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Histopathology of Skin Lesions in Leprosy

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This report deals with 13,267 cases of skin biopsies of leprosy patients, at the Instituto de Leprologia, Rio de Janeiro, Brazil, during the years 1943–1969. In it we shall give our personal experience in that study.

Our routine includes a frozen section stained by Sudan III or scarlet R, hematoxylin-eosin and Wade's technique for acid-fast bacilli. The material is fixed in 10 per cent formol solution.

The manner in which *M. leprae* enters the human body is unknown, but sometimes, without any clinical manifestation of the disease, one may find bacilli in the lymph nodes of contact persons, without any symptom of the disease. There, the reticulo-endothelial system fights against the bacilli. The results of this fight depend, partially, upon the constitutional defensive reactivity (CDR), which varies amply from patient to patient. According to this concept an infected person may or may not become a patient. Aborted cases are in the majority (approximately 95%). When the person in contact becomes a patient, skin lesions appear in the great majority of cases. The clinical and histopathologic pictures of these skin lesions vary according to the CDR of the patient. Accordingly we have found different histopathologic pictures in the skin lesions of patients, which may be summarized as follows:

I. Active Processes

1. *Nongranulomatous*
   a. Chronic histiocytic – lymphocytic inflammation
2. *Granulomatous*
   a. Prelepromatous
   b. Pretuberculoid
   c. Lepromatous
   d. Tuberculoid
   e. Borderline (bipolar)
3. *Reactional*
   a. Lepromatous exacerbation
   b. Erythema nodosum leprosum including radial Miescher's granuloma.
   c. Erythema multiforme
   d. Reactional tuberculoid
   e. Necrotizing vasculitis (Lucio's phenomenon)

II. Involutive Processes

1. Regressive lepromatous
2. Residual lepromatous
3. Residual chronic inflammation

III. Degenerative Processes

1. Fibrinoid alteration
2. Caseation necrosis

I. Active Processes

These represent the reaction of the organism against invasion by *M. leprae*, and may be divided in three main histopathologic groups as follows:

1. **Nongranulomatous process.** This is, actually, a chronic histiocytic-lymphocytic inflammation. It is represented by very small foci of large and small vessels around the nerves and skin appendages. These foci are limited to the dermis and sometimes are so mild that they become borderline with the normal skin. Very seldom (7% of cases in our material), one may find scarce, single, alcohol-acid-fast bacilli, localized mainly inside the Schwann cells of small nerves. The epidermis is practically normal or presents mild atrophy. Generally the melanin is scarce. The counterpart clinical

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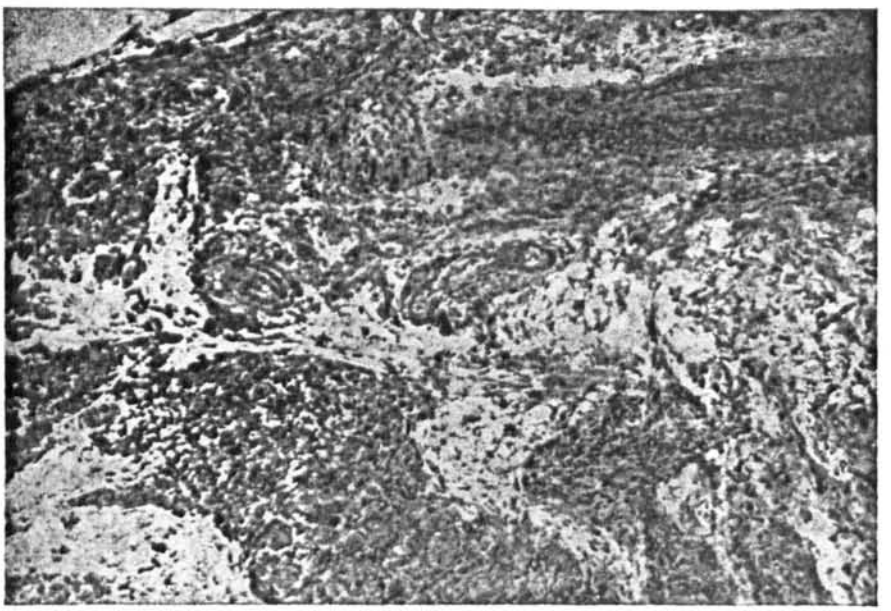

FIG. 1. Lepromatous leprosy; frozen section stained by Scarlet R to show intracytoplasmatic lipid degeneration.

picture of this structure is a hypochromic patch with hypo- or complete anesthesia and hypo- or complete anhidrosis. This simple inflammatory type of reaction is indicative of the indeterminate form of leprosy. It may go on either to spontaneous or therapeutic resolution or to prelepromatous or pretuberculoid, or even borderline structure.

2. **Granulomatous Processes.** These may be divided into the following five structures:

Prelepromatous. This structure is represented by foci of large mononuclear cells (histiocytes) mainly in the dermis. These cells do not show any vacuoles, and intracytoplasmic research for intracytoplasmic lipid in frozen sections is 100 per cent negative. Bacilli are present and in great quantity, mainly inside the cytoplasm of the cells. These cases go on to true lepromatous infiltration, if not adequately treated.

Pretuberculoid. This is represented by small groups of compact large mononuclear cells having abundant acidophilic cytoplasm. Intracytoplasmic lipids are never seen. Very seldom we may find single bacilli.

Lepromatous infiltration. The classic lepromatous infiltration is represented by a monomorphous histiocytic infiltration, either in great masses or diffusely distributed. The histiocytes harbor bacilli inside their cytoplasm which divide into clumps and globi. In time the histiocytes become altered by a cytoplasmic granular lipid degeneration, which pushes the nucleus to the periphery. The older the lesion the greater this lipid degeneration; as a matter of fact it presents the picture of a thesaurismosis (when frozen sections are stained by Sudan III or scarlet R).

In H. E. sections one sees the classic foam cells described by Virchow. In our experience the intracytoplasmic lipid degeneration (Fig. 1) is present in 98.9 per cent of these cases; only the very early cases may be lipid-negative. Besides Virchow cells one may find lymphocytes, plasma cells and even mastcells. Rarely, and only in old cases, foreign-body giant cells with lipid degeneration may be seen. The lepromatous infiltration is localized in the dermis and/or hypodermis and invades glands, follicles, nerves and arrector pili muscles, causing atrophy of those structures. The lepromatous infiltration never touches the epidermis; a band of collagen tissue (Un-

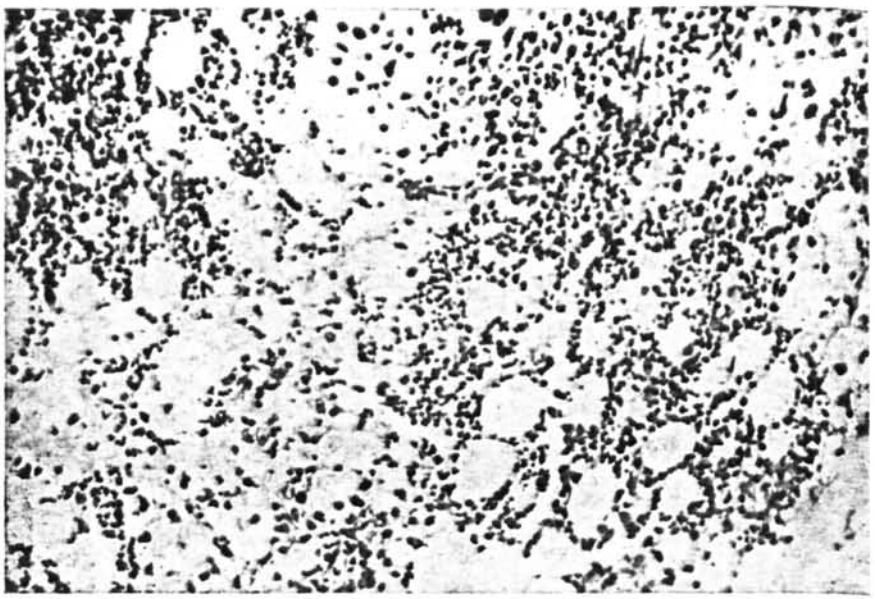

FIG. 5. Erythema nodosum leprosum; abundant polymorphonuclear cells around foci of Vichow cells.

phous). This is represented by a mixture of both types of lesion (Fig. 5), i.e. lepromatous and tuberculoid, in the same patient; these two structures may be seen in the same slide in 65 per cent of our cases, and in different lesions in 35 per cent of the cases. Sometimes these two structures may be seen in different phases of the disease in one patient. In general the lepromatous type of infiltration is localized in the superficial dermis, and one may see Unna's collagen band just as in lepromatous cases. The tuberculoid nodules are generally situated around vessels, hair follicles and nerves; sometimes the epithelioid cells present vacuoles due to edema; the lepromatous cells may or may not present vacuoles due to lipid degeneration (70% of the cases present intracytoplasmic lipid degeneration in stained frozen sections). Bacilli, clumps, and even globi are present, in variable number, in 100 per cent of cases. One must emphasize that the predominance of one structure over the other indicates a different position of the cases in the immunologic spectrum of the disease.

3. **Reactional Processes.** We describe five reactions during the evolution of leprosy, as follows:

Lepromatous exacerbation is found in the evolution of a lepromatous case. It is characterized by edema of the collagen, presence of neutrophiles and eosinophiles and an increasing number of histiocytes and young macrophages. In addition, the number of bacilli is increased and they are solid and well stained.

Erythema nodosum leprosum may appear at the first sign of the disease, but most of this type of reaction appears during treatment and more rarely even without any treatment; it is exclusive of the lepromatous type. It is represented by an exudative reaction in the hypodermis with small foci of Virchow cells and around them many neutrophiles and edema (Fig. 6). Sometimes even microabscesses are found. Dilatation of the vessels and even a low grade of vasculitis may be seen. Bacilli are few and fragmented.

Erythema multiforme. This is found, with isolated or together with erythema nodosum leprosum, and situated in the dermis over a lepromatous infiltration. Edema, dilatation of vessels, and exudative infiltration with neutrophiles and even eosinophiles are seen. Bacilli are few and fragmented.

Necrotizing vasculitis: This is known also

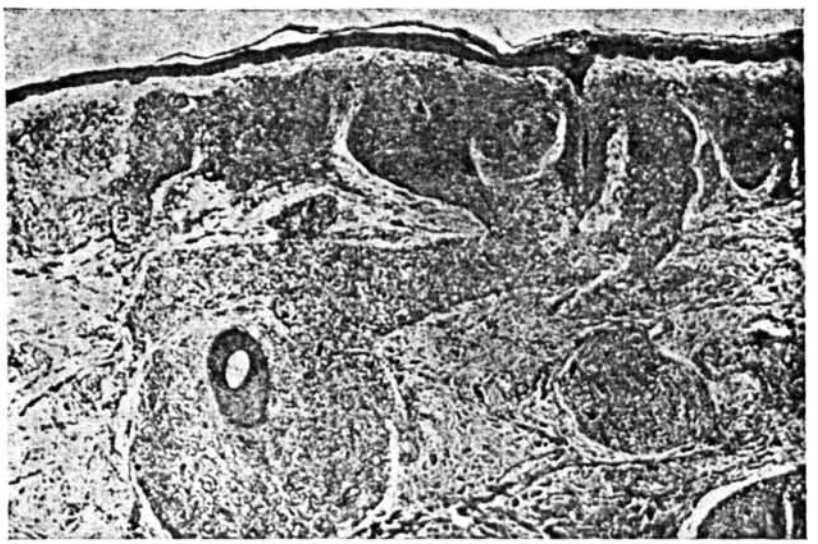

FIG. 6. Borderline leprosy.

as Lucio's phenomenon; it is frequent in Mexico but rather rare in Brazil. It is a necrotizing vasculitis of the small vessels of the dermis which goes on to necrosis; sometimes subepidermic bullae are seen. The process ends in ulceration.

Reactional tuberculoid. This may start as such or may appear during evolution of an I or T case. Histologically it is represented by a tuberculoid granuloma, as described above, with dilatation of the vessels, intense edema of the collagen and intracytoplasmic edema of the epithelioid cells. The latter have a foam appearance and give a false impression of Virchow cells, from which they differ, however, by the absence of lipid degeneration (100% negative in research for lipids in frozen sections). Single bacilli, sometimes numerous, have been found in 41 per cent of cases in our material.

II. Involutive Processes

These are found mainly as a consequence of treatment. We have divided them in three types:

1. **Regressive lepromatous.** The infiltration is reduced and formed almost exclusively by large Virchow cells, with many lipid granules in the cytoplasm and very few altered bacilli or acid-fast granules.

2. **Residual lepromatous.** This is characterized by very small foci of large Virchow cells with intense intracytoplasmatic lipid degeneration, but without bacilli or acid-fast granules. Consequently this and the regressive lepromatous are 100 per cent lipid-positive. Both pictures show that during treatment bacilli disappear before the Virchow cells.

3. **Residual chronic inflammation.** This is characterized exclusively by very small foci of mononuclear cells (lymphocytes and histiocytes); it is a result of long treatment of any form of leprosy.

III. Degenerative Processes

In the skin of leprosy patients one may see only two types of degenerative processes, as follows:

1. **Fibrinoid alteration.** This is seen very rarely in some cases of reactional tuberculoid disease, and in a very few cases of torpid tuberculoid lesions which present a granuloma annulare-like picture.

2. **Caseation necrosis.** This is seen only in high grade-immunity tuberculoid cases; there is true caseation necrosis inside nerves of the dermis. The caseation continues to the dermis and in the majority of cases there is subsequent ulceration.

SUMMARY

This report deals with 13,267 cases of skin biopsies made at the Instituto de Leprologia, Rio de Janeiro, Brazil, during the