Lofgren's Syndrome Underlying Erythema Nodosum in a Healthy Young Woman

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Case Presentation

A 21 year old woman without significant past medical history, on no chronic medications, presented to the emergency department complaining of a painful red rash on her legs. She first noticed the rash on her left calf just above the heel 3 days prior. She had seen her PCP for the rash 2 days prior and was prescribed a 10 day course of cephalexin for presumed cellulitis. Despite this, her rash had spread with new discrete lesions appearing on her left shin and right medial foot. All of her lesions were exquisitely tender to touch with some overlying warmth but no significant swelling or breakdown of the overlying skin.

In addition to her rash, she also experienced high fevers and night sweats over the 4 days prior to presentation. Fevers were accompanied by rigors, bitemporal headache, and general malaise. Her symptoms improved for brief periods of time with acetaminophen and ibuprofen. She also noted progressive painful swelling of the lymph nodes in her anterior neck bilaterally.

She also noted that for past 4 weeks she had progressive left knee pain and mild intermittent swelling. without any history of trauma. She had tried a brace without improvement in pain. Over the 2-3 days prior to presentation, she also noted worsening pain in her left ankle and had started ambulating with crutches due to severe pain with weight bearing.

Throughout the course of illness, she had had no cough, shortness of breath, nasal congestion, or rhinorrhea. She had had no abdominal pain, diarrhea, bloody stools, nausea, or vomiting. She had not had any chest pain, bleeding or bruising tendency, or weight change.

Family history was remarkable only for systemic lupus erythematosus in a maternal aunt.

The patient was pursuing a social work degree and was also interning full time. She had never smoked cigarettes or used illicit drugs. She had 2-3 drinks per month at social events.

Physical Exam

Vital signs: Temp: 38.6ºC, BP: 115/76, HR: 70, RR: 18, SpO2: 100% on room air

General: Tired appearing, in no acute distress
HENT: Pupils equal and reactive to light, no conjunctival injection, bilateral nares without discharge, oropharynx clear without exudates or erythema
Cardiovascular: Normal rate, regular rhythm, no murmurs, intact peripheral pulses
Pulmonary: Non-labored respirations, clear to auscultation in all lung fields
Abdominal: Soft, non-tender, non-distended, normoactive bowel sounds
Musculoskeletal: Pain with passive and active range of motion of left knee and ankle, no effusion, full passive range of motion
Skin: erythematous, tender blanching rash on bilateral lower extremities (see middle panel)
Lymphatics: numerous swollen, mobile, very tender lymph nodes ranging from 0.5-1cm in size in anterior cervical chain bilaterally, no inguinal adenopathy

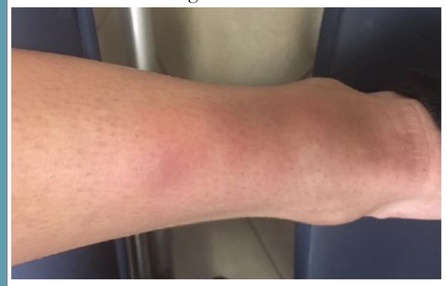
Laboratory Results

CMP: within normal limits
CBC: WBC 14.4, Hgb 12.6, Plt 287
CRP: 92.1 mg/L
ESR: 62 mm/hr

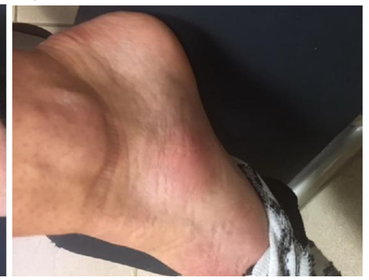
Monospot: negative
ASO titer: 21 (0-530 IU/mL)
Anti DNase B: 78 (0-300 U/mL)

Images

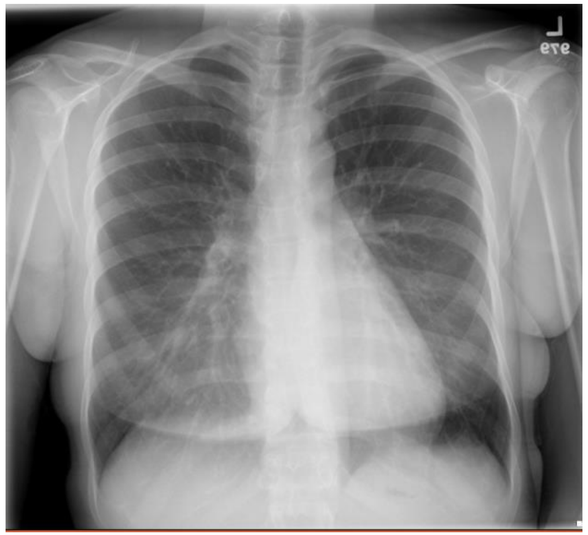
Left anterior lower leg



Right medial foot



AP Chest Radiograph



Treatment and Response

Presumptive Diagnosis: Lofgren's Syndrome

- Started on 20 mg oral prednisone daily
  - Near resolution of symptoms within 3 days
- Recurrence of erythema nodosum and arthralgias 1 week later
  - Prednisone increased to 40mg daily
- Complete resolution of symptoms, normalization of inflammatory markers after 1 month
- Prednisone was slowly weaned off over the ensuing 3 months
- No recurrence of symptoms.

Discussion

Erythema nodosum (EN) is a clinical finding consisting of subcutaneous, erythematous, tender, raised nodules or plaques. It is most commonly found on the extensor surfaces of the lower extremities. It is a panniculitis caused by a delayed hypersensitivity reaction in the subcutaneous fat. It is an uncommon clinical entity with an incidence estimated around 1-5/100,000 persons per year. It is most common in women of northern European descent in the late 2nd and 3rd decades of life. While up to 50% of cases are considered idiopathic, EN is associated with a number of disease states and should always prompt investigation for an underlying etiology.

Common etiologies:	Streptococcal upper airway infection (up to 30% of cases)
	Other infections (5-10% of cases)
	Sarcoidosis (10-35% of cases)
	Medications - sulfonamides, β-lactams, OCPs (15% of cases)
Less common etiologies:	Inflammatory bowel disease, pregnancy, malignancy.

Lofgren's Syndrome (LS) is a variant of sarcoidosis with acute systemic disease onset.
The classic triad includes EN, bilateral hilar lymphadenopathy, and arthralgias/arthritis.
LS is most common in young to middle aged women of European descent.
Lymph node biopsy with non-caseating granulomas is supportive but not required for diagnosis.
In this case, chest radiograph suggested primarily right hilar adenopathy.
This and presentation with arthralgia preceding fevers and EN (highly suggestive of LS) and rapid resolution with corticosteroids make LS the most likely diagnosis.

Cervical adenopathy in LS is unusual. Head and neck manifestations of sarcoidosis are uncommon, affecting 10-15% of all patients with sarcoidosis.
Presence of cervical adenopathy in suspected sarcoidosis should prompt clinicians to consider other causes, especially infectious etiologies and malignancy.
In this case, the patient's lack of a clear infectious prodrome, normal ASO and anti-DNase B titers, and negative monospot testing all suggested against an infectious cause.
Malignancy was considered unlikely given the acuity of onset and painful nature of her lymphadenopathy and would not have resolved with corticosteroids alone.

LS portends an excellent prognosis with >90% of cases resolving spontaneously within 2 years of disease onset. Symptoms are often mild and can be managed with PRN NSAIDs alone, however severe or refractory symptoms tend to respond rapidly to systemic corticosteroids.

Conclusion

- This case outlines the importance of considering Lofgren's Syndrome as an underlying etiology of erythema nodosum.
- Concurrent arthralgias/arthritis and erythema nodosum, especially in young women of European descent, should prompt further investigation for LS with chest radiography.
- While LS is typically self-limited and manageable with NSAIDs alone, severe or refractory symptoms often respond rapidly to systemic corticosteroids.

References

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