CASE REPORT

AN UNUSUAL PRESENTATION OF LEPROSY AT DIAGNOSIS: ERYTHEMA MULTIFORME-LIKE TYPE 2 REACTION

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ABSTRACT

This study describes a case of erythema multiforme (EM) as the first clinical manifestation of leprosy in a 35-year-old woman. She presented at the hospital with fever, arthralgia and erythematous plaques on both elbows and knees, some of them with bullous or necrotic center areas. The diagnosis was confirmed by skin biopsy, which revealed a well-known EM pattern, and also showed the presence of Virchow cells and acid-fast bacilli. Physicians should be aware that leprosy must be considered in the differential diagnosis of EM, especially in endemic regions.

KEY WORDS: Leprosy. Erythema multiforme.

CASE REPORT

A 35-year old female from Brazil presented to the hospital with a 2-month history of intermittent fever and polyarthralgia. Twenty days before admission, erythematous plaques developed on her knees and elbows, and gradually evolved into bullae and necrosis. At that time, benzathine penicillin was given to treat presumed syphilis; however, the lesions remained unchanged. The patient had an unremarkable past medical history except for phenobarbital therapy for epilepsy since the age of 13. There was no history of travel or recent infections (e.g. Mycoplasma or herpes simplex). No similar lesions were reported in family members or close contacts.

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Physical examination revealed a few large erythematous and annular skin lesions bilaterally on knees and elbows. Some of the lesions had ulcerated or bullous centers (Figure 1 and Figure 2), and there were no lesions in hands, feet or other sites. Enlarged bilateral axillary and inguinal lymph nodes were also noted. No mucosal involvement was observed. Laboratory tests for hematocrit, platelets count, creatinine, glucose, serum aspartate aminotransferase, and urinalysis showed normal ranges. Syphilis serological treponemal and non-treponemal tests were also negative.

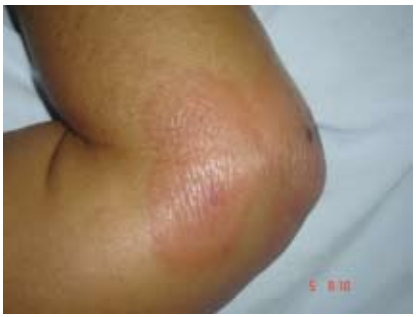

Figure 1. Targetoid lesion of the left arm.

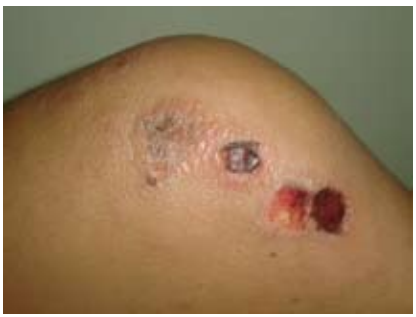

Figure 2. Bullous and ulcerous lesions on the patient's left knee, surrounded by edema and a peripheral red ring.

Skin biopsies of the targetoid lesions were obtained from elbows and knees. Histopathological examination revealed preserved epidermis thickness layered by necrotic and hematic fibrin cells, under which reepithelialization was eminent. There was also dermal inflammatory mononuclear cell infiltration with subepidermal blistering formation (Figure 3a). Taken together, these clinical and histopathological findings are compatible with the patterns described in EM. Furthermore, multibacilar leprosy diagnosis was revealed by the presence of foamy histiocytes with vacuolated cytoplasm, known as Virchow cells containing acid-fast bacilli (Figure 3b), and epithelioid cells, which characterize borderline lepromatous leprosy (BL).

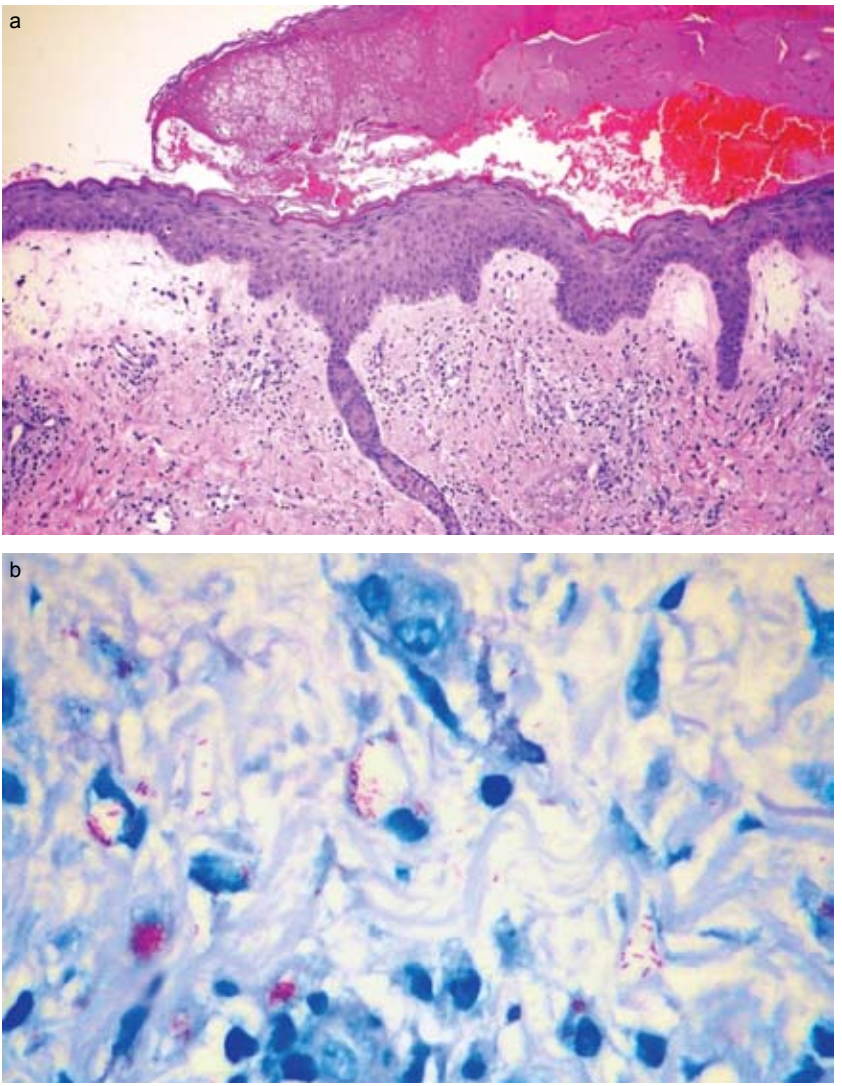

Figure 3. Histopathology of skin biopsy of targetoid lesions. a) Reepitelization of the epidermis and confluent necrosis the subepidermal blister in left arm. Mononuclear cell infiltration with vacuolated histiocytes, oedema ofthe dermis with subepidermal vesicles, likely preceding bullous formation (hematoxylin and eosin stain, x100). b) Numerous fragmented and preserved acid-fast bacilli in skin biopsy of the knee lesion (Fite-Faraco x800).

DISCUSSION

Leprosy is a dermato-neurological chronic infection caused by *Mycobacterium leprae,* an acid-fast intracellular bacilli, not cultivated *in vitro* (7). EM is an acute, self-limited inflammatory skin eruption considered to be a rare hyper reactive syndrome that usually follows infection by herpes simplex virus or *Mycoplasma pneumoniae*, and is seldom precipitated by other infections or drugs (11, 13). Besides the expression of systemic symptoms, EM has been so named because of a variety of dermatological presentations; however, its typical trait consists in localized targetoid lesions, with regular round shape and defined borders, sometimes with crusting or blistering, that detaches below 10% of the body surface area (3, 5). Despite being an unusual event, patients with leprosy infection are more prone to develop EM as a type 2 reaction, mostly those who are under multidrug therapy (MDT) (10, 12).

The patient herein described had clinical features compatible with EM, in which skin, lymph nodes, and joints were involved. The targetoid pattern and the acral and symmetrical distribution of the patient's lesions are compatible with dermatological characteristics of EM. We are aware that long-term use of phenobarbital can precipitate Steven-Johnson Syndrome and Toxic Epidermal Necrolysis (2). These clinical entities may also result in cutaneous lesions similar to the ones presented by this patient, but in such circumstances there is usually mucosal involvement, unlike the EM. Considering the possibly etiology of EM, it seems that none of the medications used by the patient contributed to the appearance of the skin lesions. The benzathine penicillin was administered just after the patient's first dermatological manifestations, and there was no worsening of those lesions nor development of new ones, even with phenobarbital maintenance. In addition, the patient had no history of any recent infection that could be implicated as a cause of EM.

Histopathological findings of EM depend on the stage of the tissue injury. In newly diagnosed lesions there is basal cell hydropic degeneration and keratinocyte apoptosis. However, as the patient had a 20 day-history of lesions, there was already necrotic and reepithelialized areas in epidermis, dermal edema and lymphocytic infiltration with subepidermal blistering, all suggestive findings of EM late stage (1, 6). The presence of Virchow cells and acid-fast bacilli established the diagnosis of leprosy and the classification as BL was based on histhopathological and clinical features, according to Ridley & Jopling criteria (15). Despite the high *M. leprae* load observed, the cause of the EM lesions cannot be ascertained by histopathology because there is not a pathognomonic pattern that defines with certainty the etiology of EM. Considering all these features, we propose that the patient developed EM probably due to leprosy infection.

Two remarkable findings in our patient were the development of type 2 reaction before leprosy multidrug therapy and EM lesions. Erythema multiforme as the first clinical manifestation of leprosy is an atypical presentation, even in

leprosy endemic regions such as Asia and South America. Table 1 summarizes the main findings of four previous publications on leprosy type 2 reaction and EM (4, 8, 9, 14). In recent reports from Brazil (4, 9) and India (8) *M. leprae* was found in biopsies of plaques or targetoid skin lesions of untreated patients. Another Brazilian study noticed that among 51% patients presenting leprosy type 2 reactions, about 8% had clinical and histopathological features compatible with EM; however, all of them were under MDT (14).

Our patient was successfully treated for a type 2 reaction with prednisone. Corticosteroid therapy, although controversial for other causes of EM, represents the main therapeutic option for leprosy reactions, as they are used to suppress the inflammatory response and the release of cytokines provoked by *M. leprae* infection (12). Specific drugs to multibacillary leprosy were started on day five consisting of one year of daily unsupervised administration of dapsone and clofazimine and monthly supervised rifampin and clofazimine, as recommended by the WHO (World Health Organization, 16).

We herein found that EM is one of the atypical skin lesions associated with leprosy. Therefore, clinicians should consider leprosy in the differential diagnosis for patients with EM, mainly in countries where the disease is endemic, but also in developed ones due to increasing immigration from leprosy endemic countries.

POTENTIAL CONFLICTS OF INTEREST

No conflicts of interest are reported.

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RESUMO

Apresentação atípica de Hanseníase ao diagnóstico: Eritema Multiforme (reação tipo 2)

Este estudo descreve um caso de Eritema Multiforme (EM) como a primeira manifestação clínica de Hanseníase (MH) em uma mulher de 35 anos. Quando atendida em um Hospital, a paciente apresentava febre, artralgia, e placas eritematosas em ambos os cotovelos e joelhos bilateralmente, algumas com bolhas e/ou necrose central. O diagnóstico foi confirmado por meio de biópsias de pele, que revelaram um padrão histopatológico compatível com EM, além da presença de células de Virchow e bacilos álcool-ácido resistentes (BAAR). Médicos em geral, especialmente os clínicos, devem considerar MH como diagnóstico diferencial de EM, especialmente em regiões endêmicas da doença.

DESCRITORES: Hanseníase. Eritema Multiforme.

Table 1. Reported cases of erythema multiforme in leprosy patients

Reference	Number of cases	Body location	Systemic symptoms	Skin lesions	Under MDT treatment	Histopathological findings (1) EM (2) Leprosy
Nery et al 1999 (14)	13	Limbs, chest	Fever, malaise, oedema	Plaques with bullae in center	All cases	(1) Epidermis necrotic cells; dermal oedema and subepidermal blister (2) Fragmented *M. leprae* bacilli*
Barreto et al 2005 (4)	1	Face, limbs, back, chest	Fever, lymphadenopathy	Plaques	No	(1) Mononuclear infiltration with vacuolar alteration (2) High load of *M. leprae* bacilli
Das Sudip et al 2007 (8)	1	Face, limbs, back, chest	Fever, lymphadenopathy	Plaques	No	(1) Mononuclear infiltration with vacuolar alteration (2) High load of *M. leprae* bacilli
Esquenazi et al 2008 (9)	3	Limbs	Fever, malaise, lymphadenopathy, oedema	Targetoid plaques, bullae and ulcers	2 cases	(1) Dermal oedema and mononuclear infiltration (2) High load of *M. leprae* bacilli
Present patient 2009	1	Limbs	Fever, lymphadenophaty	Targetoid plaques, bullae and ulcers	No	(1) Epidermis necrotic cells; dermal oedema, mononuclear infiltration and subepidermal blistering (2) High load of *M. leprae* bacilli

MDT - multidrug treatment
EM - erythema multiforme
**M leprae* bacilli load not available

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