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## OBSERVATIONS UPON THE BORDERLINE FORM OF LEPROSY<sup>1</sup>

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About 20 years ago, Wade and Rodriguez<sup>(5)</sup>, and Wade<sup>(4)</sup>, called attention to certain leprosy cases in which the type of the disease is difficult to distinguish between tuberculosis and lepromatous, because the morphologic and structural characteristics of the lesion comprise features of both types. At about the same time Cochrane<sup>(1)</sup> described such cases as "intermediate," and subsequently he has called them—among other things—"atypical."

Ever since then, many authors have studied cases of this kind, to interpret what they mean in the field of the leprosy pathology. As a matter of fact, the borderline cases have increased in importance since the WHO Expert Committee on Leprosy<sup>(6)</sup> recognized them as a distinct form, followed by the Madrid congress<sup>(2)</sup>—which, however, modified the name parenthetically to "borderline (dimorphous) B." Although such cases are not very frequent, they are not as rare as it was formerly believed.

### PRESENT STUDY

Guided principally by the descriptions of Wade and Cochrane, which are now classical, we nowadays endeavor to identify such interesting cases in our dispensary in Rio de Janeiro (A.M.A.), and to confirm them by histology (R.D.A.). To the time of writing we have found 10 cases among 240 dispensary patients. A few others are under observation, to be included in this group if the histologic diagnosis will permit. Repeated clinical and histologic examinations of these cases are being made.

<sup>1</sup> An abstract of this paper was sent to the VII International Congress of Leprology, held in Tokyo November 12-19, 1958, but another paper was chosen for the program.

## HISTOLOGIC FEATURES

The structural aspects of borderline lesions comprise the tuberculoid granuloma associated with the well-known subepithelial band of Unna and Virchow-cell infiltration. The tuberculoid structure is not well defined, and is generally without giant cells, or with only small numbers of them; and sometimes there are foamy cells in the same lesion. The foamy aspect of the cells in some cases is due to a lipid degeneration of the cytoplasm which can be demonstrated by special methods of staining, as with sudan III; and in some cases a borderline lesion can be distinguished in this way from one of reactional tuberculoid nature.

The tuberculoid and lepromatous characters are mixed in an extremely variable manner. Sometimes both are seen in the same histologic section. At other times it is necessary to take biopsy specimens from different parts of the same lesion, or from different lesions, because different sections show different aspects which, taken together, prove that the case is borderline. In general there is a mixture of tuberculoid and lepromatous characteristics, rather than a simultaneous occurrence of separate whole lesions of those two kinds.

In some of our cases we have found the two histopathologic pictures associated in the same slide, while in others they were found separately in different lesions. In 3 cases out of the 10, lipid was found in the cytoplasm of some cells.

## CLINICAL FEATURES

Considering the morphologic features of the lesions from the clinical point of view, the classical descriptions emphasize the similarity of these lesions to those of reactional tuberculoid cases, but they are more infiltrated and with a typical succulent aspect—a “soft infiltration.” The limits of these lesions are not as well marked as is usual in the tuberculoid type; they characteristically taper off into the normal skin, more in the manner of lepromatous infiltrations. These features are definitely to be seen in our cases under study. The infiltration may be so marked that it becomes an edema, which sometimes involves the hands and the feet. Also, we have observed the coexistence of tuberculoid-like lesions beside others of frank lepromatous aspect, even nodular.

Most of our patients exhibit lesions of annular aspect, as in Fig. 1, with flat central areas having no sign of involvement,<sup>2</sup> and immediately surrounding such an area the lesion presents an elevated, sharply demarked margin which is in contrast with the diffusion, or tapering off, of the outer limit. Such lesions, therefore, seem to imitate to a

<sup>2</sup>Wade regards these central zones as “immune areas,” the sites of previous major tuberculoid lesions which, on subsiding, leave the tissue with more or less complete local immunity against involvement when the case undergoes relapse.

certain extent what is seen in reactional tuberculoid cases, but contradictory characteristics are always to be found.

Figs. 2 to 4 are of a typical marked case, with multiple lesions on the buttocks and thighs (Fig. 2), those on the buttocks being particularly extensive and intricate, with several unaffected areas; on the abdomen (Fig. 3) the lesions are more of lepromatous aspect; the circinate lesion on the arm (Fig. 4) is incomplete, and has a small elevation in the central area which also is of lepromatous aspect. Figs. 5 and 6 are of another case of the many-faceted borderline condition.

The nasal mucous membrane may be ulcerated, as was seen in 2 patients of this group. This membrane had been invaded by a skin lesion in 1 case, which is an interesting finding because it is an unusual occurrence for tuberculoid lesions, although very common for those of the lepromatous kind. Ulceration of the skin lesions, which has been reported, has not been observed in our patients.

*Bacilli.*—Acid-fast bacilli are usually found, and sometimes even globi, in the lesions when examined by the scraped-incision method, and also in the affected mucous membranes. The bacteriologic examinations were negative only in 3 of our patients. One was negative in the nasal mucosa but positive in the lesions, while another showed the reverse condition. However, acid-fast bacilli have always been found in the sections, and sometimes globi. The bacilli may be of granular aspect.

*Lepromin.*—The lepromin reaction was definitely positive in 2 cases of our group, once with necrosis. Another 2 cases showed variable positivity. One was doubtful, and the other 5 were negative. Lauro de Souza Lima and Maurano (<sup>3</sup>) have reported 8 lepromin-positive cases in 35 patients of the borderline form.

Cochrane insists on general effects on the patient, as emaciation and fever of intermittent type, which the patients may suffer for several months. In our cases, we have not yet observed emaciation or any febrile state of long duration.

A tabular summary of the main clinical, bacteriologic, immunologic and histologic features of the 10 cases studied appears in Table 1.

#### DIFFICULTIES OF DIAGNOSIS

We find this form of leprosy most difficult to recognize. The clinical descriptions, although a useful guide, are not enough to make the clinician absolutely sure of the type diagnosis.

Sometimes borderline cases are identified only by the histopathologic findings, in which case they come as a surprise. The clinician is taken unaware.

At other times we are confronted by patients whose symptomatology is quite the same as is seen in unquestionable borderline cases, but, in

TABLE 1.—Summarized findings in the borderline cases reported.

Case No.	Clinical aspects	Bacilli <sup>a</sup>		Lepromin		Histology <sup>b</sup>	Evolution <sup>c</sup>
		Skin	Nose	Early	Late		
1	Annular lesions; nasal ulcer	++	+	—	—	Dimorphous; no lipids; globi	Marked improvement in 3 mos.
2	Annular lesions; nasal mucosa invaded by skin lesion	++	++	—	±	Dimorphous; lipids; globi	Great improvement, 2nd mo.
3	Prominent, circinate annular lesions	—	+	—	—	Dimorphous; no lipids; granular bacilli	Rapid improvement; lesions subsided, 2 mos.
4	Infiltration, nodules, etc.	—	—	(?)	+	Dimorphous; no lipids; few bacilli	Changed to reactional tuberculoid
5	Erythrodermic aspect	++	—	—	—	Dimorphous; scarce lipids; some bacilli	Great improvement in 3 mos.
6	Circinate erythematous spots	—	—	—	+	Dimorphous; no lipids; globi	Lesions subsided, 9th mo.
7	Circinate red spots; diffuse infiltration	+	+	+	—	Dimorphous; no lipids; granular bacilli	Improvement from 1st month; lesions residual 3rd yr.
8	Erythematous spots; infiltration; reactional tuberculoid type	+	+	+	+/-	Dimorphous; no lipids, granular bacilli	Completely negative, 3 yrs.
9	Annular circinate lesions; nasal ulcer	++	++	—	—	Dimorphous; of sarcoidal aspect; no lipids; globi	Rapid improvement; completely negative in 3 mos.
10	Hypochromic macules; papuloid aspect	—	—	—	+/-	Dimorphous; lipids; bacilli	Improved

<sup>a</sup> Cases with ++ indications for the skin are those in which globi were found, as well as isolated bacilli.

<sup>b</sup> "Dimorphous" is used in the sense that both tuberculoid and lepromatous elements were found in sections.

<sup>c</sup> Evolution refers to changes under treatment with TB-1.

spite of this, the histologic examination does not confirm the impression (Figs. 7 and 8). Even if the biopsy in such a case is repeated, the expected diagnosis may or may not be confirmed. Nevertheless, there are cases whose clinical aspects incline the clinician to the diagnosis of borderline which is not confirmed by the laboratory examination, but the subsequent evolution of the disease and response to treatment show clearly that the clinician's impression was correct.

When the histopathologist reports "lepromatous leprosy" in a case whose lesions clinically resemble the reactional tuberculoid condition and treatment gives good results more rapidly than it could in a lepromatous case, or promotes a reaction of tuberculoid type, then it stands to reason that the case must have been a borderline one in spite of the laboratory finding.

The experienced clinician has sovereignty in recognizing the types. For example, one of our patients (Case 7 of Table 1) presented infiltrations and erythematous spots with diffuse limits and rusty pigmentation on the face, a circinate and elevated erythematous spot on the right thigh, and edema of the hands and feet. Consequently, we classified him as borderline. A biopsy of the circinate lesion revealed the lepromatous histology. This patient, however, improved under treatment more rapidly than is usual with lepromatous cases. Such cases have to be investigated thoroughly, because a single histologic examination cannot suffice to define them.

Suspicion once aroused, histologic investigation will do the rest, and rapid subsidence of the lesions under specific treatment, observed within a short period, or the way the case evolves, confirms the diagnosis.

#### PROGNOSIS

With respect to prognosis, some authors consider these cases as unfavorable, perhaps because formerly they were liable to evolve to the lepromatous type. We think that a bad prognosis is not justified nowadays, because modern therapy (we now use TB-1 instead of the sulfones) has been successful in all of our borderline cases. We are convinced that the prognosis of these cases is relatively good, compared with that of cases of the lepromatous type. Some of them may become bacteriologically negative after only three months of treatment. Histologic control has shown that the lesions of 3 of our 10 cases changed to the banal chronic inflammatory condition, while another became reactional tuberculoid. The Madrid classification is not correct in describing these cases as of "malign" nature.

#### CONCLUSIONS

What we have learned from our borderline cases is summarized as follows:

1. The way in which, histologically, the lepromatous and tuberculoid



characters are associated in borderline cases varies extremely. Sometimes structures of both kinds exist in the same section; at other times it is necessary to make two or more biopsies.

2. Sometimes the clinician has no reason to suspect that a case is of borderline nature, and the histologic diagnosis comes as a distinct surprise.

3. At other times, although the clinician is able to recognize a real borderline case, the laboratory cannot confirm it because of the limited scope of the microscopic examination.

4. Smears from the skin lesions and nasal mucosa may be negative, but there will always be bacilli in the lesions that can be revealed in sections.

5. The lepromin reaction may be positive in some cases.

6. It is not correct that the prognosis of borderline cases is generally bad. Our patients have derived real benefit from modern therapy (TB-1).

7. As certain authors have stated, if the reactional tuberculoid eruption appears in a lepromatous case under specific treatment, it suggests that the case was actually a borderline one that had wrongly been taken for lepromatous.

8. The same explanation may be used to account for the lepromin positivity which appears in some supposedly lepromatous cases, after marked improvement with bacteriological negativization of the lesions.

#### CONCLUSIONES

Lo aprendido de nuestros casos limítrofes se resume así:

1. Varía sumamente la forma en que, histológicamente, se asocian las características lepromatosas y tuberculoideas en los casos limítrofes. Algunas veces existen tejidos de ambos géneros en el mismo corte; en otras ocasiones es necesario verificar dos o más biopsias.

2. Algunas veces el clínico no tiene motivos para sospechar que un caso sea de naturaleza limítrofe y el diagnóstico histológico constituye una gran sorpresa.

#### DESCRIPTION OF PLATES

FIG. 1. Case 1 of Table 1. Annular lesions resembling closely the reactional tuberculoid appearance. Histopathology: Elements of the borderline condition found.

FIG. 2. Case 9. A typical example of marked borderline, consisting largely of the "soft infiltration" with several sharply demarcated areas within it which are not affected or only slightly so.

FIG. 3. Abdominal lesions of the same patient, rather resembling lesions of lepromatous type, without trace of tuberculoid morphology.

FIG. 4. Annular lesion in the same patient, high on the right arm. This lesion, although not a complete ring, resembles those in Fig. 1 except for the small central nodulation.

3. En otras ocasiones, aunque el clínico puede reconocer un verdadero caso limítrofe, el laboratorio no puede confirmarlo debido al limitado alcance del examen microscópico.

4. Los frotos de las lesiones cutáneas y la mucosa nasal pueden ser negativos, pero habrá siempre bacilos en las lesiones, que pueden descubrirse en los cortes.

5. La reacción a la lepromina puede resultar positiva en algunos casos.

6. No es cierto que el pronóstico de los casos limítrofes sea siempre malo. Nuestros enfermos han derivado beneficio real de la terapéutica moderna (TB-1).

7. Según han declarado ciertos autores, si la erupción tuberculoidea reactiva aparece en un caso lepromatoso, esto indica que el caso era realmente limítrofe y se tomó erróneamente por lepromatoso.

8. Cabe usar el mismo razonamiento para explicar la positividad a la lepromina que aparece en algunos casos supuestamente lepromatosos después de notable mejoría con negativización bacteriológica de las lesiones.

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#### DESCRIPTION OF PLATES

FIG. 5. Case 3. Lesions of the face in another variation of borderline leprosy, in a Negress.

FIG. 6. Irregular infiltrative lesion of the left arm of the same patient, with small, irregular unaffected areas within it.

(Photographs taken after 5 months treatment with TB-1 show that the lesions seen in Figs. 5 and 6 had subsided greatly, having for the most part disappeared.)

FIGS. 7 and 8. Photographs of lesions of two patients which were of borderline aspect but which could not be verified by histopathology as of dual nature.



