Acute Necrotizing Lepromatous Lymphadenitis: an Erythema-nodosum-leprosum-like Reaction in Lymph Nodes

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Summary: Histological examination of lymph-node biopsy specimens in 12 patients with erythema nodosum leprosum showed almost complete replacement of the node by lepromatous granuloma, together with considerable polymorph infiltration. Ziehl-Neelsen staining demonstrated numerous *Mycobacterium leprae* present in the nodes. The majority of these patients were very ill, and responded to prednisolone or corticotrophin.

It is suggested that the histological appearances may represent an intensive inflammatory response in the lymph nodes followed by avascular aseptic necrosis.

Introduction

Specific lesions of lepromatous leprosy in the form of lepromatous granulomatous processes involving lymph nodes in the superficial regions of the body have been well documented (Hansen and Looft, 1895 ; Furniss, 1953 ; Khanolkar, 1964). In patients with advanced lepromatous leprosy enlargement of the inguinal, axillary, cervical, and epitrochlear glands is seen fairly commonly and often exists concurrently with hepatosplenomegaly (A. B. A. Karat, personal observation).

During the exacerbated phases of lepromatous leprosy which are characterized by erythema nodosum leprosum and a febrile illness, enlargement of the lymph nodes, liver, and spleen tends to become more pronounced in cases where there was pre-existing enlargement of these organs, and such enlargement may be noticed for the first time in a fair proportion of patients at this phase of the disease. In the majority of these patients, with the subsidence of the erythema nodosum leprosum the enlargement of the lymph nodes, liver, and spleen also clears up. Occasionally, especially in patients with severe necrotizing and/or bullous erythema nodosum lesions, the enlargement of the lymph nodes may proceed to the development of pain and tenderness in these nodes, progressing to fluctuation of the nodes, and may mimic suppurative lymphadenitis, especially in view of the hectic temperature and marked polymorphonuclear leucocytosis, which characterize this complication.

Among the reports of lymph node involvement in leprosy we were unable to find a clinical description of this complication with appropriate histological and bacteriological study of the lymph node lesions at this phase of the disease.

Present Investigation

At the Schieffelin Leprosy Research Sanatorium, Karigiri, during the past four years there were 395 admissions for management of erythema nodosum leprosum. Of these patients 78 had enlargement of lymph nodes. Thirty patients developed rapid painful enlargement of lymph nodes with fluctuation and septicaemic temperature. All the patients had leucocytosis ranging from 10,000 to 21,800/cu. mm., with polymorphs

ranging from 75 to 92%. In these patients blood cultures were done, as well as serological tests for typhoid, brucella, and infectious mononucleosis. Repeated blood examination for microfilariae was negative. In 12 patients a representative lymph node biopsy was done.

Operative Findings.—At surgery the lymph nodes were found to be oedematous, matted, and very vascular. On incision of the node a thick purulent material similar to that seen in suppurative lymphadenitis oozed from it. The purulent necrotic material obtained was tested as follows: (1) Ziehl-Neelsen and gram stains, (2) routine culture, and (3) culture for *Mycobacterium tuberculosis*. The "abscess cavity" and the lymph node excised for biopsy were also sent for histological examination.

The Ziehl-Neelsen stain of smears of the lymph nodes showed numerous acid-fast bacilli, mostly granular, a few globi, and a few solid bacilli. All the specimens examined bacteriologically were sterile on routine culture and on culture for *M. tuberculosis*.

Histological Examination showed lymph nodes practically replaced by lepromatous granuloma with loss of lymph node architecture. The striking feature in all the specimens examined was the marked infiltration of the lepromatous granuloma by large numbers of polymorphonuclear leucocytes with necrosis of the tissue. The histological picture was indistinguishable from acute suppurative lymphadenitis (Figs. 1 and 2). Ziehl-

FIG. 1.—General view of lymph node section showing abscess cavity (H. and E. $\times 30$.)

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Neelsen stain of lymph node sections showed numerous *M. leprae*—some solid and some non-solid—and a few globi (Fig. 3).

FIG. 2.—“Abscess” wall with foam-cell granuloma infiltrated with numerous polymorphs. (H. and E. $\times 300$.)

FIG. 3.—Foam-cell granuloma in the lymph node with numerous granular bacilli. (Ziehl-Neelsen. $\times 480$.)

Management.—The majority of these patients were very ill and toxic, and responded rather dramatically to prednisolone or corticotrophin, without the use of any antibiotics. A few responded to the intravenous administration of potassium antimony tartrate alone, starting at 10 mg., stepping up the dose in increments of 10 mg. to a maximum single dose of 40 mg. and a total dose of 250/300 mg. We have found a course of daily intramuscular injections of 1 g. of streptomycin with 300 mg. of isoniazid by mouth to be a very satisfactory alternative to dapsone in these patients when given for 6 to 12 weeks before institution of other specific anti-leprosy therapy (Karat *et al.*, 1967b). It should be emphasized that neither penicillin nor any of the broad-spectrum antibiotics appear to be effective in these patients.

Discussion

Faced with a patient who is severely ill with hectic temperature and progressive tender enlargement of lymph nodes going

on to suppuration, along with hepatosplenomegaly and marked polymorphonuclear leucocytosis, the clinician has a difficult diagnostic problem calling for immediate remedial measures. When these symptoms and signs appear in a patient with lepromatous leprosy concurrently with erythema nodosum leprosum it is important to consider the possibility of acute necrotizing leprosy lymphadenitis.

The pathogenesis of erythema nodosum leprosum is not yet well defined. Most leprologists favour the concept of an antigen-antibody reaction as the fundamental basis of this rather dramatic complication of leprosy (Wolcott, 1947; Ingram and Brain, 1957). The typical “cell” of response associated with erythema nodosum leprosum is the polymorphonuclear leucocyte, which is greatly increased in peripheral blood during this phase of the disease (Souza Campos and Rath de Souza, 1954), and characterizes the histological appearance of erythema nodosum leprosum in the skin (Mabalay *et al.*, 1965), nerve (Job and Bhaktaviziam, 1967), and synovial membrane (Karat *et al.*, 1967a). Ridley (1960) suggested that wherever *M. leprae* is seen one may expect an erythema-nodosum-leprosum-like reaction. This is increasingly being appreciated with more intensive study of visceral lesions in leprosy.

The rather dramatic and painful complication of necrosis of lymph nodes in leprosy may in fact represent intense inflammatory response in lymph nodes followed by avascular aseptic necrosis of the gland, on the basis of a vasculitis which is well recognized as a lesion encountered in the erythema nodosum leprosum phase of lepromatous leprosy (Latapí and Chevez Zamora, 1948).

The interest in the present report lies in the fact that this condition is being adequately documented for the first time with bacteriological and histological studies. We hope it will help in the recognition of this syndrome and thus enable the clinician to initiate appropriate therapy in a group of patients who are acutely ill and may succumb to the illness. In our series, in the early days there was one death while we were waiting for a definite diagnosis and the patient was treated with broad-spectrum antibiotics in the vain hope that he had an infection which we could not identify or recognize.

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REFERENCES

- Furniss, A. L. (1953). *Indian J. med. Sci.*, 7, 475.
- Hansen, G. A., and Looft, C. (1895). *Leprosy: In Its Clinical and Pathological Aspects*, translated by Norman Walker. Bristol.
- Ingram, J. T., and Brain, R. T. (1957). *Diseases of the Skin*, 6th ed., p. 276. London.
- Job, C. K., and Bhaktaviziam, C. (1967). *Leprosy Rev.*, 38, 243.
- Karat, A. B. A., personal observation.
- Karat, A. B. A., Rao, P. S. S., Karat, S., and Job, C. K. (1967b). *Leprosy Rev.*, 38, 163.
- Karat, A. B. A., Karat, S., Job, C. K., and Furness, M. A. (1967a). *Brit. med. J.*, 3, 770.
- Khanolkar, V. R. (1964). In *Leprosy in Theory and Practice*, 2nd ed., edited by R. G. Cochrane and T. F. Davey. Bristol.
- Latapí, F., and Chevez Zamora, A. (1948). *Int. J. Leprosy*, 16, 421.
- Mabalay, M. C., Helwig, E. B., Tolentino, J. G., and Binford, C. H. (1965). *Int. J. Leprosy*, 33, 28.
- Ridley, D. S. (1960). *Int. J. Leprosy*, 28, 254.
- Souza Campos, N., Rath de Souza, P. (1954). *Int. J. Leprosy*, 22, 259.
- Wolcott, R. R. (1947). *Int. J. Leprosy*, 15, 380.