Systemic Disease Mimickers of Genital Skin Disease

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Disclosures

I have no relevant conflicts of interest
I will discuss off-label uses of medications
Objectives

I. Genital Psoriasis
   • Recognize the frequency, impact and treatment

II. Genital Aphthosis
   • Describe systemic causes of aphthous ulcers

III. Behçet’s Disease
   • Be aware of diagnostic criteria and skin manifestations

IV. Cutaneous Crohn’s Disease
   • Describe the clinical features, lab testing and treatment
Genital Psoriasis

• 30-45% of psoriasis patients with genital involvement
• 2-5% with ONLY genital involvement
• Associated with:
  • Younger age of onset (<40 years old)
  • More frequent nail, scalp, inverse involvement
• Considerations: Superinfection
• Significant effect on quality of life, psychosexual well-being

Genital Psoriasis - Diagnosis

- A Clinical Diagnosis - Biopsy usually unnecessary
- Biopsy if treatment resistant to exclude intraepithelial neoplasia, Paget’s

Vulvar Psoriasis

- 201 Vulvar psoriasis patients
  - Symptoms: Itching (95%), pain (45%), dyspareunia (28%)
  - Exam: 90% sharp edge, 20% plaques, 17% scale
  - Superinfection: 20% of adults with C. albicans or S. aureus
  - 94% responded to topical therapy alone

Genital Psoriasis – Therapy

• Topical therapy is usually effective
• Mostly based on expert opinion (Grade D)
• Mild: low potency topical steroid until clear
• Moderate/Severe:
  • Medium to high potency steroid x 2-4 weeks → low potency steroid
  • Add vitamin D analogue, if needed, to reduce topical steroid use
  • Topical calcineurin inhibitors may substitute for steroid, if tolerated
• Avoid phototherapy, tazarotene, anthralin

Summary for Genital Psoriasis

- 30-45% of patients have genital involvement
- Biopsy is unnecessary unless refractory
- Huge impact on quality of life
- Treat possible co-infection
- Vast majority of cases may be controlled with topical therapy
  - Shorter courses of medium to high potency topical steroids
  - Maintenance with low potency steroids, vitamin D analogues, calcineurin inhibitors
DDx for Vulvar Ulcer

- **Infectious**
  - Viral (HSV, VZV, EBV, CMV, HIV)
  - Candida
  - Group A Strep
  - Mycoplasma
  - Syphilis

- **Inflammatory**
  - Aphthae
  - Lichen planus
  - Lichen sclerosus
  - Hidradenitis
  - Cutaneous Crohn’s
  - Behçet’s

- **Autoimmune**
  - Pemphigus
  - Mucous membrane pemphigoid

- **Reactive/Drug**
  - Bullous fixed drug
  - Erythema multiforme/SJS

- **Malignancy**
  - Squamous cell carcinoma
  - Extramammary Paget’s

- **Genetic**
  - Hailey-Hailey

- **Mechanical**
  - Excoriation
  - Abuse
Genital Aphthosis

- Confusing nomenclature
  - Reactive genital ulcers
  - Non-sexually acquired genital ulcers
  - Reactive non-sexually related acute genital ulcers
  - Lipschütz ulcer
  - Complex aphthosis (recurrent aphthae not due to systemic disease)
- Minor, Major (>1cm), Herpetiform
- Women>>>men
- Self-limited, 2-3 weeks
- Primary or Secondary
Genital Aphthosis

- History and physical (oral, genital, ocular mucosa)
- Family history
- Exclude infection (HSV, if constitutional sx EBV, CMV, HIV, mycoplasma, group A strep)
- Evaluate secondary causes
  - Nutritional: Iron studies, B12, folate
  - Autoimmune: Celiac, Crohn’s, Systemic lupus
  - Autoinflammatory: Behçet’s, PFAPA (periodic fever, aphthous stomatitis, pharyngitis, cervical adenitis)
- Biopsy of an acute ulcer is not usually helpful

Genital Aphthosis

• Supportive in nature
• Mild: Topical anesthetics (lidocaine, amitriptyline, ketamine)
• Moderate: Topical Class I or II topical steroids, NSAIDs
• Severe: Oral corticosteroid taper, consider colchicine, dapsone, and thalidomide

Take Home Messages - Genital Aphthosis

• A clinical diagnosis
• Exclude infection
• Consider iron studies, folate, B12, Celiac panel
• Review of systems to screen for Behçet’s, Crohn’s, SLE
• Biopsy is not helpful, except to exclude other diagnoses
• Treat with anesthetics, potent topical steroids or systemic steroids, colchicine, dapsone if needed
Behçet’s Disease

• 1937 – Described by Hulusi Behçet
• A vasculitis affecting vessels of all sizes
• Onset 20-30 years old
• Men>Women
• Turkey>Middle east>Asia>US>UK
• Ç = cedilla = Turkish origin = “Ch” sound
• “Beh-Chets”
International Criteria for Behçet’s Disease

Need ≥4 points to make diagnosis

- Oral ulcers: 2
- Genital ulcers: 2
- Ocular signs: 2
- Skin lesions: 1
- Vascular signs: 1
- Neurologic signs: 1
- Pathergy test: 1
Oral Ulcers in Behçet’s

- Occur in 95-100% of cases
- Lips, tongue, buccal mucosa, gingiva, soft palate
- Self-limited, resolves in 1-4 weeks
- Within 4 years of oral ulcer onset, 95% meet diagnostic criteria for Behçet’s

Genital Ulcers in Behçet’s

- 60-80% of cases
- Indistinguishable from other causes of aphthae
- Larger, deeper, fewer than oral ulcers
- Men: 90% on scrotum
- Women: majority on labia, can be in introitus, cervix
- May be inguinal creases, perineum, perianal skin
- May scar
- Self-limited, resolves in 2-6 weeks

Pustular lesions

• Occur in 50% of cases
• Dome-shaped pustule with a red halo
• Extremities > trunk
• Usually not folliculocentric
• Neutrophilic infiltrate, vasculitis
Pathergy Test

1. Cleanse volar forearm with alcohol
2. Use 20 gauge needle, 2-3 puncture sites
3. 24-48 hours later, observe for papule/pustule

Apremilast for Behçet’s Ulcers

Genital Ulcers:
100% in the apremilast group (n=10) vs. 50% in the placebo group (n=6) had resolution of genital ulcers by week 12, P=.04.

Behçet’s Treatment Approach

• Prevent irreversible organ damage
• Minimize morbidity of ulceration
Treatment of Aphthous Ulcers in Behçet’s

Driven by severity of symptoms

1st
- Triamcinolone paste, pimecrolimus, tetracycline/dexamethasone rinse
- Oral corticosteroid taper
- Colchicine
- Dapsone
- Apremilast

2nd
- Azathioprine
- Infliximab, adalimumab

3rd
- Anakinra, canakinumab
- Thalidomide
- Cyclosporine, interferon-alpha

Take Away Message for Behçet’s Disease

• Use 2013 International Criteria for Behçet’s Disease
• Genital ulcers occur commonly on the scrotum and labia, may heal with scarring
• Escalate treatment for ulcers as much as it bothers the patient
• Consider colchicine as 1st line systemic therapy
• Apremilast is an emerging therapy
Non-contiguous (Metastatic) Crohn’s

- The presence of cutaneous noncaseating granulomas at sites which are not contiguous with the gastrointestinal tract.
Cutaneous Manifestations in Crohn’s

1. Specific (Cutaneous Crohn’s)
   - Contiguous: Fistulae
   - Non-contiguous (Metastatic): Genital, distant sites
   - Oral: Mucosal swelling, cobblestoning, orofacial granulomatosis

2. Reactive
   - Aphthous ulcers
   - Erythema nodosum, pyoderma gangrenosum, cutaneous PAN

3. Associated
   - Psoriasiform eruptions, vitiligo
   - Acquired acrodermatitis enteropathica

Vulvar Crohn’s Disease

- Painful vulvar edema (unilateral or bilateral) - most common
- Deep linear “knife-like” fissures - most specific
- Perianal tags
- Condyloma-like lesions
- 90% also with perianal mucosal involvement
Non-contiguous Crohn’s

- In adults, 20% precede intestinal disease
- In peds, 80% precede intestinal disease
- Non-contiguous Crohn’s activity may NOT parallel intestinal Crohn’s activity

Laboratory Findings in Crohn’s Disease

- Elevated ESR, CRP
- Thrombocytosis, Anemia
- Hypoalbuminemia
- Elevated *fecal calprotectin*
- Serology
  - Positive **ASCA** (Anti-Saccharomyces Cerevisiae Antibody)
  - Negative P-ANCA
    - Specificity 91%, **Positive predictive value 88%**

Treatment Principles in Cutaneous Crohn’s

• Consider comorbidities (e.g. hidradenitis, psoriasis)
• Collaborate with GI doc involved
• Escalate therapy as if for intestinal Crohn’s disease
  • Topical/intralesional steroids, oral metronidazole
  • 6-MP/azathioprine, methotrexate
  • Adalimumab, infliximab, certolizumab
  • Ustekinumab
  • IVIG

Take Away Points for Cutaneous Crohn’s

• Painful vulvar edema is most common sign
• Knife-like fissures are most specific
• 20% adult vs. 80% pediatric cases precede intestinal disease
• ASCA, P-ANCA, fecal calprotectin are useful screening tests
• Escalate therapy as if for intestinal Crohn’s disease
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