From Cellulitis to Crohn’s: 
The Cutaneous Clues that Led Us 
to the Correct Diagnosis

Pediatric Resident Grand Rounds
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Identification #1

A) Eczema Superinfection
B) Erysipelas
C) Contact Dermatitis
D) Vasculitis

Identification #2

A) Contact dermatitis
B) Urticaria
C) Severe atopic dermatitis
D) Cellulitis

Identification #3

A) Eczema Superinfection
B) Cellulitis with abscess formation
C) Pyoderma gangrenosum
D) HSP

http://www.uptodate.com/contents/image?imageKey=GAST%2F52528&topicKey=DERM%2F5571&rank=1%7E34&source=see_link&search=neutrophilic+dermatosis&utdPopup=true
What was the point of that?

- ALL are on the SKIN
- ALL look RED
- ALL look BAD
- So how do we diagnose them?
  - Back to the basics!
Case Presentation- HPI

- 14 yo female sent from clinic for evaluation of weeping leg lesions
- Red bump on back of left leg 3 months prior
  - Drained spontaneously → Spread to both legs
  - Dermatology → Clindamycin
- 2 weeks prior to presentation, increase number of lesions
  - Became ulcerated
  - BCx at OSH, Clinda + Orapred 5mg po qd
Case Presentation - ROS

• **General**: No weight loss or gain
• **HEENT**: No oral ulcers, no vision changes, no photophobia
• **CV**: No palpitations, no chest pain
• **Resp**: No shortness of breath, no cough
• **FEN/GI**: 3 “soft” BMs/day, non-bloody
  • Watery diarrhea daily x months
• **Heme**: No pallor, no bleeding, has not started menstrual cycle
• **ID**: No fevers, + skin lesions
• **Musculoskeletal**: + intermittent knee swelling
• **Neuro**: No headaches, no weakness
• **Social**: lives with mom/dad, does well in school, denies drugs or alcohol
Case Presentation- PMHx

- **Heme/Onc: IDA of unknown etiology**
  - Iron supplementation: 120 mg elemental Fe BID
  - Alpha-thalassemia trait
  - BMA/Bx due to lack of improvement with Fe

- **Allergy/Immunology:**
  - Eczema: Tx with TAC
  - Persistent Asthma: Flovent, Albuterol prn
  - Allergies: Seafood

- **Rheumatology:**
  - Knee swelling, rash
  - Elevated inflammatory markers
  - +ANCA 1:80, Negative CT chest
    - Perinuclear ANCA usually assoc. with IBD
Case Presentation- Family History

• Family History
  • Maternal great aunt- Lupus
  • Maternal GM: Type II DM
  • Multiple family members: IDM
  • Dad: Asthma

• Medications:
  • Orapred 5mg po qd, Albuterol prn

• Allergies: shellfish, PCN
Case Presentation - Physical Exam

**Temperature (T)**: 98.1°F

**Pulse (P)**: 111 bpm

**Respirations (R)**: 20/min

**Blood Pressure (BP)**: 99/45 mmHg

**Weight (Wt)**: 36.6 kg (<5%)

**Height (Ht)**: 152 cm (8th %)

**BMI**: 15.84 (<5%)

- **Gen**: Thin, no distress

- **HEENT**: Temporal wasting, OP clear, ? Saddle nose deformity

- **CV**: Tachycardic, + II/VI SEM

- **Resp**: CTA B

- **Abd**: Soft, ND, NTTP

- **Musculoskeletal**: R knee larger than left, no erythema or warmth, FROM, NTTP

- **GU**: Tanner II, perianal fissure, skin tag
Dermatologic Exam

**L Leg:** 12 x 14 hyperpigmented area
  - Multiple punched out, healing ulcers

**R Leg:** 15 x 7 cm hyperpigmented area
  - Posterior pustular leg lesions, dusky borders, multiple firm shin nodules
Initial Lab Evaluation

ESR 79
CRP 11.1
Fecal calprotectin 1323 ug/g
   (<50 ug/g)
Albumin 2.5

Blood Cx: No growth
Wound Cx: No growth

FOBT: +
Dermatologic Evaluation

• Punch biopsies
  • Left: chronic active folliculitis with deep dermal granuloma
  • Right:
    • Dermal necrotizing suppurative inflammation with chronic active vasculitis, mild
    • Diffuse infiltrate of neutrophils, histiocytes, and lymphocytes → pyoderma gangrenosum
    • DDx: Sweet’s Syndrome; lacks nuclear destruction
    • Epidermal neutrophilic invasion and bullae formation
GI Evaluation

- **EGD:** normal
- **Colonoscopy:**
  - **Right colon**
    - Isolated site of erythematous, ulcerated colon amidst normal colon
  - **Transverse Colon**
    - Decreased disease, mild erythema
  - **Rectum, Sigmoid, & Descending Colon**
    - Erythema with friability, pus exudate, mucosal thickening

- **Pathology:**
  - **Right and transverse colon**—eosinophilia, lymphoid hyperplasia
  - **Left colon**—marked chronic active colitis with erosions and ulcerations
Colonoscopy Picture Examples

www.endoatlas.org

www.endoatlas.org
Diagnosis/Treatment

- **Diagnosis:** IBD
  - Crohn’s Disease
  - Pyoderma Gangrenosum

- **Treatment:**
  - IV corticosteroid, Remicade®, wound care
Objectives

• Become familiar with some extraintestinal manifestations of IBD
• Recognize some common neutrophilic dermatoses
• Know how to diagnose PG
• Understand treatment in PG
Extraintestinal Manifestations may find your practice!
EIM

- Involve almost every organ system
- Affect 6-47% of patients
  - Possibly higher in pediatrics
- Pathogenesis not always clear
  - Immunologic
    - Immunologic derangements → IBD
    - IBD pts have increased risk of AI diseases
  - Genetic
Growth Failure

- 15-40% of children
  - More common in CD than UC

- Z-score
  - Mean height for CD at diagnosis -0.54
  - Mean weight for CD -1.06
    - ~30% have Z-scores <3rd %
  - Mean weight for UC -0.32

- Why?
  - Discomfort eating
  - Proinflammatory cytokines \(\rightarrow\) GH resistance and decr. IGF-1 production
  - Small bowel inflammation \(\rightarrow\) PLE
  - Fat malabsorption & ADEK deficiency
  - High dose corticosteroids
Ophthalmology

- Ophtho conditions often seen in conjunction with arthritis & erythema nodosum
- Episcleritis
  - 2-5% of patients
  - Painless hyperemia of sclera and conjunctiva
  - No loss of vision
- PE:
  - Injection of ciliary vessels
  - Inflammation of episcleral tissues
- Tx:
  - Topical glucocorticoids

http://www.hopkinsmedicine.org/wilmer/conditions/episcleritis.html
Ophthalmology- Uveitis

- 0.5-3%
- Bilateral, posterior to lens
- Insidious onset, chronic
- F >>>> M
- 75% associated arthritis
- Acute or subacute onset of eye pain, blurred vision, photophobia, headaches, iridospasm
- **PE**: slit-lamp exam: inflammation in anterior chamber, corneal clouding
- **Tx**: topical or systemic steroids, covering eye
Oral Cavity

Aphthous stomatitis

• 5-10% in UC, 20-30% in CD

• Lesions parallel disease activity

• Swelling, cobblestoning of mucosa, tag-like mucosal lesions

• Tx: systemic or local corticosteroids

Liver

- Nonspecific mild elevations of aminotransferases
- Cholelithiasis (CD > UC)

**Primary Sclerosing Cholangitis (PSC)**
- Small bile duct inflammation → pericholangitis → PSC
- 3% of children and adolescents
- **Symptoms:** Fatigue, pruritus, intermittent jaundice
  - Increased risk of hepatobiliary cancer and AI disease; “overlap syndrome”
- **Diagnosis:** GGT, Alk phos, ERCP, Liver biopsy, IgG, anti-smooth muscle Ab +, anti-nuclear Ab +
- **Treatment:**
  - Ursodeoxycholic acid improves lab values
Joints

- Arthritis: within first few years of dx
  - 2x as common in CD
  - Colitis > gastroduodenal
  - Nonerosive & Asymmetric
    - Large joints: knees > ankles > hips > wrists > elbows
      - Parallel activity of intestinal involvement
    - Axial skeletal involvement (ankylosing spondylitis, SI arthritis)
      - Independent course
- Arthralgias in 17%
- Enthesopathy is frequent
- Hypertrophic osteoarthropathy- clubbing (10-30%)
Bones

- Osteopenia 41% of children with CD and 25% in UC
- Interference with bone production
  - Poor diet
  - Hypogonadism (absent menses)
  - Inadequate calcium intake or malabsorption
  - Vitamin D deficiency
  - Excessive cytokine production
  - Corticosteroid use
- Acceleration of bone loss
  - Prolonged bed rest
  - Corticosteroid use
- Secondary hyperparathyroidism
  - Vit D and calcium deficiency
Hematology

- Venous thromboembolism
  - 1-2% of hospitalized patients
  - Increased risk with CVL, severe disease, older age, PN, oral contraceptives, inherited thrombophilia
  - Prophylaxis for:
    - Severe IBD + hx of thromboembolism
    - Severe IBD + CVL, h/o familial thromboembolism, immobility
    - All: adequate hydration, mobilization, compression stockings

- Anemia
  - 50% of patients
  - IDA, B12, FA, malnutrition, hemolysis, BM suppression (AZT), chronic blood loss, anemia of chronic disease

- Thrombocytosis
  - 50% of patients
Cutaneous Manifestations

- There are many!
- We will discuss:
  - Erythema Nodosum
  - 2 Neutrophilic Dermatoses
    - Sweet Syndrome
    - Pyoderma Gangrenosum
Erythema Nodosum

• CD > UC (3%)
• Reflects increasing bowel activity
• Single or multiple tender, red or purple-blue nodules on LE extensor surfaces
  • Pretibial area
  • 1-5cm
• Histology:
  • Neutrophilic perivascular reaction w/ dermal panniculitis
  • Normal epidermis
• 75% of pts develop arthritis
• Tx: treat the IBD
Erythema Nodosum

Neutrophilic Dermatoses

- Histology: epidermal and/or dermal inflammatory infiltrates
  - Neutrophils
  - No evidence of infection

- Classification based on:
  - Clinical and pathologic features
  - Identification of associated diseases

- Pathogenesis: unknown; possibly immunologic
  - Respond to glucocorticoids and immunomodulatory therapies
Sweet Syndrome

- Acute febrile neutrophilic dermatosis – Dr. Robert Douglas Sweet 1964

- 4 primary features:
  1. Cutaneous eruption consisting of erythematous plaques and papules
     - Plaques have central yellowish discoloration (target-like)
     - Face, neck, UE (dorsum of hands)
     - Can be painful
  2. Histology: dermal nonvasculitic neutrophilic infiltration
  3. Fever
  4. Neutrophilia
Sweet Syndrome cont.

- **Associated with:**
  - IBD
  - Malignancies (AML, solid tumors)
  - Infections (URI & GI)
  - Drugs
  - Autoimmune diseases
  - Pregnancy

- **Tx:** systemic/high-potency topical corticosteroids, potassium-iodide
Sweet Syndrome

http://www.uptodate.com
Pyoderma Gangrenosum

- **Rare**: 3-10 cases/1 million people per year
  - Young and middle-aged adults, F > M
  - IBD: <1% of patients; UC > CD
- >50% associated with underlying systemic disease
  - IBD, hematologic disorders or malignancies, arthritis, PAPA syndrome
- **Pathophysiology**: dysregulation of immune system
- **DDx**: antiphospholipid-Ab syndrome, venous stasis ulcers, Wegener’s, PAN
Pyoderma Gangrenosum Subtype #1

• Ulcerative (classic)
  • Erythematous pustule or nodule → spreads peripherally → degenerates centrally → ulcer w/ violaceous border & purulent base
  • Ulcers are sterile
  • Ulcers extend to SQ tissue
  • Extensor surfaces of LE
Pyoderma Gangrenosum Subtype #2

- Bullous (atypical)
  - Related to hematologic disease
  - Rapid development of blue-gray, inflammatory bullae → erode → ulcers
  - Arms and face

Pyoderma Gangrenosum Subtype #3

- Pustular PG
  - Acute exacerbations of IBD
  - Rapid development of pustules surrounded by erythema
  - Fever + arthralgias
Pyoderma Gangrenosum Subtype #4

• Vegetative
  • “superficial granulomatous pyoderma”
  • Localized, solitary, superficial form of PG
  • Indolent, mildly painful nodule, plaque, or ulcer
  • Verrucous quality
  • Head and neck

www.uptodate.com
Pyoderma Gangrenosum Diagnosis

- **Major criteria (must have both)**
  - Rapid progression of painful, necrolytic, cutaneous ulcer
    - Irregular, violaceous, undermined border
    - 1-2 cm/day or 50% increase in size in 1 mo.
  - Other causes of cutaneous ulceration excluded

- **Minor criteria (must have two)**
  - History suggestive of pathergy or finding of cribiform scarring
  - Systemic disease associated w/ PG
  - Histopathologic findings
  - Treatment response (rapid response to systemic glucocorticoids)
Cribiform Scarring

http://www.uptodate.com/contents/image?imageKey=GAST/52528&topicKey=DERM/13782&source=outline_link&search=pyoderma%20gangrenosum&utdPopup=true
Pyoderma Gangrenosum Dx Cont.

• Biopsy
  • Include inflamed border and ulcer edge extending to SQ fat
  • Earliest lesions: perifollicular inflammation and intradermal abscess
  • Ulceration: epidermal and superficial dermal necrosis, mixed inflammatory cell infiltrate, lymphocytic vasculitis

• Labs/Studies to consider
  • CBC, CMP, ANA, ANCA, Hep panel, RF, colonoscopy
PG Treatment

- Wound care; beware of pathergy!

- Mild disease:
  - Local corticosteroids or calcineurin inhibitor

- Extensive disease:
  - Systemic glucocorticoids or systemic cyclosporine
    - 0.5-1.5mg/kg/day (max 60mg) oral prednisone or pulse IV steroids
    - Taper once progression has stopped + improvement; within 4-10 weeks
      - + glucocorticoid-sparing agent: cyclosporine, azathioprine, infliximab
  - Infliximab

- Severe, refractory disease
  - IVIG or alkylating agents

- Recurrent lesions 30%
**Infliximab for the treatment of pyoderma gangrenosum: a randomised, double-blind placebo-controlled trial**

- Brooklyn et. al
- Multicenter, randomized, placebo controlled trial
- 30 patients with PG; 19 with IBD
- Infliximab 5mg/kg or placebo infusions at week 0
- Physician & patient assessment of appearance of lesion at weeks 2, 4, & 6
  - Reduction in size, depth, and degree of undermining
  - Week 2:
    - 46% (6/13) of pts tx w/ infliximab had response compared to 6% (1/17) placebo
    - Subjects in both arms offered infliximab
      - 69% (20/29) had positive response by week 6
    - No difference in response between PG pts with underlying IBD
Progress Prior to Discharge
Continued improvement!!!
Take Home Points!

• Not all that’s red is cellulitis
• ALWAYS take a good history
• If you suspect a neutrophilic dermatosis, search for underlying disease
Special Thanks!

- Dr. Brown - Rheumatology
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References


