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SIGNIFICANCE OF THE HISTOLOGY OF BACTERIOLOGICALLY NEGATIVE LESIONS OF LEPROSY

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Questions have recently been raised about the relationships of the so-called tuberculoid variety of leprosy to the cutaneous type. In that connection it is desired to record a preliminary summary of the experience of this matter that we at the Cebu Skin Dispensary have had in the past five years. Brief reports are given here of five originally bacteriologically negative cases under our observation that have become "open" cases and in consequence have been isolated; they illustrate certain interesting phases of the matter.

Since 1931 efforts have been made in this clinic to correlate the clinical and pathological findings in cases with bacteriologically negative skin lesions. To that end biopsy specimens have been taken from one hundred and two patients; the operative work was done by Dr. F. Plantilla, or under his direction. It has been our purpose to include in the inquiry as many varieties of these skin lesions as possible, special attention being given to the earlier lesions. Some of the larger ones have been sampled repeatedly, at intervals of six months for periods of from one to two years. Most of the specimens were examined by Dr. C. Manalang, at the San Lazaro Hospital in Manila; the rest were diagnosed by Dr. H. W. Wade, at Culion.

No attempt will be made in the present report to classify or describe the cases or lesions that have been examined in this manner. As for the pathological findings, according to the reports received the specimens from 58 of 102 cases (54 per cent) showed tuberculoid changes. Of the 44 remaining cases the specimens showed only round-cell infiltration in 40, while in 4 the changes were so slight that the specimens were considered practically normal.

Upon attempting to correlate the clinical appearance and the pathology, we have found that in many instances it is impossible to predict the histological findings. However, definite tuberculoid

changes were usually associated with reddish or raised macules, with the secondary ringed or circinate lesions, and with "lichenoid" patches. On the other hand, simple round-cell infiltration was the rule in the simple, nonelevated, hypopigmented macules and in normal-appearing anesthetic skin. With reference to the latter, pigmentation and ichthyosis (keratosis) did not change this histological picture, but when there was flushing, however slight, the tuberculoid structure was the rule.

A few writers, especially in Japan, have stressed the leprolin test in connection with tuberculoid leprosy as that is recognized by them; this test is supposed to be positive and therefore to help differentiate such cases from those of the cutaneous type of the disease. We have applied this test in 42 of the cases of the series here discussed, 28 of them being among those whose specimens were reported tuberculoid and 14 in the round-cell group. Three of the former group and one of the latter proved leprolin-negative; broadly speaking the proportion of nonreactors was essentially the same in the two. Although our previous impression had been that positive leprolin reactions are apt to be less frequent in the round-cell cases, or when positive to be less strong, this particular series of cases did not show the expected difference.

The cases of the entire series here discussed have been followed for periods of from one to five years. In this time five of them became "open" (bacteriologically positive by the standard smear examination) and have been isolated in the Eversley Childs Treatment Station here at Cebu. In two of these five cases the specimens that had previously been removed for examination were found to be of the epithelioid type, in two they showed only round-cell infiltration, while one was practically normal histologically.

It is of special interest that only the two round-cell cases (Cases 1 and 2, below) have become typical cutaneous lepers. The two belonging to the tuberculoid variety of Wade (Cases 3 and 4, below), though they became bacteriologically positive, did not develop lepromatous infiltrations or nodules; one was paroled in the shortest time possible, bacteriologically negative on repeated examinations over the requisite period of time, and the other is also expected to be released in record time. The remaining case (Case 5, below), whose only lesion at the time the biopsy specimen was taken consisted of an extensive anesthetic area on the right leg, subsequently developed multiple

reddish, bacteriologically positive lesions, but the clinical appearance is not yet typical of the cutaneous form of the disease.

From the foregoing it is to be seen that our experience in Cebu, so far as it has gone, is in agreement with the general observation that cases definitely of the tuberculoid variety do not undergo conversion to the cutaneous type, at least within the period that those in this group have been observed.

REPORTS OF CASES

CASE 1.—P. E., male Filipino, aged 34, of good development and nutrition, rather light-skinned. When first seen, March 3, 1933 (Dr. Plantilla), there were two macules: (a) above right elbow, with irregularly papulate, slightly pinkish border, center slightly hypopigmented; (b) just above it one of 1 cm. diameter, also anesthetic; around both were several scattered pale and pinkish papules. Patient came for treatment irregularly (only twenty-two injections) until August 13, 1934, and not at all afterward. At that time the two lesions had fused to form one irregularly diffused patch about 10 cm. across. There was also a larger macule below the left knee. Arm lesion biopsied at the above date. Smears from specimen negative. Pathological report (Dr. Wade): round-cell infiltration, relatively marked; in the deeper tissue a small tuberculoid (?).

At the next examination, March 6, 1936: previous lesions raised and infiltrated, both earlobes infiltrated, a new small patch of infiltration on right anterior axillary fold. Smears from all lesions and both sides of the nasal septum loaded with *My. leprae*.

In the nineteen months between the last two examinations the previously existing lesions had become typically infiltrated patches of cutaneous leprosy, new lesions had appeared, and the nasal mucosa had become heavily involved.

CASE 2.—R. B., male Filipino, aged 15, of fairly good development and nutrition, rather light-skinned. When first seen, November 4, 1931, the only lesion was an area at right elbow, 4 cm. in diameter, without any abnormality of appearance but anesthetic, analgesic, and with disturbance of temperature discrimination; histamine-positive; duration claimed to be one year. Biopsy specimen (Dr. Manalang): early leprosy; smears (Dr. Chiyuto): negative. On June 7, 1932, a second specimen removed from beside the scar of the first one was submitted to the same examiners. Report: perivascular infiltration; smears: negative. During 1932-33 patient received irregular and insufficient treatment, a total of only thirty injections; none thereafter.

On June 19, 1935, patient stated that recently he had noticed numbness and loss of pain sense over certain areas on the extremities, and formication and crawling sensation over the elbow area. On left cheek is a hazy, ill-defined, pinkish, nonanesthetic macule. Earlobes infiltrated and bacteriologically positive (++). Above right patella a 4 cm. macule, faintly reddish, border best seen

from about 2 meters, anesthetic, bacteriologically negative. A similar macule completely covers left patella. Another, on left buttock, roughly triangular, 25×4 cm., is positive (++) . The anesthetic area on right elbow has extended upward and downward, to a length of about 15 cm. Scrapings from nasal septum negative. Patient admitted to leprosarium as a moderately advanced "mixed" cutaneous case.

This case is unusual in that the first lesion was an anesthetic area without visible change. It apparently progressed to a cutaneous-type case without the development of macules characteristic of the neural type.

CASE 3.—C. V., male Filipino, aged 45, of good development and fairly good nutrition; dark skin. On October 3, 1931, there were marked lesions, said to be of five years' duration, consisting of extensive, raised, copper-colored macules on the face, back and extremities. A biopsy specimen was removed from one of the smallest of these (apparently one of the latest to appear), about 5 cm. in diameter, on the left buttock; border bright copper-colored, markedly raised, center slightly lighter in color, anesthetic. Report (Dr. Manalang): tuberculoid leprosy, advanced; smears (Dr. Chiyuto): negative.

When next seen (October 18, 1935), the patient had not received any anti-leprosy treatment as he lives on another island. A smear from a macule on left cheek was positive (+). Patient admitted to leprosarium. On January 21, 1936, all lesions found negative; nine other examinations made in the following two months were all negative. The lesions have subsided, but they are still slightly reddish and the borders somewhat raised.

This case is a good example of typical "tuberculoid leprosy" and has been under observation for a period of four and half years. Though the patient was segregated because found bacteriologically positive, up to the time of writing (May 15, 1936) he has not developed lesions characteristic of cutaneous leprosy.

CASE 4.—P. M., male Filipino, aged 46, of fairly good development and nutrition, very dark-skinned. When first seen, December 18, 1931, he had very numerous (about sixty) hypopigmented macules scattered over trunk and extremities, mostly circular and ranging from the size of a rice grain to about 4 cm. The larger ones were pinkish and slightly raised, especially at the borders, and their surfaces showed coarsening of the grain of the skin; anesthesia to light touch, and pain and temperature. The smallest had normal sensibility, but in others somewhat larger there was dissociation, with loss of thermal and pain senses only. An extensive lesion extended from the middle of the left thigh anteriorly down onto the leg, where the border was indistinct. Two biopsies: (a) a small lesion, less than 1.5 cm., over left scapula; (b) a very small, slightly pale papule, believed to be an early stage of a macule. Reports: (a) tuberculoid leprosy; (b) perivascular round-cell infiltration and early tuberculoid lesions; smears negative. (These and other reports by Drs. Manalang and Chiyuto.)

On June 28, 1932, the condition was slightly worse, many of the lesions having increased in size. Treatment had been regular, once a week. Two further biopsies: (a) same lesion as the first one so identified; (b) maculo-papular lesion on back from which one bacillus had been recovered in several smears taken. Smear from macule on right chest and from one of those biopsied (b), were both positive (+). Admitted to leprosarium. Pathological report: both specimens tuberculoid leprosy.

On April 5, 1933, a third specimen was removed from the (a) macule, which had become faint and only slightly raised. The site had been injected intradermally three months previously. Other lesions also showed marked resolution. Report: fibrosis of dermis, oil globules, and perivascular infiltration. From that time until November, 1934, thirteen bacteriological examinations were made at the treatment station, all negative. At the latter time the leprolin test was + + + +. Patient paroled April 6, 1935.

This was a typical case of tuberculoid leprosy of slight degree. Although the patient was segregated because some of the lesions were found bacteriologically positive ("open" case), he has not developed lesions of cutaneous leprosy.

CASE 5.—P. M., male Filipino, aged 13, of good development and nutrition. On July 28, 1934, a biopsy specimen was removed from an extensive, anesthetic, very slightly hypopigmented area along the medial surface of the right leg; this lesion was discovered about a year and half previously. Report (Dr. Wade): practically negative. On March 3, 1936, there were numerous reddish patches varying in size from about 0.3 to 2 cm., chiefly on arms, back, buttocks and thighs; duration not known. Smears taken from buttocks, both sides, positive (usually +, in one instance ++).

Up to the present (May 15, 1936), this case has become neither typically cutaneous nor neural.