CLINICAL VIGNETTE

A Mysterious Case of Erythema Nodosum

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Case

An 18-year-old female presented to her primary care physician's office for 1 week of painful erythematous lesions on both legs. She was treated with amoxicillin 1 month prior to presentation for streptococcal pharyngitis. Review of systems was notable for fatigue and right knee pain. She was on combined oral contraceptives for acne. She was otherwise healthy without significant past medical history and denied personal or family history of easy bleeding or bruising. Physical exam revealed multiple tender, erythematous to violaceous nodules over her bilateral shins and dorsum of her feet. CBC, CMP, ESR, and PT/PTT were all within normal limits. A clinical diagnosis of erythema nodosum was made based on the patient's examination and recent history of pharyngitis, penicillin treatment and oral contraceptives. The patient was started on naproxen and ibuprofen for pain control, with consideration of stopping oral contraceptives if her symptoms persisted.

Discussion

Erythema nodosum (EN) is a type of panniculitis that commonly presents as tender, erythematous, non-ulcerated nodules on the bilateral shins. While it can occur across all age groups, it is most commonly seen in women in their second to fourth decades.[1]

EN is thought to be a type IV hypersensitivity reaction to a wide number of antigens.[2] Thus, it is important to keep a broad differential in mind. Infectious etiologies are the most commonly identified with streptococcal infections the most common cause. Drug-induced etiologies include oral contraceptives, penicillins, and sulfonamides. Inflammatory etiologies include inflammatory bowel disease, sarcoidosis, and Behcet's disease. Malignancy and pregnancy are other potential causes. Despite extensive evaluation, no cause can be identified in 37-53% of patients.[3,4]

The diagnosis of EN is largely clinical. The classic firm, tender, non-ulcerated, fixed nodules of erythema nodosum most often present on the bilateral shins. They are frequently preceded by a nonspecific prodrome of fever, upper respiratory symptoms, polyarthralgia, and/or fatigue. Associated symptoms include joint pain, swelling, and stiffness. The diagnosis of EN should prompt an evaluation for potential triggers or underlying conditions (Table 1).[1,2] Common etiologies include streptococcal infection, sarcoidosis, and tuberculosis.[5] Complete review of systems and comprehensive physical exam, including the throat and tonsils can help direct the clinician's evaluation. Medication history should be performed to evaluate for drug-induced EN. Laboratory studies may guide the clinician towards an underlying etiology, however, there are no laboratory abnormalities specific to EN. Dermatologic evaluation should be sought if the diagnosis remains unclear and a biopsy may be warranted for atypical features including: atypical location, scarring, ulceration, or large lesions over 5cm.[2]

Table 1: Erythema Nodosum Workup to Consider

Complete Blood Count for underlying infection and/or malignancy
Inflammatory markers (ESR and/or CRP)
Throat culture and/or ASO-titer for streptococcal pharyngitis
Chest X-ray can reveal signs of pulmonary infections such as TB or sarcoidosis
TB skin test and/or Quantiferon Gold
Stool evaluation for infection or inflammatory bowel disease

EN is self-limited and spontaneously resolves over days to weeks. It is not typically associated with sequelae and resolves without scarring, ulceration, or necrosis. Associated skin discoloration may take longer to completely clear, up to several months. If joint pain occurs, it can persist for months, but without injury to the joint. A small proportion of patients will have a relapsing course with flares over months to years.[4]

The mainstay of management is symptom control through rest, elevation of the legs, compression stockings, and treatment of the underlying condition if identified. Analgesics and anti-inflammatory medications including colchicine can be used. Some patients fail to respond to conservative treatment or have severe and debilitating symptoms that are refractory to analgesics and anti-inflammatories. In these situations, systemic or intralesional glucocorticoids can help.[1]

Conclusion

One month after her initial diagnosis of EN, the patient developed a new onset of multiple oral aphthous ulcers within one week. The five ulcers were self-limited and resolved within

a few days without intervention. The following month, she developed left eye pain, and was diagnosed with iritis. By this time, her EN lesions had self-resolved. Her diagnosis of iritis prompted a referral to rheumatology. Extensive rheumatologic testing was only notable for the presence of the HLA-B51 gene, which is associated with an increased risk of Behcet's disease, though she did not meet all diagnostic criteria for Behcet's.[6]

This patient's EN exemplifies the complex presentation and sometimes multifactorial etiologies associated with this inflammatory condition. Etiologies included the use of oral contraceptives, recent antibiotic use, recent strep throat infection, and a possible underlying systemic disorder. The possibility of Behcet's disease highlights the importance of maintaining a broad differential when a patient presents with erythema nodosum.

REFERENCES

1. **Requena L, Requena C**. Erythema nodosum. *Dermatol Online J*. 2002 Jun;8(1):4. PMID: 12165214.
2. **Hafsi W, Badri T**. Erythema Nodosum. 2020 Sep 20. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 29262192.
3. **Cribier B, Caille A, Heid E, Grosshans E**. Erythema nodosum and associated diseases. A study of 129 cases. *Int J Dermatol*. 1998 Sep;37(9):667-72. doi: 10.1046/j.1365-4362.1998.00316.x. PMID: 9762816.
4. **Mert A, Kumbasar H, Ozaras R, Erten S, Tasli L, Tabak F, Ozturk R**. Erythema nodosum: an evaluation of 100 cases. *Clin Exp Rheumatol*. 2007 Jul-Aug;25(4):563-70. PMID: 17888212.
5. **García-Porrúa C, González-Gay MA, Vázquez-Caruncho M, López-Lazaro L, Lueiro M, Fernández ML, Alvarez-Ferreira J, Pujol RM**. Erythema nodosum: etiologic and predictive factors in a defined population. *Arthritis Rheum*. 2000 Mar;43(3):584-92. doi: 10.1002/1529-0131(200003)43:3<584::AID-ANR15>3.0.CO;2-6. Erratum in: *Arthritis Rheum* 2000 May;43(5):1061. PMID: 10728752.
6. **Maldini C, Lavalley MP, Cheminant M, de Menthon M, Mahr A.** Relationships of HLA-B51 or B5 genotype with Behcet's disease clinical characteristics: systematic review and meta-analyses of observational studies. *Rheumatology (Oxford).* 2012 May;51(5):887-900. doi: 10.1093/rheumatology/ker428. Epub 2012 Jan 11. PMID: 22240504.