Erythema Nodosum

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Rheumatology Fellow
Objectives

- Be able to identify characteristic lesions of erythema nodosum
- Be familiar with the differential diagnosis of erythema nodosum and have an approach
- Know the implications of erythema nodosum in different clinical conditions
Overview

- Theory
  - Description of the EN lesion
  - Histology of the EN lesion
  - Differential Diagnosis of the EN
  - Workup

- Case Discussions
Dermatological Lesion

- Tender red raised nodules
- 1-5 cm
- Commonly on shins
- Less commonly on extensors of arms, thighs and trunk
Histology

- Septal panniculitis
- Inflammatory infiltrate with neutrophils, lymphocytes and histiocytes
- Eventually granuloma form with multinucleate giant cells
Differential diagnosis of erythema nodosum

- **Common causes**
  - Idiopathic
  - Streptococcal
- **Associated with hilar lymphadenopathy**
  - Sarcoid
  - TB
  - Histoplasmosis, Coccidoidomycosis, Blastomycosis
  - Hodgkin’s Disease
  - Yersiniosis
- **Associated with GI disease**
  - IBD
  - Behcet’s
  - Pancreatitis
  - Whipple’s disease
  - Yersiniosis
- **Pregnancy**
- **OCP, Sulfa, omeprazole, hepatitis B vaccine, isotretinoin**
- **Others**
  - Leprosy
  - SLE, Churg-Strauss, Takayasu’s, Relapsing Polychondritis, Wegener’s
  - HIV
  - Syphilis
  - Cat-scratch disease
- **Weber-Christian panniculitis**
- **Nodular vasculitis (erythema induratum)**
- **Nodular lymphangitis (Sporothrix, Mycobacterium marinum, bacterial)**
- **Subcutaneous granuloma annulare**
Differential diagnosis of erythema nodosum

- Common – Idiopathic, Streptococcal
- Drugs
- Pregnancy
- Associated with Hilar Adenopathy
- Associated with GI Disease
- Others
- Histopathologically not erythema nodosum
Work-Up

- Drug screen
- CBC
- S. chemistry, lipase
- Beta-HCG
- ASOT, throat swab
- ESR, CRP
- CXR
Case 1

- 25 yr. female
- Presented with raised tender lesions on shins that measured 1-2 cm in diameter
- Arthralgias in wrists
Case 1

- No recent sore throat
- Otherwise healthy
- Not pregnant
- No gastrointestinal symptoms
- No cough / SOB
- No TB risk factors
- No fungal exposure / travel
- Did receive Septra for a UTI infection 1 week ago
- Physical exam confirmed EN but was otherwise unremarkable including MSK exam
- ASOT negative, throat swab negative, CXR normal, CBC normal, serum chemistry normal
Case 1

- Diagnosis: Drug related EN - Sulfa
Case 1

Most common causes

- Idiopathic
- Streptococcal
- Drugs – sulfa, OCP, iodide / bromide containing drugs
- Pregnancy
Case 1

- Treatment
  - NSAIDs
Case 2

- 35 yr. female
- Presented with raised tender lesions on shins 2-4 cm in diameter x 4 weeks
- Pain and redness in both ankles x 4 weeks
Case 2

- Otherwise healthy
- No sore throat
- No respiratory / GI symptoms
- Not pregnant
- No meds / OCP
- No red eye / photophobia / ocular pain
- No TB / fungal RFs
- P/E confirmed EN and red tender ankle joints with no effusions, otherwise unremarkable
- ASOT, throat swab, CBC and serum chemistry unremarkable
- ESR 65
Case 2
Case 2

- Diagnosis: Sarcoidosis

- Have to ask 2 critical questions because of diagnostic and therapeutic implications?
  - Are there RF’s or history suggestive of another granulomatous process?
  - Does this fit with Sarcoidosis?
Lofgren’s syndrome

- Fever
- Arthritis
- EN
- Hilar Adenopathy
Heerfordt-Waldenstrom’s Syndrome (Uveoparotid Fever)

- Fever
- Uveitis
- Parotid Enlargement
- Facial N. Palsy
Case 2

- Treatment: Corticosteroids or NSAIDs
- Lofgren’s generally self limited
- Heerfordt’s not self limited and requires corticosteroids
Case 3

- 43 yr old female
- Aboriginal
- Transferred down from rural Manitoba with 3 wk history of EN not resolving
- Also has fevers, chills and sweats mostly in evenings x 3-4 wk
- Poor appetite, no previous weight to compare with but not cachetic
- CXR - ? UL infiltrate
Case 3

- Lives in rural Manitoba
- Multiple family members with previous TB (none in last year)
- No respiratory / GI symptoms
- Not pregnant
- No meds / OCP
- No sore throat
- No arthritis
- No fungal RFs
- P/E confirmed EN. Patient was febrile at 38° at admission. Sweats observed. Exam was otherwise unremarkable.
- CXR showed hilar adenopathy but no parenchymal disease
- Mild NCNC anemia, rest of routine blood work was normal
Case 3

- Further W/U
  - ACE level normal
  - Ca$^{2+}$ normal
  - 24 hr. U. Ca$^{2+}$ normal
  - Sputum AFB negative
Case 3

- Mediastinoscopy with hilar lymph node biopsy
  - Caseating granuloma
  - AFB seen
  - No evidence of lymphoma
Case 4

- 16 yr. female
- Presented with EN and arthritis 3 mths ago
- No respiratory / GI complaints
- ASOT, throat swab, CXR, CBC and chemistry were unremarkable
- CRP 80, ESR 90
- Resolved over 4 weeks with NSAIDs
Case 4

- Now presents with recurrent EN, arthritis and fever
- No respiratory symptoms
- Stomach sore but no diarrhea or blood and mucus in stool, abdomen was benign
- Weight stable
- Wrists tender and swollen
- ASOT, throat swab, CXR and chemistry unremarkable
- Anemic with Hgb 116, normocytic
- CRP and ESR 120
- Started on NSAIDs and brought back to clinic in 2 weeks
Case 4

- No better
- Father accompanied patient this time and reported significant weight loss
- No diarrhea or blood and mucus in stool
- Abdomen was benign
- Arthritis persisting
- No respiratory symptoms
Case 4

- No improvement in stomach soreness or appetite with prednisone 30mg (arthritis improved but recurred as soon as prednisone stopped)
- ASCA positive
- Urgent assessment with Pediatric GI arranged the same week
  - Now microcytic anemic with Hgb 80 (but still not describing melena or BRBPR)
  - Admitted and nuclear scan lit up from terminal ileum to rectum
  - Subsequent urgent endoscopy with biopsies and then started on Prednisone 60 mg daily
  - Biopsy of terminal ileum confirmed Crohn’s disease
Case 4

- Common causes less likely in *recurrent EN* and should always prompt a detailed reassessment.
- Extraintestinal manifestations of IBD that indicate active disease:
  - EN, PG
  - Scleritis / Episcleritis
  - Peripheral arthritis
  - Aseptic osteomyelitis
  - Aseptic meningitis
  - Thrombosis
Case 5

- 42 yr. female
- Presented with abdominal pain x 2yrs
  - Symptomatic and incapacitated for a few days and then it resolves. Episodes occur every 2-4 wks. Sometimes associated with diarrhea
- Arthralgias involving hands
- Red bumps on her shins that come and go over weeks to months, has current lesions consistent with EN
- Non-descript headaches
Case 5

- Blood and mucus in stool
- Orogenital ulcers (recurrent x 5 yr.)
- Neck stiffness
- Pustular eruption on upper trunk (history of acne type lesions off and on but nothing this severe in the past)
- Developed uveitis 2 months later
- Developed DVT a year later
## Diagnostic Criteria for Behcet’s Disease

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Required features</th>
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<tbody>
<tr>
<td>Recurrent oral ulceration</td>
<td>Aphthous (idiopathic) ulceration, observed by physician or patient, with at least three episodes in any 12 month period</td>
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**Plus any two of the following**

<table>
<thead>
<tr>
<th>Criterion</th>
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<tr>
<td>Recurrent genital ulceration</td>
<td>Aphthous ulceration or scarring, observed by physician or patient</td>
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<tr>
<td>Eye lesions</td>
<td>Anterior or posterior uveitis cells in vitreous in slit lamp examination; or retinal vasculitis documented by ophthalmologist</td>
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<td>Skin lesions</td>
<td>Erythema nodosum-like lesions observed by physician or patient; papulopustular skin lesions or pseudofolliculitis with characteristic acniform nodules observed by physician</td>
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<td>Pathergy test</td>
<td>Interpreted at 24 to 48 hours by physician</td>
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Summary-Approach to EN

Recurrent?

Common Causes
1. Idiopathic
2. Streptococcal
3. Drugs
4. Pregnancy

Hilar Adenopathy
1. Sarcoid
2. TB/Fungal
3. Yersinia
4. Lymphoma

GI
1. IBD
2. Behcet’s
3. Pancreatitis
4. Whipples

Others (great mimickers)
1. CTD
2. HIV
3. Syphilis

Not EN
1. Nodular lymphangitis
2. Nodular vasculitis
Questions?