Histoid Variety of Lepromatous Leprosy
A Histopathologic Study

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The term 'histoid' was used by Wade (1) to designate an unusual form of lepromatous leprosy which presents certain characteristic clinical and histopathologic features. The term seems to have been based on the histologic appearance of the lesion which is very similar to that of a tumor (2) derived from a single element namely the spindle-shaped histiocyte. Several workers in different parts of the world have recognized this interesting form of leprosy, and recently there have been two publications (3,4) describing the morphology of such lesions. This paper records certain observations on cases which fulfill the clinical and histopathologic criteria of Wade's histoid leprosy.

MATERIALS AND METHODS

Biopsy tissues obtained from the skin lesions of 109 patients clinically diagnosed as cases of histoid leprosy, constitute the materials for this study. One or more such typical lesions from each subject was removed, for histologic examination. In some cases, a biopsy was also performed on a lesion of conventional lepromatous in the same patient. After standard fixation and embedding, paraffin sections of the tissue were stained with haematoxylin-eosin stain, Elt's modification of Ziehl-Neelsen's method, and Mallory's aniline blue method for connective tissue.

Only those cases which, on histologic examination, fully satisfied the criteria laid down by Wade were designated as histoid leprosy. Histologic features characteristic of histoid leprosy were observed in 25 of 109 cases. In 42 other cases, although the picture was not in complete conformity with the description given by Wade, the lesions were considered as being consistent with a histoid leprosy. This group of cases has been designated separately as "comparable with histoid." In the remaining 42 cases, there was no evidence to support the diagnosis of histoid. These cases presented a picture of conventional lepromatous leprosy with some atypical features.

RESULTS

The striking histologic feature observed in all cases was the circumscribed nature of the lesion. The epidermis was usually elevated, stretched and thinned, due to the expanding lesion in the dermis. In an occasional case, however, with ulceration due to pressure from an underlying lesion, an uninvolved sub-epidermal zone was not distinguished. Dense bundles of collagen were usually seen in the peripheral part of the lesion, and a well-formed "pseudo-capsule" (Fig. 3) was recognized in 12 cases. The appendages of the skin were pushed aside by the growth of the lesion (Fig. 1). As such, these appendages were generally outside the lesion, or at the periphery but seldom within the lesion. These features of expansive growth were in contrast to the infiltrative growth observed in the conventional variety of lepromatous leprosy. In the latter, irregular branching and finger-like processes of the leproma were seen to infiltrate the layers of the dermal collagen and invade the appendages. Such of the appendages as were encircled by the leproma were ultimately destroyed and totally replaced.

The location of the lesion was usually in the dermis. In 15 cases, a large lesion was seen to occupy the entire extent of the dermis. In eight cases, the lesion was found mainly in the deeper parts of the dermis,
and in two others, it was immediately subcutaneous. As observed by Wade, these lesions have a tendency to migrate towards the superficial reaches of the skin so that they become nodular, and are protuberant or even pedunculated.

The cellular architecture of the lesion was the most classical feature of the histoid variety of lepromatous leprosy. In a typical old and well-established lesion, numerous thin spindle-shaped cells were seen forming interlacing bands, whorls, and at times, tight curlicues (Fig. 2). Such a structure was frequently indistinguishable histologically from a neurofibroma or a dermatofibroma. However, palisading of the nuclei was not observed and no giant cells were seen. The constituent spindle-shaped cells had a moderate amount of cytoplasm with nuclei that were oval or lightly
Fig. 2. Cellular details of a histoid lesion. Note the arrangement of the spindle-shaped cells in wavy bands, very similar to that seen in a neurofibroma. (H & E × 120)

stained. In some cases, the constituent cells were predominantly polygonal or irregular shaped (Fig. 3). This was a feature of comparatively early cases with younger lesions. The polygonal cells had abundant cytoplasm which was eosinophilic and granular. Vacuolation was rarely observed, and foamy macrophages were not seen. The nuclei were round and vesicular, and nucleoli could usually be distinguished (Fig. 4). Mitotic features indicative of the increased rate of growth were also sometimes made out. Among the 25 cases included as characteristic of histoid, ten showed predominantly spindle-shaped cells; in six cases a predominantly polygonal cell population was seen, and the remaining nine contained admixtures of both
types of cells. In addition to these principal cells, there was also seen a variable admixture of inflammatory cells. While mononuclears appeared prominent, in a few cases polymorphonuclears were also seen. Such inflammatory cells were usually found at the periphery of the lesion.

There was considerable variation in the content of connective tissue. As could be expected, the lesions with spindle-shaped cellular architecture contained abundant connective tissue. However, even in the younger lesions with polygonal cellular elements, Mallory-stained sections revealed fine blue collagen fibers almost around every individual cell in the lesion. Connective tissue was abundant in 13 cases, moderate in seven and sparse in the remaining five.
The histoid lesions contained an unusually large number of acid-fast bacilli, very much more than were seen in the conventional lepromatous lesions in the same case. The organisms were packed tightly into bundles and groups completely occupying the entire extent of the cell, without, however, disturbing its normal contour. This arrangement has been designated by Wade as the "histoid habitus" and is considered to be one of the characteristic histopathologic aspects of histoid leprosy. The acid-fast organisms were generally of the uniformly stained (solid), well-preserved variety. Seven cases in this series revealed predominantly solid stained forms, 12 showed solid as well as nonsolid forms, while in the remaining six cases, the organisms ap-

Fig. 4. A high power view of a young histoid to show cellular details. Note the large polygonal histiocytes with abundant granular cytoplasm and vesicular nuclei. (H & E X 480)
The epithelioid cell collections described by Wade, and referred to by him as 'tuberculoid contamination' were not encountered in any of the cases in our series. Coexistent conventional lepromatous leprosy was found in 15 of the 25 cases of histoid leprosy. In the 42 cases labeled as being compatible with histoid leprosy, some but not all the typical features described above were present. Thus, while the spindle-shaped cells formed the predominant cell type, in 14 cases there was an admixture with vacuolated cells. Likewise, while 'histoid habitus' was an exclusive feature in 14 cases, globi were present in the remaining twenty-eight. Finally, in 30 of these 42 cases, the lesions were not circumscribed, but were seen to infiltrate the adjacent connective tissue and appendages.

The remaining 42 cases which clinically mimicked histoid leproma were, in effect, conventional lepromatous leprosy with some atypical features. No further description is warranted in these cases.

**DISCUSSION**

The outstanding clinical features which distinguish the lesions of histoid leproma are that they appear as cutaneous or sub-cutaneous nodules or occasionally as plaques, and they are sharply circumcribed. The lesions are generally firm and occasionally appear pearly. Microscopic examination of smears from these lesions generally reveal a large number of intact rod-shaped bacilli. This contrasts sharply with the irregularly stained and fragmented forms usually seen in conventional lepromatous leprosy.

The circumscribed nature of the lesion described above would suggest that in its mode of growth it is expansive, the lesion growing either sideways or from the depths to the skin surface. The cellular architecture is striking in as much as the lesion is seen to be composed predominantly of either one or another cell type instead of the conventional polymorphous character of a leprosy. In some instances, the histoid lesion is seen to consist almost exclusively of spindle-shaped histiocytes forming whorls and interlacing bands. In other cases, polygonal cells are seen. Varying amounts of connective tissue are found in the lesion and a very large number of bacilli are seen overloading each cell and arranged in characteristic formation described as the 'histoid habitus.' While the lesion can be suspected clinically, it is necessary to have histopathologic confirmation. This is clear from the findings in the present series where, of 109 cases that were clinically diagnosed as histoid, only 25 conformed to all the characteristics of the histoid lesion, with another 42 presenting features that were considered as suggestive of the histoid variety.

The very striking histologic features of a histoid leproma makes the condition more than a mere clinical curiosity or a structural variant. The morphology of the lesion which mimics a neoplasm would suggest a possible cellular alteration which may be caused by several variable factors in the long natural history of the development and the progress of lepromatous leprosy. The enormous number of bacilli in the lesion with a striking sparsity in the neighboring areas would indicate the failure of immunologic mechanisms or the presence of iatrogenic factors resulting in uninhibited multiplication of bacilli in a restricted area. In particular, the morphology of the bacilli, which is similar to that seen in untreated cases of leprosy, is significant. Further, the connective tissue fibers found in abundance in the older lesions and their relation to the histiocytes, would indicate that these cells have assumed a fibrogenic activity.

Although structurally resembling a neoplasm, the histoid lesion is essentially an inflammatory condition. This is borne out by the fact that many of these cases respond well to specific treatment for leprosy. It, however, presents certain morphologic similarities and possible pathogenic parallelisms with certain conditions known to be in the borderland between inflammation and neoplasms. Among such conditions are lesions such as nodular subepidermal fibrosis, histiocytosis X, and dermatofibrosarcoma protuberans. In all these conditions...
doubts exist whether they represent an inflammatory proliferation or a neoplastic growth. Civatte (1) regards the histiocyte as a precursor of the fibroblast which by a process of normal growth and development, forms the nodules of fibroma simplex. The ability of the histiocyte to produce collagen fibers has been observed in the lesions of the lepromatous leprosy (3), both in the skin as well as in nerves. This property of the histiocyte appears to be exaggerated in some cases of histoid lepro- 

ma, as the histiocytes are seen to lay down abundant collagen fibers. Although the fibrogenic propensity of the histiocyte is accepted, there is no clear evidence to indicate that in histoid leprosy these cells have undergone any neoplastic change. Price et al. (4) consider that nodular subepidermal fibrosis probably represents a type of reaction to an inflammatory process. This is supported by Montgomery (5) who considers it a hyperplasia often induced by mild local injury which is often disregarded or forgotten and which sets up an inflammatory process resulting in a nodule. By analogy it would seem that in histoid leprosy the chronic inflammatory process set up in response to the low virulence M. leprae could provide a continuous stimulus resulting in a tumor-like lesion. The fact that this does not happen more frequently would indicate that there are more factors than such continuous stimulus responsible for the development of the histoid lesion. It may be that during the prolonged course of the disease, there could occur alterations in certain groups of histiocytes so that they behave in a manner different from others in the same patient. It is also tempting to speculate that the histiocytes which form the cell population of histoid leprosy are derived from biologically distinct cells of this type which do not exhibit the classic behavior when confronted with large loads of M. leprae. In conventional lepromatous leprosy, the histiocytes can be converted into macrophages which are able to harbor large numbers of M. leprae. In histoid leprosy an even greater unrestricted growth of bacilli seems to be permitted within the macrophages.

The enormous bacillary population and the character of the individual organisms in the histoid lesion strongly suggest the absence of any therapeutic effect by antile- 

prosy drug. The fact that the histoid lesion develops in patients who have had long years of therapy, lends support to this contention. Such lack of therapeutic effect could theoretically result from circumstances where the drug is prevented from reaching the organisms in adequate concentrations. It is very difficult to imagine the operation of such a situation in histoid leprosy especially since these lesions are multiple and are situated adjacent to conventional lepromatous lesions where ther- 

apeutic actions of antileprosy drug are clearly evident as judged by marked fragmentation of the bacilli. Therefore, the alternate possibility that these lesions result from the development of small foci of drug-resistant forms of M. leprae, which would be of serious import, needs very thorough investi- 

gation. It is particularly noteworthy that a few cases of lepromatous leprosy, known to be drug-resistant, appear to belong to the histoid variety of this disease (6, 7). However, the experience at this Institute has been that a proportion of these cases respond to standard DDS therapy in the same way as conventional lepromatous leprosy. The development of drug resistant variants in M. leprae has to be borne in min- 

d, but it is felt that this cannot be very common especially in view of the fact that M. leprae is a slowly growing microorgan- 

ism. Even so, since sulphones have been employed in the therapy of leprosy for about 20 years now, this possibility should be borne in mind and investigations insti- 

tuted to ascertain whether some of these histoid forms of lepromatous leprosy are due to sulphone resistant mutants of M. leprae.

SUMMARY

A summary of clinical and histopathological aspects of an unusual form of leproma- 

tous leprosy, namely histoid leprosy is presented. The manner in which the struc- 

ture of this lesion mimicks a neoplasm has been described in detail and possible sig- 

nificance discussed. The pathogenesis of
Histoid leproma is still an enigma and merits further investigation.

RESUMEN

Se presenta un resumen de los aspectos clínicos e histopatológicos de una forma poco usual de lepra, que se conoce como lepra histoide. Se describe en forma detallada la manera como la estructura de esta lesión se asemeja la de un neoplasm y se discute el posible significado de este hecho. La patogenia del leproma histoid es todavía un enigma y merece mayor estudio.

RESUME

On présente ici un résumé des aspects cliniques et histopathologiques d’une forme inhabituelle de lépre lépromateuse, à savoir le léproma histoid. La façon dont la structure de cette lésion ressemble à un néoplasme est décrite dans le détail, la signification possible de ce fait est discutée. La pathogénie des lépromas histoides reste un énigme et mériterait d’être étudiée plus avant.

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REFERENCES