Leprous Lymphadenitis

Demonstration of Tuberculoid Lesions[1]

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Leprous lesions in lymph nodes have been described from very early times. The first scientific paper of Armauer Hansen on leprosy in 1869 was on a study of lymph nodes. In this he observed the "yellow granules" reported earlier by Danielssen (Vogelsang ([17])). Later, Klingmüller ([10]) and Basombrio ([2]) described lesions in lymph nodes in lepromatous leprosy. Gross autopsy findings in all organs, including lymph nodes, were described in detail by Mitsuda and Ogawa ([12]). They observed characteristic "grayish or yellowish lipoid degeneration" in lymph nodes, considering it as conclusive proof of lepromatous leprosy. The histologic appearance of the nodes in lepromatous leprosy was described in detail by Furniss ([7]). He found no lesion in the lymph nodes in tuberculoid cases. These findings were later confirmed by Sharma and Shrivastav ([15]), who also failed to see any lymph node lesions in the tuberculoid type of leprosy. Absence of lesions in the nodes of tuberculoid leprosy might be explained on the generally accepted ground that tuberculoid cases do not show a widespread dissemination of the infection. Lymph node enlargement, however, has been observed by us clinically and has also been reported by others ([5, 15]). It is possible, as Furniss believes, that many of the cases observed might represent nonspecific enlargement; but there is a significant number of cases with lymph node enlargement, in which skin lesions can be observed in the area drained by the affected nodes. It was felt therefore that a study should be made of lymph nodes in tuberculoid and borderline leprosy, based on selected cases where lymph nodes draining the lesions were enlarged.

MATERIALS AND METHODS

Lymph node biopsy specimens for study were obtained from patients attending the Schieffelin Leprosy Research Sanatorium, Karigiri, India. The patients were examined carefully and classified according to the system suggested by Ridley and Jopling ([14]) for research purposes. There were thus four groups of cases: lepromatous (LL), borderline (BB), borderline-tuberculoid (BT), and tuberculoid (TT). The borderline-lepromatous (BL) cases were included in the lepromatous group. The material was collected from a total of 33 cases. These included 12 cases in the lepromatous group (LL), eight cases in the borderline group (BB), eight cases in the borderline tuberculoid (BT) group and five cases in the tuberculoid (TT) group.

The sites of biopsy in the cases studied are shown in Table 1. In every case there were skin lesions in the area drained by the biopsied lymph node.

A portion of each lymph node was cultured for acid-fast bacilli in six of the lepromatous (LL), four of the borderline (BB), three of the borderline-tuberculoid (BT), and all five tuberculoid (TT) cases. For the purpose one-half of the node was homogenized, inoculated on Petragnani's medium, and incubated at 37°C for a minimum period of nine weeks. The other half was used for histologic examination. All the tissues for histologic examination were fixed in formol-Zenker's fluid and processed.

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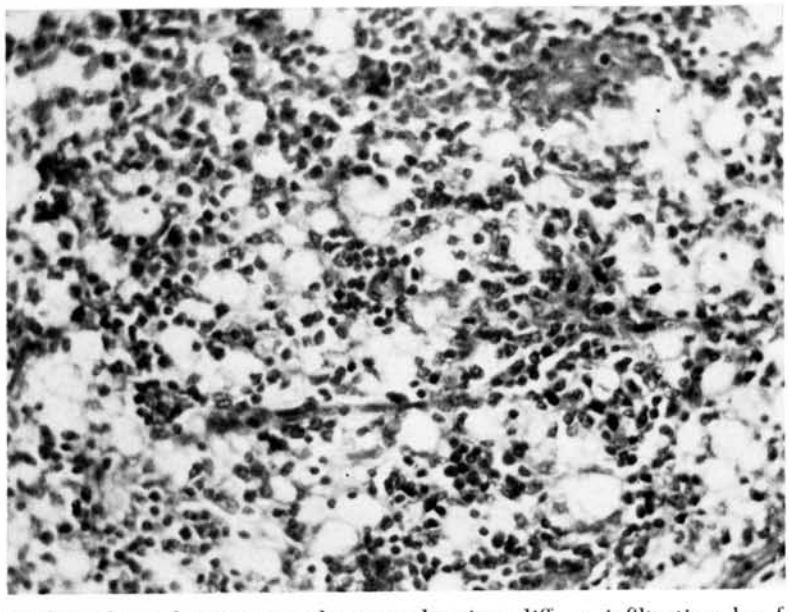

FIG. 1. Lymph node in lepromatous leprosy showing diffuse infiltration by foamy macrophages. H & E stain. × 300.

Paraffin sections 6 microns thick were stained with Ehrlich's hematoxylin and eosin stain and Fite's modification of the Ziehl-Neelsen stain. In a few cases, the sections were stained by Bielschowsky's method for reticulum.

OBSERVATIONS

The lymph nodes in all the lepromatous cases showed a picture similar to that observed by earlier workers. They were much enlarged, firm and discrete. On section, the cut surface showed a light brown color with yellowish streaks. Microscopically there was extensive replacement of the nodes by large collections of foamy macrophages (Fig. 1), which contained clumps of acid-fast bacilli. The medullary sinuses were infiltrated in all cases. Eight cases showed infiltration of marginal sinuses also. Reticulum fibers were seen around the macrophages, forming a characteristic net work of fine fibers (Fig. 2).

In the borderline group of cases the lymph nodes showed moderate enlargement, the largest of the specimens measuring 2.5 × 1.5 × 1.5 cm. The outer surface was smooth. The nodes were firm in consistency and discrete. The cut surfaces showed a uniform pink appearance. Microscopically the capsule was thickened and infiltrated by lymphocytes in seven cases. The lymph node structure showed an extensive granulomatous infiltration involving the cortex and medulla. The follicles were extensively replaced by the granulomata. Most of the remaining follicles were large, with prominent germinal centers. Four

TABLE 1. *Sites of lymph node biopsies in cases studied.*

Group	Nodes			Total
	Axillary	Inguinal	Epitrochlear	
LL	4	8	—	12
BB	2	1	5	8
BT	1	—	7	8
TT	1	1	3	5
Total	8	10	15	33

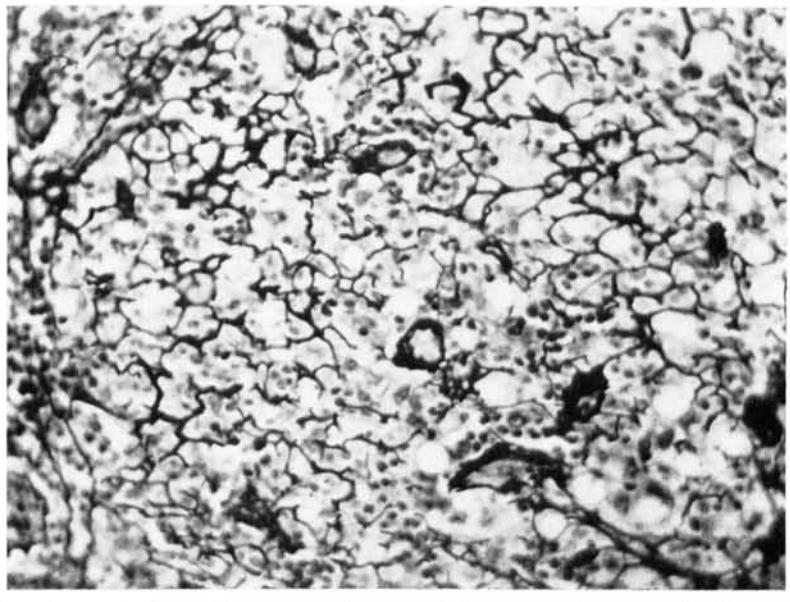

FIG. 2. Note the reticulum fibers around most of the macrophages in the lepromatous granuloma, which is typical of this type of lesion. Reticulum stain. ×300.

cases showed infiltration of the marginal sinuses with foam cells. The medullary sinuses were infiltrated by granulomatous tissue in six cases. In all the cases the sinuses that were not infiltrated by the macrophages were dilated, and there was also hyperplasia of the littoral cells. The granuloma in all the cases was composed chiefly of collections of macrophages having an abundant eosinophilic granular cytoplasm with large, pale, vesicular nuclei. Intermingled were macrophages with vacuolated cytoplasm. Scattered collections of epithelioid cells were also present in every

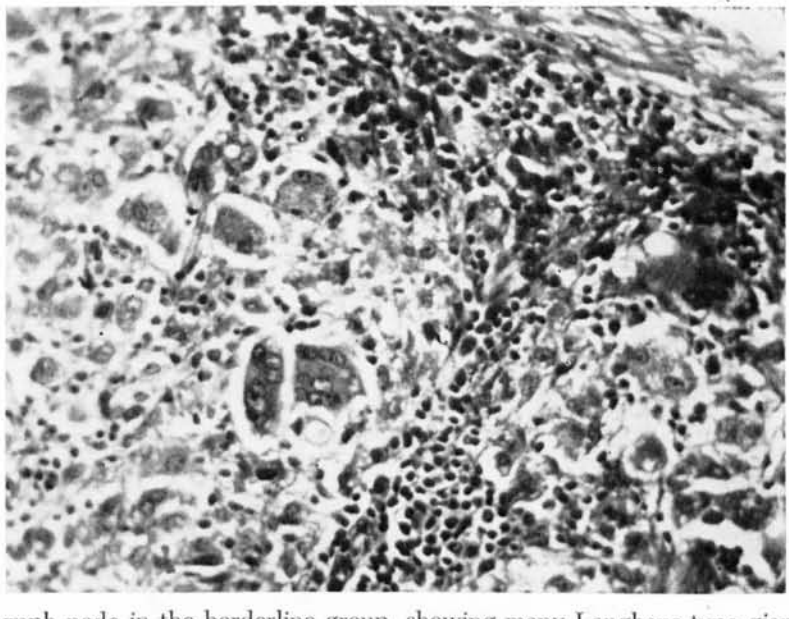

FIG. 3. Lymph node in the borderline group, showing many Langhans type giant cells and a few epithelioid cells scattered irregularly. Along with these, several marophages are also seen. H & E stain. ×300.

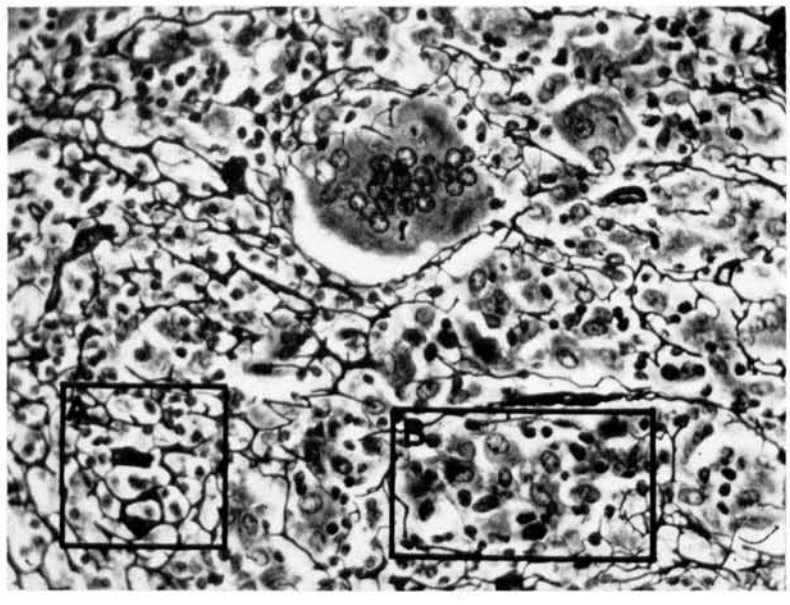

FIG. 4. The reticulum stain shows well formed reticulum fibers around macrophages (**A**), and destruction of the fibers in the focus of epithelioid cell collection (**B**). Reticulum stain. ×300.

case. Several Langhans type giant cells were scattered irregularly in the granuloma (Fig. 3). There was some increase in vascularity. Acid-fast bacilli were seen in clumps inside the macrophages in six out of the eight cases. Reticulum stains showed well formed reticulum enclosing most of the reticuloendothelial cells. The germinal centers stood out prominently, with hardly any reticulin fibers in them. In the granuloma there were reticulum fibers around the macrophages, but they were destroyed around the epithelioid cell collections and giant cells (Fig. 4). Since the epithelioid cells were irregularly scattered, the destruction of the reticulum fibers showed an irregular pattern unlike the arrangement in the tuberculoid cases, where well-defined tubercles could be made out. All four of the lymph nodes cultured for acid-fast bacilli showed no growth.

In tuberculoid cases the nodes were small and discrete. The largest of the biopsied nodes measured 2 × 1 × 1 cm. The outer surface was smooth. The cut surface showed a uniform pink appearance. Microscopically the lymph nodes in the borderline-tuberculoid (BT) group of cases showed a pronounced involvement by the granuloma. The capsule was infiltrated by lymphocytes in five cases. There was extensive and diffuse infiltration of the lymph node, and in one case almost entire replacement of the lymph node structure by granuloma. In other cases many of the follicles or medullary cords were infiltrated. The remaining follicles were large, with prominent germinal centers. Marginal sinuses were infiltrated in four cases, and two showed infiltration of medullary sinuses also. The granuloma was composed of clusters of epithelioid cells and giant cells. The clusters were quite large and showed well formed tubercles (Figs. 5 and 6). There was no caseation in any of them. The lesions were similar to those seen in sarcoidosis. In one case only acid-fast bacilli were present, and they were few. In the reticulum stain there was destruction of the reticulum fibers at the center of the granuloma and at the periphery; the fibers were coarse and condensed (Fig. 7). In three cases, the lymph nodes were cultured for acid-fast bacilli; there was no growth.

The cases of the tuberculoid (TT) type showed a slightly different distribution of the lesions. Of the five cases studied, two showed lymphocytic infiltration and thickening of the capsule. Small tubercles, com-

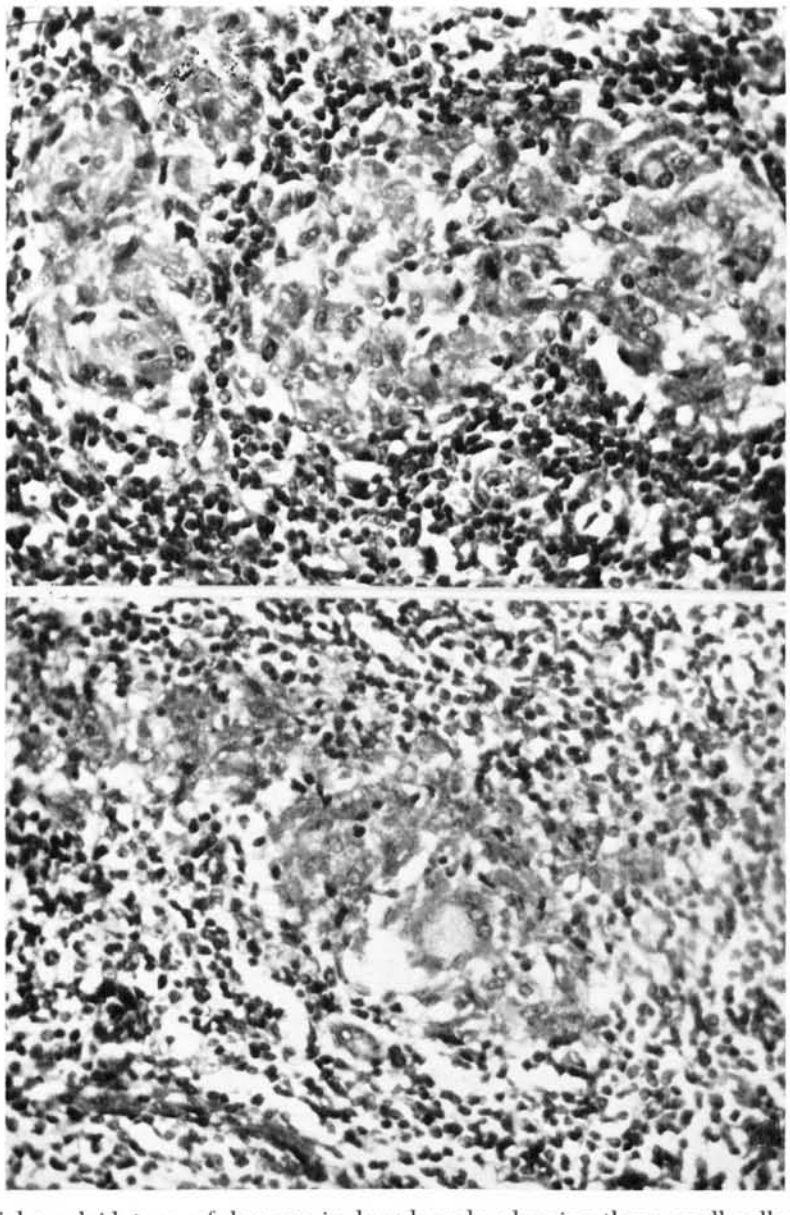

FIG. 5. Tuberculoid type of leprosy in lymph node, showing three small collections of epithelioid cells. H & E stain. ×300.

FIG. 6. Another field from a tuberculoid lesion showing a typical tubercle with a Langhans type giant cell surrounded by epithelioid cells. H & E stain. ×300.

posed of epithelioid cells and giant cells, were distributed both in cortex and medulla. Caseation was not seen. Both marginal and medullary sinuses were free from granuloma in all cases. The sinuses were dilated and showed hyperplasia of the littoral cells. Some contained histiocytes. Acid-fast bacilli were not seen in any of the cases. Reticulum stains showed a picture similar to that seen in cases of borderline-tuberculoid (BT) leprosy. The lymph nodes in all the five cases were cultured for acid-fast bacilli, and no growth was seen in any or them.

DISCUSSION

The lesions in lymph nodes in lepromatous leprosy have been described in great

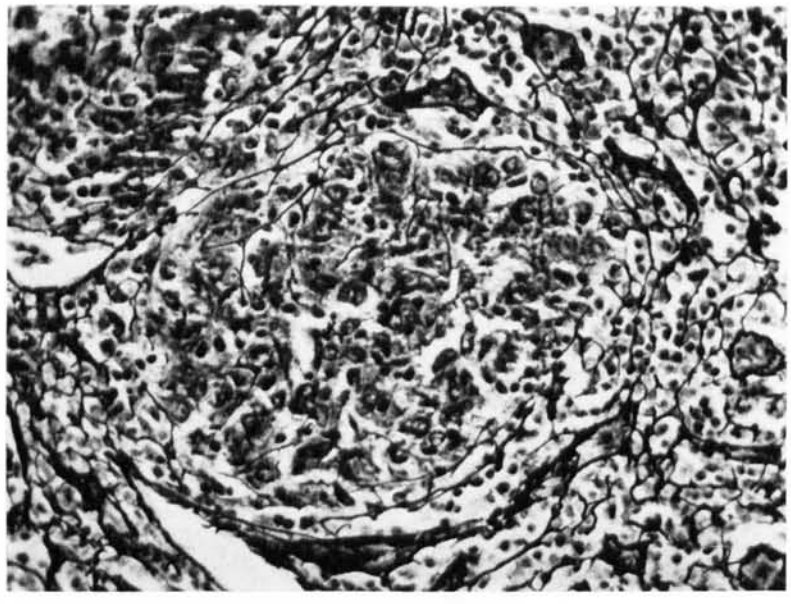

FIG. 7. Reticulum stain of the tuberculoid lesion shownig destruction of the reticulum fibers in the region of the granuloma and condensation of the fibers at the periphery. Reticulum stain. ×300.

FIG. 8. Clinical picture of one of the polar tuberculoid cases that showed lesions in the lymph nodes.

detail by Furniss (7) and Sharma and Shrivastav (15). Our observations are in general agreement with those of these authors.

The finding of leprous lesions in the lymph nodes in borderline or tuberculoid cases is of special interest in the present study. Dharmendra (5) mentioned enlargement of lymph nodes in some cases of tuberculoid leprosy and Sharma and Shrivastav (5) examined lymph nodes in 16 tuberculoid cases and Furniss (7) in nine cases. They found no lesions in any of these cases. Lowe (11) reported definite tuberculoid change in the lymph nodes of six out of 11 cases, but no culture or guinea-pig inoculation was made to exclude tuberculosis. Sharma and Shrivastav (15) quoted Schuman and Voccaro, who produced some evidence to suggest glandular and visceral involvement in tuberculoid leprosy, but indicated that the evidence was not unequivocal. In the series here reported the lesions in the lymph nodes of tuberculoid cases were histologically characteristic. There is, of course, a close similarity with lesions of tuberculosis and sarcoidosis. Tuberculosis is ruled out by the failure of growth of acid-fast bacilli in culture. Sar-

coidosis is very rare in our experience in South India.

It is generally believed that in the tuberculoid type of leprosy a widespread dissemination of infection does not occur. On this ground one would expect the true polar type of tuberculoid cases to show the least dissemination in the body. We have therefore divided the tuberculoid leprosy cases into two groups as suggested by Ridley and Jopling (14), viz., a borderline-tuberculoid group (BT), which is more toward borderline, and tuberculoid (TT), which is the classic polar type. In all the cases the classification was confirmed histologically and by lepromin test, and the lymph nodes were cultured to exclude tuberculosis. We have been able to demonstrate lesions in the lymph nodes in the polar type of tuberculoid cases also.

Lymph node lesions in leprosy may throw some light on the spread of the disease in the human body. Ermakova (6) has revived the older theories of ascending neural infection in lepromatous leprosy. Khanolkar (8, 9) has suggested that the organisms spread through the axoplasm of nerves in both tuberculoid and lepromatous cases. The demonstration of the tuberculoid type of leprosy lesions in the liver (1, 3, 13, 16) would strongly indicate that there is dissemination by the blood stream even in the tuberculoid type of leprosy. Cochrane (4) has emphasized the existence of two forms of tuberculoid leprosy, and has suggested two types of spread in the two forms, viz., blood stream spread in the "low-resistant" tuberculoid type (BT), and multiple infection by direct inoculation into the skin in polar type tuberculoid cases (TT). Our finding of lesions in the lymph nodes in the polar tuberculoid (TT) cases would indicate that a lymphatic spread occurs in this group also.

SUMMARY

A study of lymph node lesions in 33 cases of leprosy is presented, with special reference to the borderline group and tuberculoid type of cases. The tuberculoid type has been subdivided into the "low-resistant" and the classic polar types on clinical, histologic and immunologic bases. In lepromatous leprosy, the changes observed are consistent with the observations of other workers. The borderline and tuberculoid cases showed histologically characteristic lesions in the lymph nodes. Lesions of tuberculoid leprosy have been conclusively demonstrated in the low-resistant as well as in the classic polar types of tuberculoid leprosy.

RESUMEN

Se presentan lesiones encontradas en ganglios linfáticos en 33 casos, con especial referencia al grupo límite (borderline) y los tipos tuberculoides. El tipo tuberculoide ha sido dividido entre el de "baja resistencia" y el clásico tipo polar, sobre bases clínicas, histológicas e inmunológicas. En la lepra lepromatose, los cambios observados fueron consistentes con la observaciones de otros autores. Los casos límite (borderline) y tuberculoide mostraron características lesions histológicas en los ganglios linfaticos. Las lesiones de lepra tuberculoide han sido demostradas conclusivamente en los de baja resistencia como así también en los clásicos tipos polares de lepra tuberculoide.

RÉSUMÉ

On présente ici une étude sur les lesions des ganglions lymphatiques dans 33 cas de lèpre, avec mention particulière pour ce qui concerne les cas du groupe dimorphe (borderline) et du type tuberculoïde. Le type tuberculoïde a été divisé en "cas de faible résistance" (low-resistant) et en cas polaires typiques, sur la base de critères cliniques, histologiques et immunologiques. Dans la lèpromateuse, les modifications observées sont en accord avec les observations faites par d'autres chercheurs. Les cas dimorphes et tuberculoïdes ont montré des lésions histologiquement caracteristiques dans les ganglions lymphatiques. Des lésions de lèpre tuberculoïde ont été mises en évidence de manière conclusive dans les cas de faible résistance, ainsi que dans les cas atteinte du type polaire classique de lèpre tuberculoïde.

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