Case Report

Erythema nodosum migrans successfully treated with indomethacin: A rare entity

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Abstract

Erythema nodosum migrans (subacute nodular migratory panniculitis) is a panniculitis characterized by migrating subcutaneous nodules or plaque on the lower extremity. We describe a 75-year-old woman with idiopathic erythema nodosum migrans which was manifest centrifugally spreading, slightly morpheaform erythematous plaque on the lower left leg successfully treated with indomethacin. She was initially diagnosed and treated as a case with cellulitis and with poor clinical response. A biopsy specimen from this lesion showed that the septal was thickening; fibrous tissue was also seen with lymphohistiocytic infiltrate and occasional multinucleated giant cells with some inflammatory cells infiltrated into the periphery of the fat lobules. Erythema nodosum migrans should be kept in mind in the differential diagnosis of any morpheaform centrifugally expended plaque, especially in the lower extremities in cases of unknown etiology.

Key Words: Chronic erythema nodosum, erythema nodosum migrans, panniculitis, vilanova disease

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INTRODUCTION

Erythema nodosum (EN), the most frequent variant of panniculitis, is a septal panniculitis with possible association with a wide variety of factors and disorders such as infection, pregnancy, drug intake, and some systemic conditions.[1] Some clinical variants of EN have been described under different names, including erythema nodosum migrans, subacute nodular migratory panniculitis, and chronic erythema nodosum, but probably they are just clinical variants which may all be included within the spectrum of EN.[2] Erythema nodosum migrans, a disorder characterized by migrating erythematous subcutaneous nodules or plaque on the legs, was first described by Bafverstedt in 1954[3] and was named subacute nodular migratory panniculitis by Vilanova and Piñol Aguade in 1956.[4] In this study, we describe a 75-year-old woman with idiopathic erythema nodosum migrans plaque on the lower left leg that was initially diagnosed as a case with cellulitis and with poor clinical response. Therefore, erythema nodosum migrans should be kept in mind in the differential diagnosis of any morpheaform centrifugally expended plaque, especially in lower extremities in cases of unknown etiology.

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CASE REPORT

A 75-year-old otherwise healthy woman was referred to us with a large tender erythematous morpheaform plaque without ulceration on the lower part of her leg. This plaque had begun as a small nodule on the shin 1 month prior to this visit. It had gradually extended outward in a centrifugal pattern despite oral antimicrobial treatment by her family physician. She was initially diagnosed and treated as a case with cellulitis and with poor clinical response. This patient denied having had a sore throat or arthralgia in the previous months. Other than diabetes mellitus type II, she had no significant medical history. She had been taking oral hypoglycemic agents for many years. On physical examination, it became evident that she had a large erythematous plaque measuring 30 × 30 cm^2 on the anterolateral aspect of her lower left leg [Figure 1]. There was mild edema and local tenderness on the leg plaque. The color of this morpheaform plaque varied from red to brown, and its surface was mildly scaling. A skin biopsy specimen was then taken from the newly extending area on the left calf. Histopathological examination revealed that the pathologic changes were mainly in the subcutaneous tissue, in which the septa were thickened and there existed lymphohistiocytic infiltrate and a few neutrophil and occasional multinucleated giant cells. Some inflammatory cells had infiltrated into the periphery of the fat lobules (Septal panniculitis) [Figure 2]. The vessels have not any obvious pathology. A mild perivascular inflammatory infiltrate was also present in the dermis. The overlying epidermis was mildly acanthotic and hyperkeratotic. These findings suggested a diagnosis of erythema nodosum migrans. The results of laboratory investigations were within normal limits. A skin test of PPD and the titer of antistreptolysin O (ASO) proved negative. The chest radiograph has normal appearance. On the basis of the clinical pathological findings, we diagnosed the patient's eruption as erythema nodosum migrans. The patient was treated with oral indomethacin, and topical clobetasol propionate lotion twice daily; this resulted in significant gradual improvement over a period of 1 month.

DISCUSSION

Erythema nodosum migrans, which is seen predominantly in women, is often unilateral. According to Bafverstedt's original descriptions, it presents itself as persistent nodular lesions where these nodules are enlarged by confluence or peripheral extension (centrifugal extension with central clearing) to form plaques. Compared to classic EN, the symptoms are milder, and the course is prolonged and is characterized by nodules that migrate or expand in a centrifugal manner[3] and may assume a yellowish or morpheaform appearance.[5] Lesions tend to be less tender than those of classic EN. There may be few, if any, associated systemic symptoms.[3] Most reported cases of EN migrans such our case are women aging between 15 and 65 years old, with a solitary lesion and a recent history of sore throat with streptococcal infection (as evidenced by elevated antistreptolysin O and anti-DNase B titers), arthralgia, or thyroid disease.[3,6,7] Some of its clinical and pathological characteristics are similar to chronic EN, and it is believed by many to represent a variant of the latter (septal panniculitis).[4,8] However, microscopically, in contrast to more classic forms of EN, subacute nodular migratory panniculitis shows greater septal thickening, more prominent granulomatous inflammation along the borders of widened subcutaneous septa, absence of phlebitis, and rare hemorrhage.[6] A cellulitic variant simulating erysipelas, although rare, was recognized in a previous report. Because of septal panniculitis,

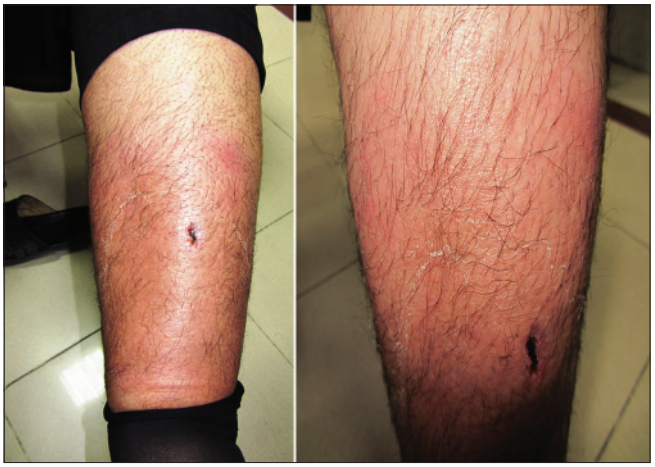

Figure 1: Erythema nodosum migrans. Erythematous subcutaneous plaque on anterolateral lower ex-tremity, with peripheral extension later in the course and without ulceration

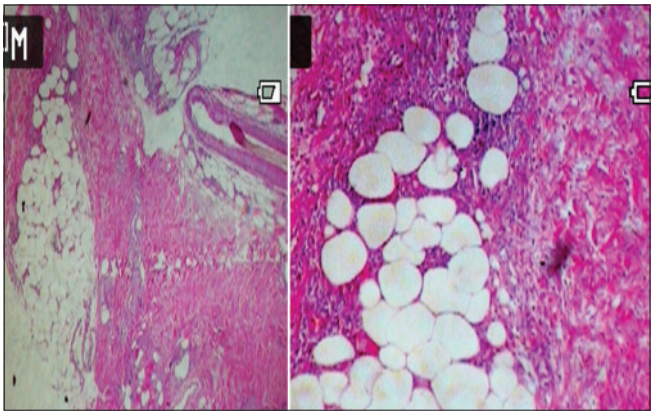

Figure 2: Erythema nodosum migrans. The lymphohistiocytic infiltrate mainly in the edematous thicken septum (H and E, ×40(left), ×100(right)

histopathology of EN and EN migrans is relatively specific. The other form of septal panniculitis such as morphea and α_1-antitrypsin deficiency panniculitis has an additional finding that helps to differentiation of these entities. In our patient, the histological finding consists of the EN migrans. Yu-Chih Lin *et al.* also reported this variant in a 69-year-old man on anterolateral of his calves similar to our patient.[9] The cause and mechanism of classic EN or EN migrans are obscure. It has been associated to thyroid infectious and inflammatory diseases, drugs, and malignant neoplasms. Pregnancy has also been reported to be a triggering factor. The triggering events of EN migrans are slightly different from those of classic EN. In Hannuksela's series of EN migrans, pregnancy was reported most frequently, followed by streptococcal infections.[10] While in the series of De Almeida Prestes *et al*., the most frequently reported associated condition of EN migrans was streptococcal infection.[6] Lazaridou *et al.* present a case of ENM in a 33-year-old male patient with hepatitis B infection. The patient was under treatment with antiviral drugs for hepatitis B infection and had an excellent response to treatment with potassium iodide.[11] In our patient, no diseases or conditions underlying the eruption were found. The culture of throat swab were considered normal flora of the oropharynx. According to the observation of De Almeida Prestes *et al.*, severe septal fibrosis, multiple granulomas, and granulation tissue-like capillary formation are correlated with unilateral migratory diseases. The chronic EN group tends to show milder septal fibrosis and lymphohistiocytic perivascular inflammation with only focal granulomas.[6] In our case, the biopsy specimen showed septal fibrosis and granuloma formation was milder compared to the previous reported case. Untreated, subacute nodular migratory panniculitis can last for months or years. However, treatment with potassium iodide is usually effective, resulting in clearing of lesions within several weeks.[5] The treatment of EN migrans is nonspecific. Bed rest, firm supportive bandage, or stockings are helpful. Many patients respond to potassium iodide 360-900 mg daily for 3 to 4 weeks. Naproxen, other NSAIDs, and hydroxychloroquine have sometimes been effective.[12] Ubogy *et al.* reported that the three patients with EN secondary to streptococcal pharyngitis were treated with indomethacin 100-150 mg orally for 2 weeks with excellent results, after having failed to respond to treatment with erythromycin, penicillin, and aspirin.[13] In addition, Barr *et al.* reported chronic idiopathic EN in a 32-year-old woman that had been unsuccessfully treated with aspirin, resolved with indomethacin 25 mg three times daily for 1 month.[12]

Our patient responded to the treatment of oral indomethacin administered over a 3-week period. Similar therapy is reported to have been effective in both classic erythema nodosum and erythema nodosum migrans. In conclusion, our experience and success with indomethacin for EN migrans is observational and not the result of a randomized, controlled trial.

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REFERENCES

1. Papagrigoraki A, Gisondi P, Rosina P, Cannone M, Girolomoni G. Erythema nodosum: Etiological factors and relapses in a retrospective cohort study. Eur J Dermatol 2010;20:773-7.
2. Requena L, Requena C. Erythema nodosum. Dermatol Online J 2002;8:4.
3. Bafverstedt B. Erythema nodosum migrans. Acta Derm Venereol 1968;48:381-4.
4. Vilanova X, Pinol Aguade J. Subacute nodular migratory panniculitis. Br J Dermatol 1959;71:45-50.
5. Ross M, White GM, Barr RJ. Erythematous plaque on the leg. Vilanova's disease (subacute nodular migratory panniculitis). Arch Dermatol 1992;128:1644-5, 7.
6. de Almeida Prestes C, Winkelmann RK, Su WP. Septal granulomatous panniculitis: Comparison of the pathology of erythema nodosum migrans (migratory panniculitis) and chronic erythema nodosum. J Am Acad Dermatol 1990;22:477-83.
7. Perry HO, Winkelmann RK. Subacute Nodular Migratory Panniculitis. Arch Dermatol 1964;89:170-9.
8. White WL, Hitchcock MG. Diagnosis: Erythema nodosum or not? Semin Cutan Med Surg 1999;18:47-55.
9. Chen Y-CLJ-S, Chiu HC. Erythema Nodosum Migrans Mimicking Cellulitis: Report a case. Dermatol Sinica 2009;19:63-7.
10. Hannuksela M. Erythema nodosum migrans. Acta Derm Venereol 1973;53:313-7.
11. Lazaridou E, Apalla Z, Patsatsi A, Trigoni A, Ioannides D. Erythema nodosum migrans in a male patient with hepatitis B infection. Clin Exp Dermatol 2009;34:497-9.
12. Lehman CW. Control of chronic erythema nodosum with naproxen. Cutis 1980;26:66-7.
13. Barr WG, Robinson JA. Chronic erythema nodosum treated with indomethacin. Ann Intern Med 1981;95:659.

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