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Erythema Nodosum Leprosum in Malaysians

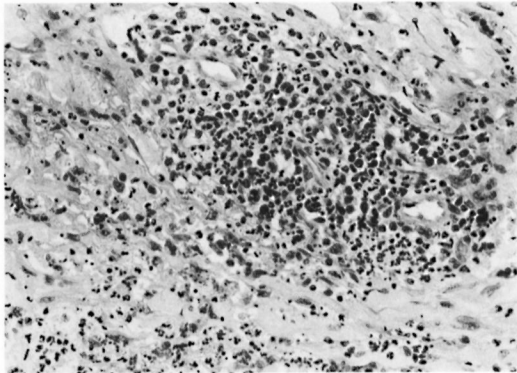
TO THE EDITOR:

Reactions and relapses in leprosy pose major problems in the management of the disease. A reaction is an allergic inflammatory process which is not an essential part of the infective process of leprosy. Reactions which occur in the multibacillary type of leprosy are erythema nodosum leprosum (ENL), exacerbation reactions, the Lucio reaction, and reversal or upgrading reaction (¹). Clinically, it is difficult to differentiate reactions from relapse. Microscopic examination of the lesion is very useful for the proper diagnosis. This study documents the histological features of ENL with clinical correlation in Malaysian patients.

Skin biopsies from leprosy patients sent to the Institute of Medical Research, Kuala Lumpur, Malaysia, during the period between January 1988 and December 1992 were reviewed. Sections cut from paraffin-embedded material were stained with hematoxylin and eosin (H&E) and Fite's stain for acid-fast bacilli (AFB). In addition, Mar-

tius' scarlet blue stain for fibrin and immunohistochemical stains were performed in suspected cases of ENL. Specifically, the immunoperoxidase method of Sternberger (¹⁰) was applied with modification. Antisera were obtained from Dakopatts and included immunoglobulin IgG and complement component C3. The diagnosis was based on the criteria of Ridley and Jopling (⁷).

A total of 189 biopsies from suspected leprosy patients were reviewed. The histological diagnosis was tuberculoid leprosy (TT) 5 cases, borderline tuberculoid leprosy (BT) 38 cases, borderline leprosy (BB) 2 cases, borderline lepromatous leprosy (BL) 49 cases, and lepromatous leprosy (LL) 95 cases. The features of ENL were observed in 6 LL patients and 1 BL patient. These patients were composed of 6 males and 1 female. The age range was between 19 to 32 years. All 7 patients with ENL presented with tender nodules, 5 of the 7 having concomitant fever. Two patients had edema of the legs. All 7 patients except one had re-



THE FIGURE. Erythema nodosum leprosum showing infiltration of the granuloma by neutrophils (H&E $\times 500$).

ceived antileprosy therapy consisting of multiple drug therapy (5 cases) and dapsone (1 case).

Histology showed infiltration of the granulomas by neutrophils in all cases (The Figure). The interstitium also showed minimal infiltration of neutrophils in all cases. The primary site of inflammation was mainly in the dermis in 6 cases, with extension of inflammation into the subcutaneous fat in 2 cases. Mild edema of the upper dermis was observed in 2 cases. Vasculitis involving a medium sized vein in the dermis was noted in 1 case. None of the cases had ulceration of the skin. Acid-fast stain revealed a few highly fragmented AFB in 1 case. Immunocytochemical stains did not show deposits of IgG or complement in any of the cases.

ENL is a known complication occurring in patients with multibacillary (MB) leprosy, and it is one of the most common type of reactions in leprosy (2). ENL usually occurs after the commencement of chemotherapy (1) but sometimes it can develop prior to any medication. (5).

In our study, the histological diagnosis of ENL was made in 4.8% (7/146 cases) of MB leprosy. Some of the histologic features noted in our study, such as inflammatory reaction with predominant involvement of the upper dermis, absence of ulceration and low incidence of vasculitis are similar to those seen in Malaysian patients in the previous report by Ridley, *et al.* (8). In that study, the workers noted well-developed edema in the dermis. In contrast, in our study subepi-

dermal edema was noted only in 2 (28.5%) cases and it was mild in both. In Mexican patients, the primary site of inflammation was mainly in the deep dermis and subcutis in 15/18 cases (83.3%). In Singapore, biopsies of patients with ENL showed four patterns: classic, subepidermal bulla or edema, vasculitis, and nonspecific change. Subepidermal bulla with upper dermal edema was the predominant pattern (3).

The etiology of ENL is uncertain. There are two hypotheses regarding the pathogenesis of ENL. Modlin, *et al.* (4) proposed that the cell-mediated immune response plays an important role in ENL pathogenesis based on a study of the subsets of T lymphocytes in LL patients with and without ENL. They noted a high ratio of helper-suppressor cells in ENL tissue and low ratio in LL patients without ENL.

Wemambu, *et al.* (11) observed deposits of complement components and immunoglobulin in the vessel walls of an ENL lesion, and suggested that ENL is a manifestation of the Arthus phenomenon. Ridley and Ridley (10) observed deposits of bacterial antigen, immunoglobulin IgG, IgM, and complement components at the site of ENL lesions. These deposits were seen extracellularly and intracellularly in the neutrophils and degenerating macrophages. They concluded that ENL is an immune complex phenomenon, but differs from the classic serum sickness because the immune complexes are extravascular. In our study there were no deposits of complement or immunoglobulin.

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Follicular Keratoses in Leprosy and Post-Kala-Azar Dermal Leishmaniasis

TO THE EDITOR:

The term "follicular keratoses" refers to a group of varied etiology in all of which there is a prominent plug of keratin in the follicular orifice (¹). Keratosis pilaris, keratosis pilaris atrophicans, keratosis circumscripta, phrynoderma, lichen spinulosa, follicular ichthyosis, to name a few, are the disorders in which this pathology is prominently seen (¹). In most of these disorders, the exact cause of keratinization is unclear. In some the type of keratitis is abnormal, in others the shedding mechanism or the rate of production is at fault. The histopathological changes are distinctive in a few instances, but often the morphological differences are more striking.

Many inflammatory conditions of the skin tend to develop a follicular keratosis. Two types of follicular keratoses, keratosis spinulosa (²) and comedo (³) have been described over the lesions of borderline tuberculoid (BT) leprosy. We report such le-

sions in three patients, one each with borderline lepromatous (BL), lepromatous leprosy (LL) and post-kala-azar dermal leishmaniasis (PKDL).

Case 1. A 45-year-old woman with polar lepromatous leprosy (LLp), with a bacterial index of 4+ and a morphological index of 1%, was receiving the World Health Organization multibacillary multidrug regimen (WHO-MDT-MBR). During her sixth monthly follow up, multiple, 1- to 3-mm keratotic pigmented papules with follicular atrophy at places were seen over some of the infiltrated plaques present on her forearms and legs.

Case 2. A 33-year-old man suffering from borderline lepromatous (BL) leprosy for the last 3 years presented in one of the episodes of type 1 lepra reaction. There were multiple, hyperkeratotic, pigmented follicular papules over a few of the erythematous infiltrated plaques on his back. No follicular scarring or atrophy was appreciated. Ac-