



Clinical Pathology Conference

A 34 year old woman with “cellulitis”

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Today's speaker has no conflict of interest to disclose.

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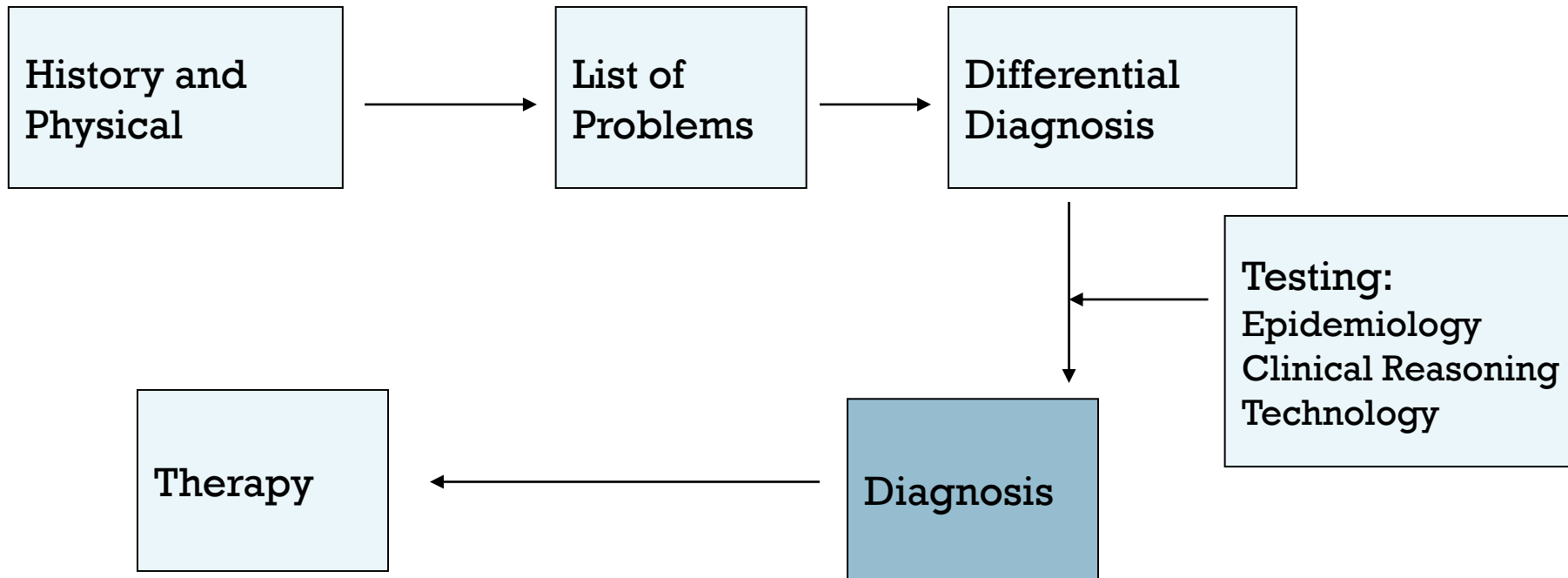
Goals of the talk



- Model clinical reasoning and self directed learning
- Emphasize a mechanistic approach to understanding key findings
- Discuss the differential diagnosis for the key findings
- Share some pearls along the way



The sequential process of making a diagnosis



+ Road Map



- Review of the protocol
- Development of a problem list
- Discussion of key clinical findings
- Review and discussion of the differential
- Selection of the final diagnosis



Case: HPI



- 34 yo AAF with ulcerative colitis:
 - 2d history of F/C with right hand pain and swelling
 - Started initially at fourth digit and progressed to include wrist
 - Now entire area erythematous and painful
 - Small scattered macules progressed to pustules on both upper extremities



Case: HPI--Continued



- Similar, less severe skin eruptions X 3 yrs.
 - Usually preceded by fever and arthritis
 - Never sought care for these episodes, as they were relatively asymptomatic, resolving in 1-2 weeks.
- ROS notable for:
 - Arthralgias-- chronic, but worse with recent illness.
 - Pruritis—chronic
 - 8 non-bloody, non-bilious episodes of diarrhea daily



Case: PFSH



■ PMH:

- Ulcerative Colitis- Diagnosed 2003
- Primary Sclerosing Cholangitis with mild fibrosis (recent biopsy due to chronic AP elevation)

■ PSH:

- Gastric Bypass (laparoscopic Roux-en-Y) Feb. 2004
 - Complicated by mesenteric volvulus and bowel ischemia → resection of ~12 cm of small bowel
- Cholecystectomy- 2006
- C-section x3- uncomplicated



Case: PFSH



- **Allergies:** Metronidazole
- **Meds:** Mesalamine, Zolpidem, B12, MVI
- **Social:**
 - No tobacco, alcohol, or drug use
 - Married with 4 children
 - Currently in nursing school
 - Monogamous with her husband/no prior high risk sexual behavior
- **Family Hx:** Father with Crohn's disease



Case: Physical Exam



- **VS:** T97.8F HR84 BP102/59 RR20 O2sat 96% on RA
- **GEN:** WD/WN AAF in NAD.
- **HEENT:** PERRL, EOMI, Anicteric Sclera, No Conjunctival Pallor, OP Benign with MMM
- **NECK:** supple. No lymphadenopathy, JVD, or thyromegaly.
- **CHEST:** CTAB CV: RRR. No murmurs, rubs, or gallops
- **ABD:** soft, ND, NT NABS
- **NEURO:** no focal deficits



Case: Physical Exam



■ MSK:

- Active synovitis to right 3rd, 4th PIPs and right wrist.
- Extension to digits three, four, and five is limited, secondary to pain

■ SKIN:

- 1 cm pustule over PIP with erythematous halo.
- Erythema extends from tip of fourth digit proximally to mid forearm.
- Scattered pustules with erythematous base are noted to extensor surfaces of BUE

+

Case: Basic Labs



137	107	3	72
3.4	26	0.5	

Anion Gap=4 (9 corrected)

7.5	11.8	407
	34	

Diff 50P/38L/7M/5E

LFTs:

Normal except AP- 1050

TP 6.4/Alb 2.4



Case: Imaging



■ **X-ray, Right hand:**

- The joint spaces are within normal limits
- There is moderate soft tissue swelling, predominantly along the dorsum of the hand
- No erosions



A diagnostic test was performed
and a diagnosis was made.

Background History

Gastric Bypass surgery (2004)

Surgical complications:

bowel ischemia and volvulus,
resection of small bowel
(2004??)



Cholecystectomy (2006)

PSC Diagnosis (“recent”)

UAB admission (2011)

Ulcerative Colitis Dx (2003)

History of Present Illness

Diarrhe

Worsening arthralgias

Fevers and Chills

Pain, redness and swelling of 4th digit → whole hand/wrist

Scattered macules on hand → Pustules all over both upper extremities

2 days

1 days

UAB admission

Intermittent episodes of similar skin eruptions, preceded by fever and arthritis-(1-2wks)

Diarrhea

Worsening arthralgias

Fevers and Chills

Gastric Bypass surgery (2004)

Surgical complications:
bowel ischemia and volvulus,
resection of small bowel
(2004??)

Pain, redness
and swelling
of hand

Pustular rash
over both upper
extremities

3 years

2 days

1 days

UAB
admission

Cholecystectomy (2006)

PSC Diagnosis ("recent")

Ulcerative Colitis Dx (2003)



Initial Distillation of Findings



- Synovitis of the hand (finger → wrist)

- Additive?
- Asymmetric, distal involvement

- Systemic symptoms:

- Fever/chills
- Worsening Arthralgias
- Diarrhea

History

- Pustular rash over BUEs (also started on hand)

- PMH: UC, Recently diagnosed PSC, Gastric Bypass

- Pustule over PIP with erythematous halo

PE

- Confluent erythema from tip of fourth digit to mid forearm.

- Scattered pustules with erythematous base, extensor surfaces BUE

- Active synovitis of 3rd and 4th PIPs and wrist on same hand

- Limited extension of digits

+ Initial Distillation of Findings

- Labs only notable for:
 - Chronically elevated Alk Phos
 - Hypoalbuminemia

Diagnostic Tests

- Hand Xray: moderate STS, negative for erosions

+ Simplified Problem List

- Additive Inflammatory Polyarthrititis of Right hand
- Pustular rash over BUEs
- Systemic symptoms (F/C, arthralgias, diarrhea)
- History of IBD (UC) and Gastric Bypass
- Recently diagnosed Sclerosing Cholangitis

+ PEARLS for the approach to polyarthrititis



Severe, prolonged morning stiffness, swelling in multiple joints, fatigue, weight loss, or fever suggests a systemic inflammatory process.

+ PEARLS for the approach to polyarthrititis



History and physical examination findings are much more important than laboratory findings in establishing the diagnosis in a patient with inflammatory polyarthrititis.

Initial Clinical Characterization of Arthritis

Clinical feature	Variable		
Duration	Acute (hours to days)	Chronic (\geq weeks)	
Number of joints involved	Monoarticular	Oligoarticular (2-4)	Polyarticular(\geq 5)
Pattern of involvement	Symmetric or asymmetric	Additive or Migratory	
Inflammation	Yes	No	
Constitutional symptoms	Yes	No	
Extra-articular disease	Yes	No	
Comorbid conditions	Yes	No	

Initial Clinical Characterization of Arthritis

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Comorbid conditions	Yes	No	



Initial Clinical Characterization of Arthritis: **OUR PATIENT**



Clinical feature	Variable
Duration	Acute (hours to days)
Number of joints	Oligoarticular (2-4)
Pattern	Asymmetric and Additive
Inflammation	Yes
Constitutional sx's	<ul style="list-style-type: none">•Fever•Diarrhea•Arthralgias (other joints)
Extra-articular dz	Pustular skin lesions
Comorbid conditions	IBD, PSC Gastric Bypass

+ DDX: ACUTE OLIGOARTHRITIS



Infection	Postinfection	Spondyloarthropathy	Other
DGI	Reactive arthritis	Reactive Arthritis	Oligoarticular presentation of RA, SLE, Stills, Relapsing Polychondritis etc.
Septic arthritis	Rheumatic Fever	Ankylosing Spondylitis	Gout
Bacterial endocarditis		Psoriatic Arthritis	Pseudogout
Viral		IBD associated arthritis	

+ DDX: Chronic OLIGOARTHRITIS



Common	Uncommon or Rare
Spondyloarthropathy <ul style="list-style-type: none">•Reactive Arthritis•Ankylosing Spondylitis•Psoriatic Arthritis•IBD associated arthritis	Bacterial Endocarditis (SBE)
Early Disseminated Lyme Dz.	Sarcoidosis
Rheumatoid Arthritis (atypical)	Bechet's disease
Gout	Relapsing Polychondritis
	Secondary Syphilis
	Celiac disease



Fever and ARTHRITIS



Active infection	Not due to active infection
Septic arthritis	SLE/Drug-induced lupus
Disseminated gonococcal infection	Still disease
Endocarditis	Gout/Pseudogout
Acute viral infections	Reactive arthritis (esp. early phases)
Mycobacterial	Acute rheumatic fever (post-strep)
Fungal	Inflammatory bowel disease
	Acute sarcoidosis
	Systemic vasculitis
	Familial Mediterranean Fever
	Paraneoplastic arthritis

+ IBD associated arthritis

- Arthritis occurs in 9 to 53 percent of patients with IBD.
 - More likely to occur in patients with large-bowel disease and in those patients with complications
 - Males and females are affected equally
 - Subclinical gut inflammation, documented by endoscopy, has been described in up to 2/3 of pts. with spondyloarthropathies
- Manifestations:
 - Spondylitis/sacroiliitis
 - Type I peripheral arthritis --acute and remitting (knee)
 - Type II peripheral arthritis--chronic problem with frequent relapses (MCP, multiple)





Other Diseases: Bowel And Joint Involvement



- Reactive arthritis
- Whipple's disease
- Behcet's disease
- Celiac disease
- Intestinal bypass arthritis
- Parasitic rheumatism
- Pseudomembranous colitis



working DIFFERENTIAL



- Reactive Arthritis
- IBD associated arthritis
- Psoriatic arthritis
- Disseminated Gonococcal Infection
- Others:
 - Behcet's
 - Secondary Syphilis
 - ?Intestinal Bypass arthritis

+ PEARLS for the approach to polyarthriti



Extra-articular manifestations often provide definitive diagnostic information in a patient with polyarthriti, particularly ocular and dermatologic involvement.

+ Simplified Problem List

- Additive Inflammatory Polyarthrititis of Right hand
- Pustular rash over BUEs
- Systemic symptoms (F/C, arthralgias, diarrhea)
- History of IBD (UC) and Gastric Bypass
- Recently diagnosed Sclerosing Cholangitis

+ Pustular skin lesions

- Pustules are **elevated skin lesions containing collections of purulent fluid.**
- Papules or vesicles (clear fluid) are common; pustules occur less frequently
- Differential diagnosis of pustules is broad
- Key distinguishing features:
 - The patient's age and general health
 - The distribution of lesions
 - The duration of the lesions



Differential diagnosis of pustules

Acne rosacea/perioral dermatitis
Acne vulgaris
Arthropod bite (fire ants)
Drug eruption
Eosinophilic folliculitis
Erythema toxicum neonatorum
Folliculitis
Fungal or yeast infections (especially tinea capitis and Majocchi's granuloma)
Furunculosis
Gonorrhea (disseminated)
Herpes simplex/zoster
Impetigo
Keratosis pilaris
Neonatal pustulosis
Pseudofolliculitis barbae
Pustular psoriasis
Pyoderma gangrenosum
Syphilis
varicella

+ Pustules With Fever (or other Systemic Symptoms)

- **Varicella**
- **Medications (AGEP, others)**
- **Disseminated gonococemia**
- **Secondary syphilis**
- **Pyoderma gangrenosum**
- **Deep fungal infections**
- **Pustular psoriasis**

Disseminated gonococcal infection



Typical small postular skin lesion in a patient with disseminated gonococcal infection.

Courtesy of Don L Goldenberg, MD.

+ Disseminated Gonococcal Infection

Pros

- Pustular skin lesions in extremities
- Fever, arthralgias
- Young adult, female
- Migratory polyarthrititis
 - often involving hands/feet

Cons

- Limited # of pustules
 - Rarely >40, usually 2-10
- Lack of tenosynovitis
- Localized involvement
- No known exposure (monogamous etc.)
- Prior similar milder episodes

+ Neutrophilic Dermatoses

- Group of disorders characterized by recruitment of PMN leukocytes to various layers of the skin
 - Histology: intense epidermal and/or dermal inflammatory infiltrates composed of neutrophils without evidence of infection
- Cutaneous findings are variable
 - Vesiculopustules, plaques, nodules, or ulcerations
- Lesions may be localized or widespread
 - Depends on underlying disorder

+ Neutrophilic Dermatoses

- Extracutaneous involvement may be present
- Pathogenesis unknown. It is believed that these disorders represent a state of altered immunologic reactivity.
- Frequently associated with underlying conditions
 - Malignancy, infections, autoimmune, IBD, meds etc.



The non-infectious neutrophilic dermatoses without vasculitis

Involving predominantly the epidermis
Pustular psoriasis
Drug-induced/acute generalized exanthematous pustulosis
Keratoderma blennorrhagicum
Sneddon-Wilkinson disease (subcorneal pustulosis)
IgA pemphigus (subcorneal pustular dermatosis type, intraepidermal neutrophilic IgA dermatosis type)
Antimicrobial pustulosis of the folds
Infantile acropustulosis
Transient neonatal pustulosis
Involving predominantly the dermis
Sweet's syndrome
Pyoderma gangrenosum
Behçet's disease
Bowel-associated dermatosis-arthritis syndrome
Inflammatory bowel disease (may also have small vessel vasculitis)
Neutrophilic eccrine hidradenitis
Rheumatoid neutrophilic dermatitis
Neutrophilic urticaria
Still's disease
Erythema marginatum
Hereditary periodic fever syndrome

Data from: Moschella, SL, Davis, MDP. Neutrophilic dermatoses. In: *Dermatology, 2nd ed*, Bologna, JL, Jorizzo, JL, Rapini, RP (Eds), Mosby Elsevier, Spain 2008.

Classification of neutrophilic dermatoses associated with arthropathy

Papulopustular dermatosis
Generalized pustular psoriasis
Subcorneal pustulosis
Reactive arthritis
Bowel associated dermatosis-arthritis syndrome
Palmoplantar pustulosis
Dermal and subcutaneous infiltration with or without ulceration
Sweet's syndrome
Behcet's disease
Rheumatoid neutrophilic dermatosis
Pyoderma gangrenosum

+ Sweet's syndrome



- The prototype of the neutrophilic dermatoses
 - In 1964, Sweet described 8 female patients with acute onset of:
 - Fever, leukocytosis, and erythematous plaques infiltrated by neutrophils
 - He called the disorder acute febrile neutrophilic dermatosis
- Rare disorder with striking female predominance (4:1)
- Associated with underlying disease in as many as 50%
 - 20-25% have malignancy
 - IBD (Crohn's and UC)

Proposed diagnostic criteria for Sweet's syndrome*

Major criteria
Abrupt onset of typical cutaneous lesions
Histopathology consistent with Sweet's syndrome
Minor criteria
Antecedent fever or infection
Accompanying fever, arthralgia, conjunctivitis, or underlying malignancy
Leukocytosis
Good response to systemic corticosteroids and no response to antibiotics

* Two major and two minor criteria are needed for diagnosis.
Adapted from Su, WP, Liu, HN, Cutis 1986; 37:167.

+ Sweet's syndrome: Cutaneous findings



- Tender erythematous plaques and papules
 - Plaques are usually a few centimeters in diameter
 - May have a central yellowish discoloration, creating a target-like appearance.
 - Lesions may progress to vesicles and bulla formation
 - Pustules can also be seen
- Distribution: most often found on the face, neck, and upper extremities, especially the dorsum of hands, but can occur anywhere

Sweet's syndrome



A brightly erythematous plaque with a pustular component is visible on this patient with Sweet's syndrome.
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Sweet's syndrome: Plaque



+ Sweet's Syndrome

Pros

- Pustular skin lesions
- Fever, arthralgias
- Predilection for UEs
- Strong female predilection
- Association with IBD
- Inflammatory arthritis

Cons

- Lesion characteristics (large plaques)
- Lack of signs of inflammation on labs (often ↑WBC, ESR etc.)
- Previous milder episodes

+ Pyoderma Gangrenosum

- Ulcerative disease of the skin of unknown origin.
 - Significant morbidity: up to 50% of pts. require long term treatment to prevent recurrences
- Earliest clinical lesion: pustule with an inflammatory base, an erythematous nodule, or hemorrhagic bulla on a violaceous base.
 - Lesions evolve to form shallow or deep ulcers, and can expose underlying tendons or muscle
 - The ulcers have a purulent base and a ragged, undermined, violaceous gunmetal colored border which spreads peripherally
- Lesions occur most commonly on the legs, (esp. pretibial area), but can develop in any area of the body

+ Pyoderma Gangrenosum:

association with underlying disease



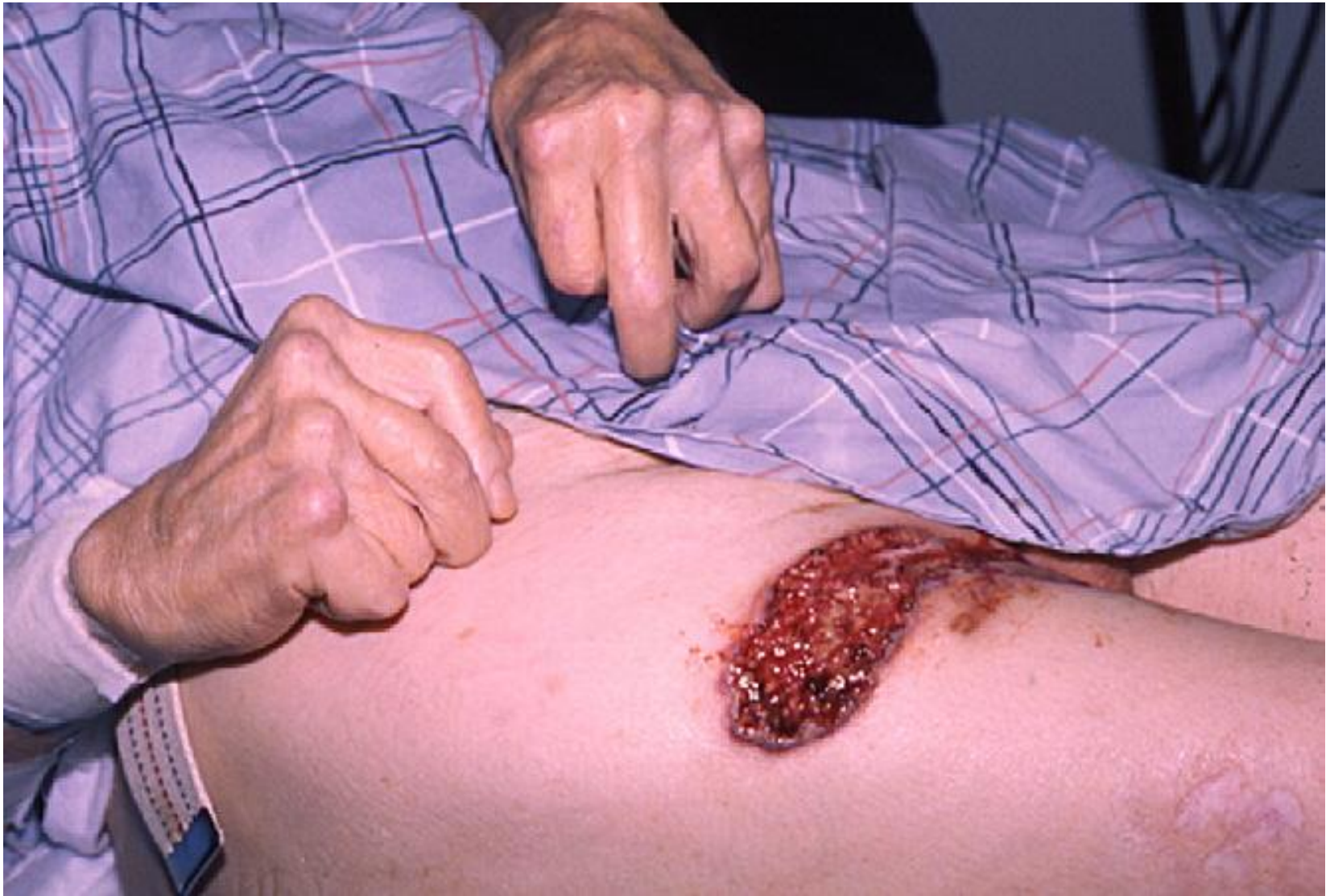
- Underlying systemic disease ~50% of cases
 - IBD, arthritis, or lymphoproliferative disorders
- IBD associations:
 - PG seen in up to 5 percent of UC patients, 2 percent of Crohn's patients
 - PG activity may or may not parallel IBD activity
 - Pustular variant most likely to parallel
 - Colectomy may be helpful if extensive colitis present

Pyoderma Gangrenosum—Early Pustular Lesion



(Courtesy Dr. Jodi Ganz.)

Pyoderma Gangrenosum—Ulcerated Lesion



+ Pyoderma Gangrenosum

Pros

- Pustular skin lesions
- Fever, arthralgias
- Female predilection
- Strong association with IBD
- Associated inflammatory arthritis

Cons

- Lesion characteristics (large ulcers--unless pustular variant)
- Distribution (usually lower extremity)
- Previous milder episodes



Other neutrophilic dermatoses



- **Reactive arthritis**
- **Subcorneal pustular dermatosis**
- **Generalized pustular psoriasis**
- **Behcet's disease**
- **SAPHO syndrome**
 - synovitis, acne, pustulosis, hyperostosis, and osteomyelitis
- **Bowel-associated dermatosis-arthritis syndrome**



Generalized Pustular Psoriasis

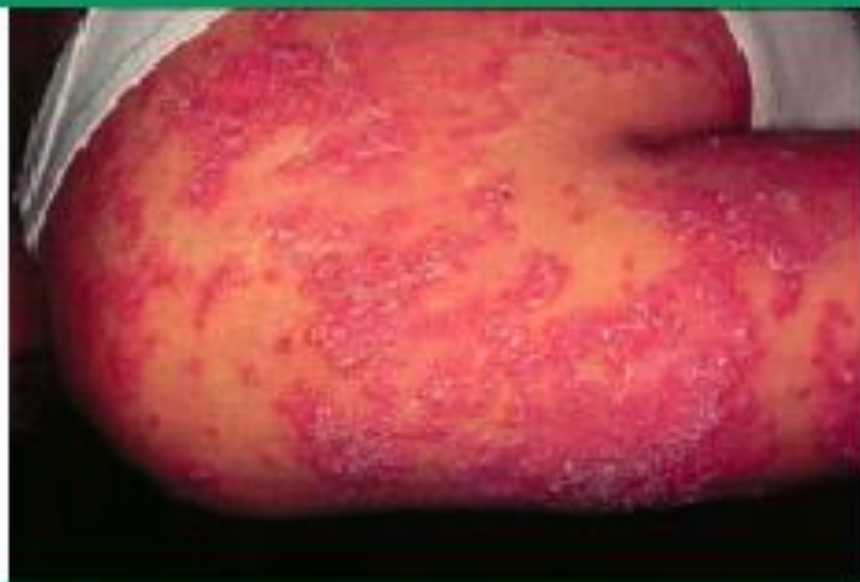
Pros

- 2- to 3-mm pustules over an erythematous base
- Distribution: The trunk and extremities may be involved
- Fever, arthralgias
- Acute onset
- Arthritis

Cons

- No preceding history of psoriasis type lesions
- No nail bed involvement
- Lesions usually on flexural surfaces
- No “lakes of pus”
- No precipitating cause (meds), IBD association

Pustular psoriasis



Pustular psoriasis is characterized by widespread erythema and scaling and sheets of superficial pustules.

Courtesy of James C Shaw, MD.

Generalized Pustular Psoriasis



+ Behcet's Disease

Pros

- Pustular skin lesions in extremities
- Fever, arthralgias
- Associated inflammatory arthritis
- GI symptoms

Cons

- GI involvement usually diffuse colic and recurrent ulceration (IBD mimic)
- No aphthous stomatitis
- No genital ulceration
- No eye findings



SAPHO syndrome

synovitis, acne, pustulosis, hyperostosis, and osteomyelitis



- Epidemiology:
 - Primarily seen in children and young adults (rare >60)
 - No racial or sexual predilection; more common in Japan and Europe
 - Association with IBD and HLA-B27 haplotype
- Sterile neutrophilic infiltration of skin, articular surfaces, and bone. Patients present with painful arthritis and fever.
 - Skin: varied expression
 - Palmoplantar pustulosis most common
 - Acne may present as vulgaris, conglobate, or fulminant
 - Articular lesions:
 - most common in the anterior chest wall joints, may present as synovitis, osteitis, and aseptic osteomyelitis

+ SAPHO syndrome

Pros

- Pustular skin lesions in extremities
- Fever, arthritis
- Association with IBD
- Young adult

Cons

- No acne described
- Usually palpopustular
- Usually prominent pain in anterior chest wall



revised DIFFERENTIAL



- Sweet's Syndrome
- Pyoderma Gangrenosum
- Disseminated Gonococcal Infection
- Secondary Syphilis
- Pustular Psoriasis
- Other Neutrophilic Dermatoses

+ Simplified Problem List

- Additive Inflammatory Polyarthrititis of Right hand
- Pustular rash over BUEs
- Systemic symptoms (F/C, arthralgias, diarrhea)
- History of IBD (UC) and Gastric Bypass
- Recently diagnosed Sclerosing Cholangitis



Complications of Bariatric Surgery

Roux-en-Y gastric bypass (LATE)



- Surgical/Local
 - Gastric remnant distension
 - Stomal stenosis
 - Marginal ulcers
 - Cholelithiasis
 - Ventral incisional hernia
 - Internal hernias
- GI disturbances
 - Short bowel syndrome
 - Dumping syndrome
 - Change in bowel habits
- Metabolic
 - Metabolic and nutritional derangements
 - Postoperative hypoglycemia
- Failure to lose weight and weight regain



Final DIFFERENTIAL?



- Behcet's disease
- Generalized Pustular Psoriasis
- Reactive arthritis
- Sweet's Syndrome
- Pyoderma Gangrenosum
- Disseminated Gonococcal Infection

Bowel-associated dermatosis-arthritis syndrome – a relapsing, extremely rare extraintestinal sign of acute flare-up in Crohn's disease

[European Journal of Dermatology, Volume 21, Number 3, 443-5, May-June 2011, Correspondence](#)

 [Full Text](#)

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Bowel associated dermatosis – arthritis syndrome: a case report

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Abstract

We report a rare case of Bowel Associated Dermatitis – Arthritis Syndrome in a young patient with complex Crohn's disease who presented with fever, arthritis, rash and worsening of diarrhea with abdominal pain, who promptly responded to a short course of steroids.



Bowel-associated dermatosis- arthritis syndrome (BADAS)



- Uncommon syndrome: assoc. with GI pathology
 - Originally described after jejunio-ileal bypass in 1960s/70s
 - Since described with other surgical procedures
 - Creation of a blind loop of bowel, pancreatobiliary diversion
 - **Also described with IBD**
- Pathogenesis uncertain
 - Bowel bacterial overgrowth → immune complex formation
 - Deposition in tissue target sites → activation of complement
 - Ab's against bacteria and complement isolated in patients



BADAS: Clinical Manifestations



- **Serum sickness-like syndrome**
 - F/C, malaise, arthralgia, arthritis, and myalgia
- **Polyarthritits**
 - Nonerosive, asymmetric, episodic, +/- tenosynovitis
 - Predominantly small peripheral joints (fingers and wrists)
- **Diarrhea and malabsorption** are additional features
- **Skin**
 - **Erythematous macules** (up to 1 cm), which develop **a central papulovesicle or pustule** over 1 to 2 days
 - Eruption usually concentrated on the UEs and torso
 - Lesions last 2 to 8 days (with recurrences possible)

Disseminated papulopustular hemorrhagic dermatosis



Scattered papulopustular lesions due to neutrophilic infiltration of the skin is seen in the bowel-associated dermatosis arthritis syndrome in patients with inflammatory bowel disease.

Courtesy of Samuel Moschella, MD.

+ BADAS: Diagnosis



- No specific lab findings
- Histologic findings:
 - Described as identical to Sweet syndrome
 - Mature neutrophilic infiltrate in the dermis with papillary dermal edema
 - BADAS characteristically does not result in vessel destruction

+ BADAS: Treatment



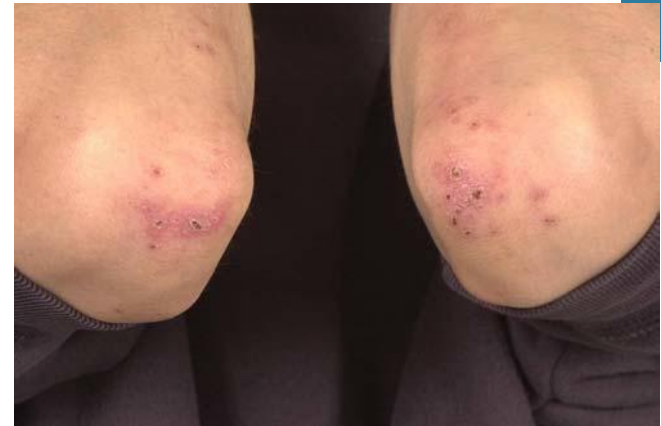
- Abx: Tetracycline and metronidazole (etc.)
 - Inconsistent results
- NSAIDs and Prednisone
- Reversal of bypass
 - Curative in majority of patients who have had it
- Rx of underlying GI disease
 - i.e. IBD without bowel bypass



BADAS: Pustular skin lesions



Clinics in Dermatology (2006) 24, 470– 481



Journal of Medical Case Reports 2007, 1:81



Bowel-associated dermatosis-arthritis syndrome: **Pros**



- Characteristic skin lesions and distribution
 - Pustules on erythematous base
 - Predilection for Upper extremities
- Fever/systemic illness (serum sickness)
- Inflammatory arthritis and arthralgias
 - Often involving hands/fingers
- History of IBD, Gastic Bypass
- Diarrhea
- Prior similar milder episodes

+ Bowel-associated dermatosis-arthritis syndrome: **Cons**

- No definitive diagnostic test
- Very similar in many ways to other neutrophilic dermatoses (PG, Sweet's etc.)
- BUT...



+ Final diagnosis

Bowel associated dermatitis and arthritis syndrome (BADAS)

- Related to IBD and/or prior gastric bypass surgery

Diagnostic Test:

- Typical Clinical Features PLUS
- Biopsy of skin lesion showing typical histology and no signs of infection or vasculitis
- Response to therapy?





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