



Correspondence

Effectiveness of restoring vitamin B12 levels in the resolution of a case of erythema nodosum

Dear Editor,

Erythema nodosum (EN) is an inflammatory with acute onset. It is characterized by panniculitis, the presence of bilateral, symmetrical subdermal palpable, warm, and painful nodules, localized in the pretibial areas and rarely in the trunk, upper extremities, or other areas of the body. In adults it may be accompanied by fever, malaise, and arthralgias, whereas in children arthralgias and fever occur rarely. The diagnosis of EN is based on clinical evidence, and a skin biopsy should only be performed if the clinical picture, presentation, distribution, or duration of the lesions is atypical. Patients should be carefully evaluated for underlying causes which can be treated for lesion resolution. Treatment depends on the patient's specific needs and includes non steroidal anti-inflammatory drugs, corticosteroids, antibiotics, potassium iodide, hydroxychloroquine, topical heparin, and colchicine.^[1] Healing usually occurs in approximately 6–8 weeks.

We report the case of a 53-year-old woman who had an 18 months history of painful subcutaneous nodules in the pretibial areas [Figure 1a]. A deep skin punch biopsy was performed, and findings were consistent with EN [Figure 2]. The patient did not respond to classic therapies. She was in menopause for 3 years, did not have any history of immune-dermatological diseases, recent viral, bacterial, or fungal infections, hematological diseases, or neoplasms, did not report neuropathies, and followed a balanced and varied diet.

The laboratory investigations showed no abnormalities. Vitamin B12 was below the normal range 185 pg/ml (normal range 211–911), with negative anti-parietal cell antibodies and normal peripheral blood picture: Red blood cells $5.09 \times 10^6/\mu\text{L}$, HB 15.00 g/dl, mean cell volume 91 fL; white blood cells $5.97 \times 10^3/\mu\text{L}$. Chest X-ray, abdominal ultrasound, and esophagogastrroduodenoscopy were negative for anomalies.

The patient received intramuscular injections of 1,000 μg cyanocobalamin once a week for 5 weeks. After 2 weeks, the subcutaneous nodules were reduced by 50%; by the end of the injection therapy, the nodules had disappeared [Figure 1b]. After 1 year, the patient was in complete clinical remission and presents vitamin B12 values of 476 pg/ml.

The etiology of EN is difficult to identify given the plethora of possible causes. The mainstay of treatment is the identification and removal of the causative factor. Volkov *et al.*^[2] reported for the first time, the association of EN and vitamin B12 deficiency in a woman following a vegetarian diet and the regression of the dermatosis after cyanocobalamin supplementation.

Moreover, Milman and coll.^[3] described the case of EN and pernicious anemia and Eugénio *et al.*^[4] reported an unusual association between EN and autoimmune atrophic gastritis. In both cases, Vitamin B12 supplementation caused the regression of EN. Vitamin B12 is crucial for DNA synthesis and is derived from animal foods. Vitamin B12 deficiency is associated with hematological, neurological, psychiatric, gastrointestinal, and dermatological disorders.^[5]

Vitamin B12 deficiency is associated with an increased occurrence of inflammation and metabolic complications. Antitumor necrosis factor- α a hallmark of inflammation, shows an inverse correlation with serum levels of B12.^[6]

Adequate amounts of vitamin B12 provide the proper functioning of cell-mediated innate immunity, such as the



Figure 1: (a) The presence in the pretibial area of erythematous/violaceous nodules; in (b) almost total resolution of the lesions after the administration of Vitamin B12

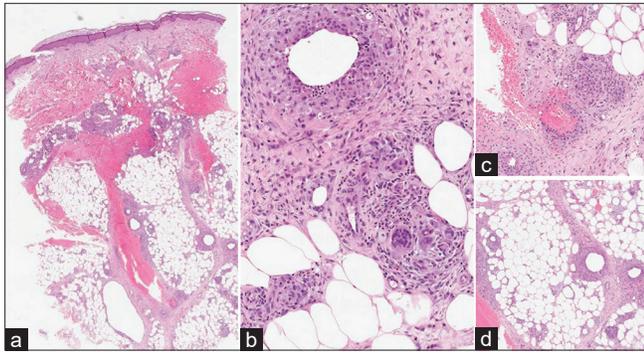


Figure 2: (a) Cutaneous pathology of erythema nodosum (EE, $\times 10$). (b and c) Inflammatory infiltrate along the fibrous septa between the fat (infiltrate constituted by neutrophils, lymphocytes, and histiocytes with the formation of noncaseating granulomas) (EE, $\times 20$)

ability to mount an effective oxidative burst together with cell movement, function, differentiation, and proliferation facilitates T-cell production and helps to regulate ratio between T helper and cytotoxic T-cells.^[7] Vitamin B12 deficiency is also associated with a decline in natural killer cell activity and a reduction of B lymphocytes.^[8]

We hypothesize that these immunomodulatory properties of the molecule, alone or in concert, may contribute to the resolution of EN.

Following the three cases described above, this is the first report of persistent, treatment-resistant EN associated with vitamin B12 deficiency “sine causa,” which quickly regresses after administration.

Unlike what reported by previous authors, in our patient, we could not demonstrate any cause to justify the vitamin B12 deficiency (diet/malabsorption).

Our experience suggests the importance of assessing vitamin B12 levels in EN, even in patients without an apparent cause of vitamin B12 deficiency. Being just a single case report, we cannot determine with certainty that the resolution of EN was, due to vitamin B12 administration, however, there are good reasons to hypothesize it. Even if the blood level of vitamin B12 was only slightly below the normal range, it suggests that even the supplementation in the presence of adequate levels of the molecule can be effective, as it is known to reduce local inflammation after peripheral nerve injury.^[9] The administration of cyanocobalamin induces resolution of the EN lesions, thus confirming the possible immunomodulatory role of vitamin B12, in inducing the resolution of the cutaneous inflammatory process.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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