

CLINICAL VIGNETTE

A Case of Erythema Nodosum as Harbinger of Pulmonary Tuberculosis

Nima Golzy, MD and Michael E. Lazarus, MD

A 32-year-old female presented to clinic with a rash on her lower extremities that was diagnosed as erythema nodosum (Fig. 1). Several months later, she developed a persistent cough and fevers. The patient did not have a significant past medical or surgical history. She was not taking any medications, had never smoked tobacco products, and had no significant occupational inhalation exposures. She had no pets or known allergies. She moved to Arizona from Vietnam three years prior to presentation and her family history was remarkable for an uncle who died of lung cancer. After evaluation in Arizona, she received a diagnosis of pulmonary sarcoidosis and began treatment with several courses of high-dose oral prednisone. Although the steroids led to an improvement clinically, upon tapering her symptoms would recur. She had one hospitalization that required admission to the intensive care unit where she was treated with bronchodilators, antibiotics, and steroids. Due to ongoing difficulty in controlling her symptoms, the patient was referred to our tertiary care hospital for a diagnostic bronchoscopy under conscious sedation.

After the procedure, she developed a fever to 41.9 °C (107.4 °F) and was admitted to the hospital. Airborne precautions were instituted. X-ray of the chest showed bilateral interstitial and airspace opacities (Fig. 2). Computed tomography of the chest showed bilateral airway thickening and bronchocentric micronodularity (Fig. 3). Sputum samples were strongly acid-fast bacilli smear positive and cultures grew *Mycobacterium tuberculosis* (MTB). Steroids were rapidly tapered and she was treated with standard antituberculous therapy with improvement in symptoms.

Erythema nodosum (EN) is a nonspecific cutaneous finding associated with several underlying conditions, including disorders that also present with constitutional and respiratory symptoms. We describe a case of erythema nodosum associated with chronic cough that was initially presumed to be due to pulmonary sarcoidosis but was in fact a sequela of MTB infection. We report this case to remind clinicians of the differential diagnosis of erythema nodosum and to remain cognizant of anchoring bias.

EN is associated with many conditions, most commonly infection but also drugs, inflammatory bowel disease, malignancy, pregnancy, and other inflammatory disorders such as sarcoidosis and Behçet disease. Histologically, EN is a delayed-type hypersensitivity panniculitis and the clinical presentation is that of tender erythematous subcutaneous nodules, usually on the shins.¹ EN has a known association with

MTB that varies with population demographics and geography. In a case-control study in a Chinese population, there was a positive association between EN and MTB infection.² However, in a retrospective study in a French population, 28% of EN cases were due to streptococcal infections and 11% due to sarcoidosis, with only the rare case of EN attributable to MTB infection.³ There is evidence that in the context of MTB, EN represents primary infection. A Turkish review of twenty years of hospitalized MTB cases found that all cases of primary MTB were associated with EN. Additionally, they separately analyzed ten years of EN cases and reported 20% of them were secondary to primary MTB infection.⁴ Interestingly, EN may serve a protective role in both sarcoidosis and coccidioidomycosis; it remains unknown whether this same effect is seen with MTB infection.^{5,6}

Given that EN is associated with various underlying etiologies with divergent therapies, it is important for the clinician to maintain a broad differential diagnosis and remain cognizant of the epidemiology behind this cutaneous finding.

Figures



Figure 1. Erythema nodosum of the patient's lower extremity.

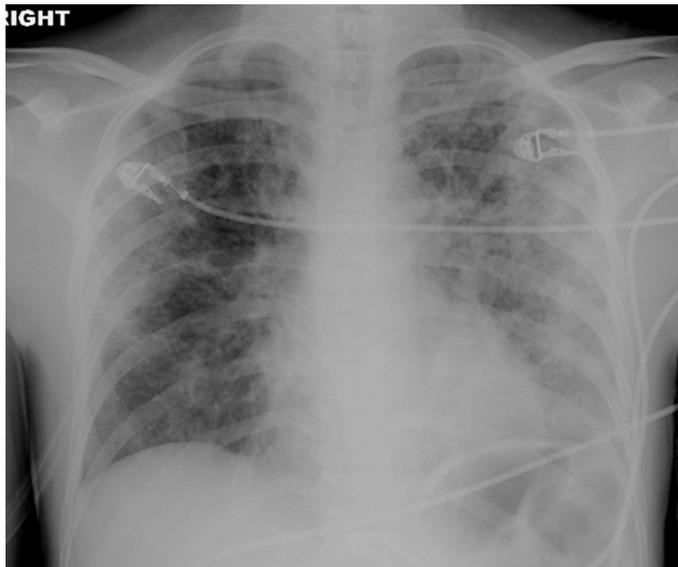


Figure 2. X-ray of the chest upon admission to the hospital. Diffuse bilateral interstitial, granular, and patchy airspace opacities in left greater than right lung.

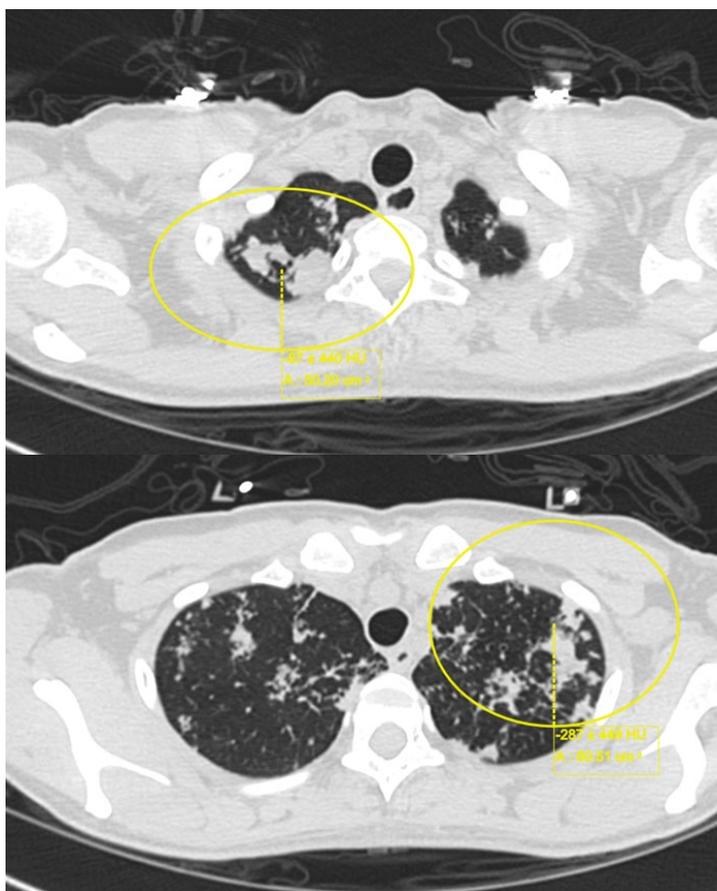


Figure 3a and 3b. Computed tomography of the chest, axial sections, upon admission to the hospital. Diffuse airway thickening and clustered broncho-centric micronodularity in upper greater than lower lobes with areas of coalescence.

REFERENCES

1. **Requena L, Requena C.** Erythema nodosum. *Dermatol Online J.* 2002 Jun;8(1):4. Review. PubMed PMID: 12165214.
2. **Chen S, Chen J, Chen L, Zhang Q, Luo X, Zhang W.** Mycobacterium tuberculosis infection is associated with the development of erythema nodosum and nodular vasculitis. *PLoS One.* 2013 May 1;8(5):e62653. doi: 10.1371/journal.pone.0062653. Print 2013. PubMed PMID: 23650522; PubMed Central PMCID: PMC 3641092.
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. PubMed PMID: 9762816.
4. **Mert A, Ozaras R, Tabak F, Ozturk R.** Primary tuberculosis cases presenting with erythema nodosum. *J Dermatol.* 2004 Jan;31(1):66-8. PubMed PMID: 14739509.
5. **Mañá J, Gómez-Vaquero C, Montero A, Salazar A, Marcoval J, Valverde J, Manresa F, Pujol R.** Löfgren's syndrome revisited: a study of 186 patients. *Am J Med.* 1999 Sep;107(3):240-5. PubMed PMID: 10492317.
6. **Braverman IM.** Protective effects of erythema nodosum in coccidioidomycosis. *Lancet.* 1999 Jan 16;353(9148):168. PubMed PMID: 9923870.

Submitted October 7, 2018