinical Dermatology.* 2006.
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