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SOME OBSERVATIONS ON BORDERLINE LEPROSY

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The inclusion of the borderline group in the classification adopted by the Madrid Congress (1), as previously done by the WHO Expert Committee on leprosy (4), was a valuable contribution to the understanding of leprosy, both because of the frequent occurrence of such cases and because it strengthens the individualization and fixation of the polar types. Wade (3) has urged leprologists to publish studies of cases of this group. In the hope of contributing to information about this interesting form of leprosy the following account of our observations is given.

In total, there have been studied 286 cases of borderline form from the different dependencies of the Leprosy Division, namely, the Central Dispensary in Caracas, the Cabo Blanco Leprosarium, the Isla de Providencia Leprosarium, and the different regional dispensaries. These cases represent 3.2 per cent of the 8,872 known cases of leprosy existing in Venezuela as of June 1956. Of the total, 100 cases were hospitalized at Cabo Blanco. The other 186 cases were reported by the leprologists of the leprosy service in the interior, who are familiar with the borderline condition. They sent to the service's central office clinical records, including the results of bacteriological examinations and lepromin tests, and also biopsy specimens by means of which the diagnoses were confirmed.

MATERIAL AND METHODS

The material on which the present report is based consists of the 100 cases that were hospitalized and studied thoroughly by us. Their distribution as regards age and sex is shown in Table 1.

Two-thirds of the cases were of reactive nature, one-third nonreactive. With respect to their principal clinical features they may be grouped as follows:

Reactive Cases (68)

With severe impairment of general health ..... 16 cases
With moderate impairment of general health ..... 31 cases
Without impairment of general health ..... 21 cases

Nonreactive Cases (32)

With infiltrating, diffuse lesions ..... 10 cases
With infiltrating, plaque-like lesions ..... 22 cases

TABLE 1.—*Age and sex distribution of the 100 borderline cases studied.*

Age	Male	Female	Total
0–14	5	1	6
15–29	25	16	41
30–44	14	12	26
45–59	11	7	18
60 and over	6	3	9
TOTALS	61	39	100

Clinical study.—The evolution of the cases was followed clinically from the initial examination to their present stage, with detailed descriptions of their lesions, tests for sensory changes, histamin tests, and complementary laboratory tests including in some cases electrophoresis. Methylene blue injections were made in one group.

Bacteriological tests.—Smears made by the scraped-incision method were taken from active lesions and also from apparently healthy skin. Smears from the nasal cavity were made by scraping, after cleaning the mucous membrane. All smears were stained for acid-fast bacilli.

Immunological tests.—Standard lepromin, and in some cases the Dharmendra-type bacillary lepromin, were used for the Mitsuda test, which was applied at different sites. The readings were made after 24 and 48 hours and after 21 days. Tuberculin tests with PPD were also made.

Histological examinations.—Material for skin biopsies was taken from lesions of different aspects, the sections regularly stained with hematoxylin and eosin and in some cases with Sudan IV. Fite's 1947 method was used for staining bacilli in the sections.

FINDINGS

Facies dimorpha.—We use this term to designate the lesions of the face. In many cases where we are dealing with infiltrations these lesions —taken as a whole, on the forehead, between the eyebrows, on the bridge of the nose, and on the chin, together with those of the cheeks—give a bat-like figure that is easily recognizable. We have found it in 63 per cent of the cases.

Hypochromic halo.—The presence of a hypochromic halo around some lesions, especially the infiltrated ones, seen in 27 per cent of the cases, is a sign that should be taken into consideration in the diagnosis of the borderline group. We interpret it as the condition secondary to the process

of regression, which begins in the outward part of the infiltrated lesion and increases as the regression progresses. However, in some cases it is also found in connection with very active lesions and gives the impression of being a peripheral disturbance of pigmentation.

Hypochromic patches.—We refer especially to those hypopigmented areas of the skin that are secondary to the regression of infiltrated lesions. They vary with respect to number, size, form and the definition of the border. It is almost the rule that they are numerous and occupy extensive areas, regardless of whether the skin is atrophied or not, and they can be present together with active, infiltrated lesions. We have observed them in 61 per cent of our cases.

Differential diagnosis: The most important diagnostic problem, as we see it, is the differentiation between the hypochromic patches of this borderline group and those of the indeterminate group, since those seen in the tuberculoid type are easily distinguished by the immunologic reactions of the cases, and since such patches in the lepromatous type are rare. In dealing with this problem various possibilities must be borne in mind:

1. Diagnostic errors in which hypochromic patches may be classified as indeterminate when in reality they are borderline lesions in the process of regression.

2. Cases of the borderline kind evolving falsely from indeterminate. This possibility exists in those hypochromic borderlines which in former stages showed active, erythematous infiltrations. If they were erroneously classified as indeterminate to begin with, one would get the impression that they were borderline cases evolving from indeterminate, when in reality they were simply different stages of borderline lesions.

3. Borderline cases may transform into lepromatous. When this occurs with the hypochromic borderline stage as a transitory phase, one could certainly get the false impression that the lepromatous condition was evolving from the indeterminate one, and not from its true source, i. e., borderline.

4. Similar reasoning could be applied to eventual transitions of the hypochromic stage of borderline towards the tuberculoid type.

Evolution: For several years we have had the opportunity to observe how the secondary hypochromic patches of the borderline group follow different courses of development:

(*a*) They may become repigmented.

(*b*) They may persist for a long time.

(*c*) They may give origin to new erythematous infiltrations of their own borderline form.

(*d*) They may be transformed into tuberculoid, although not very frequently.

(*e*) They may be transformed more frequently into the lepromatous type.

(*f*) They may grow centrifugally.

This process of growth individualizes the hypochromic stage of the borderline group, for one thing as a potentially active phase which can give origin to new reactive phenomena or change into either of the polar types (most frequently into lepromatous), and for another thing as a phase in which the patches may be active and progress in the hypochromic phase itself. This concept is supported by the presence of the borderline histopathological structure in some of them. This finding, however, is not very frequent, and it may be stated almost as a rule that the hypochromic patches of borderline cases are productive, infiltrating, perivascular processes.

When hypochromic patches with the borderline histopathology are found in patients who affirm that they have never had any different form of lesion in the same spots, we are compelled to believe that the same patches have existed as initial lesions. As this may be of considerable interest in connection with the indeterminate group, it may be necessary to recognize a new form of borderline leprosy, namely the hypochromic. The hypochromic patch of this group may thus not only be a lesion in process of regression, potentially active or active *per se*, but it may have existed as a borderline lesion from the beginning.

Nerve disturbances: Our experience has shown that there are three possible eventualities as regards sensory changes and the result of the histamin test in these patches.

1. The histamin reaction may be abnormal (i. e., with no reflex erythematous halo), this abnormality being accompanied by sensory disturbances. This is the classical finding.

2. The histamin reaction and sensitivity may, on the other hand, both be normal. This integrity of the nerve elements within the patches is interesting, as it shows a divergence from the accepted rule that hypochromic skin lesions in leprosy are accompanied by sensory disturbances and an abnormal histamin reaction, with the inference that the absence of these phenomena is a sign that the patches are not of leprous origin. The further absence of the Hansen bacillus would give stronger support to the possibility of error.

3. There may be normal sensation, but an abnormal histamin reaction. It has long been an accepted notion that the abnormal histamin reaction is always accompanied by sensory disturbances, but we have found in some hypochromic patches of borderline cases a lack of association of the two phenomena. In other words, the pathways of conduction of superficial sensation have remained intact, while those that conduct the Lewis vascular reflex, which is concerned with normal histamin reaction, have been affected. The existence of this discordance in hypochromic patches of borderline cases stands in contrast with what is observed in similar patches of indeterminate cases, in which it is a rule that sensory disturbances and an abnormal histamin reaction go together.

The situation that arises from the existence of hypochromic patches of cases of the borderline group in relation to similar patches of the indeterminate group is very interesting from our point of view, in that the latter group loses importance.

TESTS WITH METHYLENE BLUE IN BORDERLINE LEPROSY

In view of the interesting observation of Montel ([2]) of the retention of methylene blue in parts of a lesion of a borderline case, to which attention was called by Wade ([3]), we have applied that test to 21 such cases.

The methylene blue solution employed was of 1 per cent concentration, the injections intravenous. Starting with a dose of 3 cc. on the first day, 4 cc. on the second day, and 5 cc. on the third day, it was increased until by the 15th day it was 10 cc. In the cases that remained without colored lesions this dose was repeated daily until the 21st day. In a few cases the injections were continued for as long as four months.

It was found that some cases which show retention of the dye do so only in certain sites, such as the earlobes, the ciliary region, the alae nasi, and the cheeks, with no retention of the pigment in the rest of the lesions. From this observation it might be expected that lepromatous foci were present in the parts that retained the methylene blue, and that was proved to be a fact by histological examination. It was found that the failure of other lesions (borderline patches) to retain the pigment was due to their lack of lepromatous elements.

In some cases we have found, in areas contiguous to highly-retentive, histologically-proved lepromatous foci, certain lesions that retained the blue pigment diffusely and in which a lepromatous component was found concomitantly with a borderline element. On the other hand, we have also found cases in which the methylene blue was not retained at all even after repeating the injections for fifteen days, or—in some cases—as much as four months.

On the basis of this experience we are convinced that the pure borderline lesions do not retain methylene blue, and those cases which do hold the pigment do so in direct proportion to the amount of lepromatous granuloma they contain. These granulomas may sometimes be found concentrated in certain areas, and sometimes distributed within the borderline patches themselves.

A noteworthy fact is that there is a marked difference in the time that is needed to fix the methylene blue in lepromatous and borderline cases. In the former, the lesions become intensely blue in 1 or 2 days, while in the latter the blue color appears only after 4 to 7 days. We refer here to those cases in which the lepromatous granulomas are found distributed in the borderline patches.

In our opinion, the test with methylene blue will not be useful in studying the cases of pure borderline leprosy, but it should serve to

distinguish those cases of this class which have a lepromatous component. As the quantitative presence of that component is directly proportional to the intensity with which the pigment is retained, the test is prognostically useful.

ELECTROPHORETIC INVESTIGATION OF PLASMA PROTEIN

We have subjected the sera of 30 of our cases to electrophoresis, and found that the albumin-globulin ratio was normal in 60 per cent of them. These cases showed important regressive activity. In the remaining 40 per cent, the albumin-globulin quotient was below the normal value, ranging from 1.01 to 1.46. In this group the lesions showed a tendency to persist and spread.

SUMMARY

From the various units of the leprosy service, data has been collected on 286 cases of the borderline form of leprosy, these constituting 3.2 per cent of the 8,872 known cases of the disease. The present report is based on personal study of 100 hospitalized cases.

What is described as the "*facies dimorpha*" was seen in 63 of these cases. Hypochromic halos around some lesions, usually a consequence of their retrogression, was seen in 27. Hypochromic patches, secondary to regression of infiltrated lesions, seen in 61, are discussed in some detail.

The problem of differentiation of these secondary patches from lesions of cases of the indeterminate group is considered first. Concerning their evolution there are several possibilities, including change to tuberculoid (infrequent), or to lepromatous (more frequent), or centrifugal progression as such. It is believed that such hypochromic lesions, with borderline histopathology, may exist as initial lesions. Findings regarding sensory disturbance and the histamin test are variable.

Intravenous injections of methylene blue daily for various periods, given to 21 cases, resulted in retention of the dye where there were histologically-proven lepromatous changes. Sometimes this was only about the face, sometimes in parts of borderline patches which contained lepromatous elements, but sometimes there was no retention of the dye even after long courses of injections. It is concluded that pure borderline lesions do not retain methylene blue.

Brief mention is made of electrophoresis tests of the plasma of 30 cases. The albumin/globulin ratio was normal in 60 per cent of them, these being regressive cases.

RESUMEN

De los varios departamentos del servicio de lepra, se han acopiado datos acerca de 286 casos de la forma limítrofe de lepra, constituyendo 3.2 por ciento de los 8,872 casos conocidos de la enfermedad. La comunicación actual se basa en el estudio personal de 100 casos hospitalizados.

La llamada "facies dimorpha" fué observada en 63 de estos casos. En 27, se notaron auréolas hipocrómicas alrededor de algunas lesiones, por lo general consecuen-

cia de la regresión de las últimas. Se discuten con algún pormenor las placas hipocrómicas, secundarias a regresión de lesiones infiltradas, observadas en 61 casos.

Se considera primero el problema de la diferenciación de estas placas secundarias de las lesiones de casos del grupo indeterminado. En cuanto a su evolución, caben varias posibilidades, incluso cambio a la forma tuberculoidea (infrecuente) o lepromatosa (más frecuente) o progresión centrífuga (como tal). Parece que esas lesiones hipocrómicas, de histopatología limítrofe, pueden existir como lesiones iniciales. Son variables los hallazgos relativos al trastorno sensorial y a la prueba de la histamina.

A 21 enfermos se les dieron diariamente durante varios períodos de tiempo inyecciones intravenosas de azul de metileno, dando por resultado retención del colorante cuando había alteraciones lepromatosas comprobadas histológicamente. Algunas veces esto sucedió unicamente alrededor de la cara, algunas veces en placas limítrofes que contenían elementos lepromatosos, pero a veces no hubo retención del colorante, ni aun después de largas series de inyecciones. Dedúcese que las lesiones limítrofes puras no retienen el azul de metileno.

Se hace breve mención de las pruebas electroforéticas del plasma de 30 enfermos. La proporción de albúmina/globulina fué normal en 60 por ciento de ellos, tratándose de casos regresivos.

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