

Brucella as an unexpected cause of erythema nodosum

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ABSTRACT

Erythema nodosum (EN) is the most common panniculitis which affects individuals from all ages. Etiologically most of the cases are idiopathic EN and infections rank the second. Its clinical presentation is sudden, hot erythematous nodules or plaques in legs, knees or ankles with a diameter ranging between 1 and 5 cm. In the majority of cases, healing is observed within two to eight weeks without any scar tissues. It may occasionally manifest itself as the first symptom of systemic diseases such as sarcoidosis, inflammatory bowel diseases, Behçet's disease, and other rheumatological conditions. Therefore, EN cases must be carefully examined in terms of their etiologies. Herein, we report an interesting Brucella case presenting as a EN case consulted for rheumatological etiology investigation.

Keywords: Brucellosis, erythema nodosum, rheumatology.

Erythema nodosum (EN) is the most common panniculitis in clinical practice. Its prevalence is 5/100,000 with 1/6 male-to-female ratio in adults.^[1,2] Although it is most commonly seen in the second or third decade of life, it can affect individuals from all ages. It is equally common in both sexes of children.^[3] Etiologically, 55% of cases are idiopathic and streptococcus infections rank the second in 28 to 48% of cases. Other common causes include sarcoidosis (11 to 25%), medications (3 to 10%), pregnancy (2 to 5%), and enteropathies (1 to 4%).^[2-4]

Erythema nodosum is a non-specific skin reaction which may occur against many different antigens and, histopathologically, it is the inflammation of septa in subcutaneous fat tissues (septal panniculitis). It has no association with vasculitis; however, inflammation and hemorrhage may be observed in small veins.^[5] Its clinical manifestations are sudden hot erythematous nodules or plaques in legs, knees or ankles. Lesions may also appear on the face or in other body parts. They are typically bilateral, symmetrical and have a

diameter ranging between 1 to 5 cm. In most of the cases, healing is observed within two to eight weeks without any scar tissues.^[6]

Erythema nodosum may occasionally manifest itself as the first symptom of systemic diseases such as tuberculosis, bacterial and fungal infections, sarcoidosis, inflammatory bowel diseases, and cancer.^[5] On the other hand, the most common rheumatological disease which causes EN is Behçet's disease. Therefore, EN cases must be carefully examined in terms of their etiologies. In this article, we report an interesting Brucella case presenting as a EN case consulted for rheumatological etiology investigation.

CASE REPORT

In December 2019, a 39-year-old female patient was referred to the rheumatology clinic by the treating dermatologist with the extensive, painful, erythematous plaques in her body. She had no history of such complaints before and she never smoked or consumed

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Figure 1. Extensive erythema nodosum on front side of legs.



Figure 2. Extensive erythema nodosum on gluteal region.

alcohol. Lesions began acutely and progressed in the last two weeks and there were no other symptoms. She did not use any medication recently. On physical examination, her vital signs were normal. She had extensive EN on the front side of her legs (Figure 1) and on the gluteal region (Figure 2). She had no complaints of arthritis, enthesitis or inflammatory low back pain. Further examinations for rheumatic conditions revealed no oral aphthae, genital ulcer, or uveitis. The pathergy test was negative. No inflammatory bowel disease was detected, and other rare rheumatic causes such as vasculitis connective tissue disease were ruled out. She had no history of respiratory tract infection or gastroenteritis inducing EN. Laboratory test results were as follows: erythrocyte sedimentation rate: 39 mm/h and C-reactive protein (CRP): 8 mg/dL; complete blood count and biochemical test results were normal; rheumatic factor (RF) and viral hepatitis serology (HBsAg and Anti-HCV) were all negative. Full urinalysis and plain chest X-ray results were normal. The purified protein derivative of tuberculin test was 3 mm. Although she had no history of apparent contact with animals or animal products, a Coombs anti-serum Brucella agglutination test was performed, as the patient lived in a rural area, and the result was 1/640 positive. She was referred to the infectious

diseases department and diagnosed with brucellosis. A six-week combined antibiotherapy consisting of rifampicin 600 mg/day and tetracycline 200 mg/day was initiated. During follow-up examinations, EN completely regressed, CRP returned to normal, and Brucella agglutination test was found to be positive at a 1/160 titer lower than baseline. A written informed consent was obtained from the patient.

DISCUSSION

Although EN is usually idiopathic, it may also be associated with many etiological factors. Brucellosis, on the other hand, is a rare condition observed in the etiology of EN and there are few cases reported in the literature.^[7-12] Etiologies of EN may vary depending on demographic characteristics.^[13] In the study by Kisacik et al.^[14] in Turkey, the etiologies of EN were idiopathic in 34.6% of cases and underlying conditions in 65.4% of cases. Behçet's disease was detected in 40 cases (37.4%) of a total of 107 cases.^[14]

Rheumatic diseases are not the most common causes of EN; however, EN may be observed in different groups of rheumatic diseases (such as Behçet's disease, systemic vasculitis, and autoimmune collagen vascular diseases). Among rheumatic

cases, EN occurrence is most common in Behçet's disease cases with a percentage of approximately 50%.^[15] The EN prevalence in Takayasu's arteritis was detected to be 6.25% in a retrospective study with 80 patients.^[16] Although skin involvement is 28 to 60% in polyarteritis nodosa (PAN), EN is not an expected symptom and the histopathology of nodules appearing in PAN cases is usually compatible with cutaneous vasculitis. The histopathology of subcutaneous nodules detected at a ratio of 80 to 100% in cutaneous PAN cases is compatible with vasculitis and may be confused with EN.^[17] Among Wegener granulomatosis cases with skin involvement, clinically and histopathologically confirmed EN was present.^[18] Brucellosis is an endemic infection in developing countries which can affect many organs including the musculoskeletal system, thus it is a great masquerader for rheumatologists. In a series of 400 Brucellosis cases, the prevalence of joint involvement was 26%, and the most prevalent manifestations were sacroiliac joint (26%) and knee joint (25%) involvement.^[19] Despite extensive joint involvement, skin involvement was detected in 6% of 436 brucellosis cases (n=27) and EN-like lesions were observed only in 11 cases.^[20] A review of brucellosis cases in the literature indicates that different symptoms accompanying EN were reported. Extensive arthralgia in addition to extensive EN in Goldstein's case,^[7] systemic symptoms such as fever and fatigue in Mazokopakis et al.'s^[9] case, 40°C fever prior to EN in Nardiello et al.'s^[10] case, fever, night sweating, fatigue and hepatosplenomegaly in Tanyel et al.'s^[11] case, and history of arthralgia prior to EN in Tanveer et al.'s^[12] case were among the reported symptoms. In our case, distinctively, no symptoms other than EN were observed before or during the diagnosis. The presence of EN for two weeks and early diagnosis and treatment of brucellosis may have prevented the occurrence of other symptoms. The high prevalence of brucellosis in the patient's area of residence was the most valuable clue for the differential diagnosis.

In conclusion, EN is a non-specific symptom which may occur in many different groups of diseases, during pregnancy or medication use, or in malignant processes. Although it is often idiopathic, it must be examined carefully with a multidisciplinary approach in terms of its etiologies. As in our case, it may occur as the initial symptom and contribute to early diagnosis and treatment of a systemic disease.

Declaration of conflicting interests

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