

SPECIFIC TISSUE ALTERATIONS IN LEPROUS SKIN

I. TRANSFORMATION OF THE TUBERCULIN REACTION IN LEPROUS PATIENTS INTO LEPROMA-LIKE LESIONS

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The development of persistent, leproma-like dermal lesions following tuberculin skin tests was observed in two leprosy patients of the Hospital for Hansen's Disease in Jerusalem. To our knowledge this unusual reaction in leprosy has not been previously described among the many reports on the complex problem of tuberculin reactions in this disease (1-10). The cases in which this unusual response occurred are presented in detail.

CASE 1. A 55-year-old woman, born in Lebanon, was hospitalized in 1949. She had been ill with leprosy for 15 years, and had received chaulmoogra oil treatment at a leprosarium near Damascus. At the time of admission the only clinical signs of leprosy were a bluish-brown discoloration of the lower extremities; some faintly delimited, slightly atrophic patches of hyper- and hypopigmentation on the trunk and extremities; partial loss of the eyebrow hair; and palpable cubital glands in the right arm.

No acid-fast bacilli were found in smears from the mucous membrane of the nose. A few were observed twice in smears from the earlobe in 1949. All later examinations were negative up to January 1951, when the patient left the hospital. The lepromin test, Wassermann and Kahn reactions, and Takata-Ara test were all negative. Thymol turbidity was 4+, cephalin flocculation was positive, and the Weltman was 8.

Two biopsies of atrophic patches on the extremities revealed small foci of a nonspecific perivascular infiltration, mostly lymphocytic.

The patient received a total of 500 cc. of promin during 1947, 67 gm. of diasone, and later sulphetrone.

A tuberculin test with PPD (5 units per 0.1 cc.) was performed on her left forearm on May 8, 1950. The reaction was positive, measuring 2 x 1 cm. after 48 and 72 hours. On

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May 24, the reaction was still positive and a biopsy specimen was removed.

The histological examination revealed a granuloma indistinguishable from lepromatous leprosy. The epidermis was atrophic, with absence of rete pegs (Fig. 1). A granulomatous structure occupied the whole thickness of the dermis up to the epidermis. A narrow subepidermal zone was free of infiltrations (Fig. 2). The granuloma was composed predominantly of histiocytic cells with pale, elongate nuclei. Many small or a few large sudanophilic vacuoles filled their cytoplasm, which was faintly basophilic and poorly defined at the periphery. A varying number of fibroblasts, fibrocytes and lymphocytes was scattered among the lipid-laden histiocytes. Lymphocytes and fibroblasts tended to be more numerous in regions in which histiocytes contained many small vacuoles, and quite sparse among the foam-cells with large vacuoles (Figs. 3 and 4). Smaller irregular-shaped infiltrations of similar composition were found elsewhere in the dermis, often situated around skin appendages and subpapillary blood vessels. No acid-fast bacilli were found.

This reaction to the tuberculin test persisted for six months as a papule surrounded by an erythematous zone. During this time several small nodules, brownish-red in color, developed around the original papule. The clinical appearance was that of a flat leproma. The lesion has remained like this up to January 1951 (Fig. 5).

A second tuberculin test was made on June 5, 1950, with old tuberculin, 1:50,000, on the back. The reaction was positive after 48 hours. A biopsy at this time revealed nests of foam-cells clustered around the small vessels of the subpapillary layer of the dermis.

CASE 2. A 58-year-old man, born in Yemen, was admitted to the hospital in 1944. At the time of admission there were slightly raised patches spread all over the trunk. The skin was atrophic, especially on the extremities, and resembled an acrodermatitis atrophicans. The muscles of the face and hands were slightly atrophic; the thenar and hypothenar eminences were flattened. The lateral part of the eyebrows showed partial loss of hair. Cubital glands were palpable. Sensitivity to pain and temperature on the extremities was diminished. These findings persisted without change up to 1947, despite treatment with chaulmoogra oil. At this time diasone therapy was started and the patches on the skin gradually disappeared.

In 1949 a few bacilli were occasionally found in smears from the nasal mucosa and the earlobe. The lepromin test was positive after 48 hours and negative after 21 days. Urine and blood examinations, Wassermann and Kahn reactions, Takata-Ara and cephalin flocculation tests were all negative. Thymol turbidity was 1+.

Two skin biopsies from the upper extremities showed dermal atrophy without changes characteristic of leprosy.

The patient received a total of 1,102.5 gm. of diasone up to 1950. Since 1950 he has been under treatment with diaminodiphenyl sulfone

(Avlosulfon I.C.I.), receiving a total of 64.1 gm. The skin lesions have now disappeared completely, and the cubital glands are no longer palpable. The atrophy of the skin remained unchanged.

On June 13, 1950, a tuberculin test with old tuberculin, 1:10,000, was performed on the right arm. The reaction was strongly positive after 48 hours. A biopsy specimen of the test site was removed after 5 days.

Histological examination revealed a slightly atrophic, hyperkeratotic epidermis, with absence of the rete pegs. Throughout the dermis were scattered numerous varying-sized oval-shaped foci of infiltrations, with their long axes parallel to the epidermis. The smaller ones were usually perivascular in position. A thin border zone of uninvolved dermis was present between the epidermis and the foci. The composition of the infiltrates was the same as that described in Case 1. Lymphocytes tended to accumulate at the periphery of the foci and were also found scattered throughout the dermis.

The reaction remained positive and a deep infiltrate developed, which enlarged to 2 cm. in diameter (Fig. 6). This lesion persisted up to May 1951, and then gradually disappeared. The tuberculin test was repeated on March 3, 1952 with old tuberculin, 1:10,000. A biopsy ten days later revealed the same histological picture as seen in the previous one of June 1950.

DISCUSSION

The skin reactions to tuberculin tests in two leprosy patients, clinically free of symptoms of active disease, caused leprosy-like lesions which persisted for 6 and 11 months, respectively. Histological examination of the first tuberculin-test lesion in Case 1, and of both lesions in Case 2, taken 16, 5 and 10 days, respectively, after the tests, showed circumscribed granulomas composed of foam cells, fibroblasts and lymphocytes, characteristic of lepromatous leprosy. The second tuberculin reaction of Case 1, examined 48 hours after injection of PPD, showed only perivascular nests of foam cells in the subpapillary layer of the skin. Acid-fast bacilli were not demonstrated in any of the histological sections. Smears from the floor of the excision wounds revealed a few acid-fast bacilli in the first instance and acid-fast granules in the second one of the first case. Only acid-fast granules could be detected from the biopsy fields in the second case.

Biopsies of the skin of these two patients from two different sites before the tuberculin test was performed revealed atrophic skin but no evidence of leprosy.

The significance of these observations will be discussed in

a future publication which reports a more extensive and systematic study of the tuberculin skin test in leprous patients.

SUMMARY

In two patients with lepromatous leprosy who had become free of clinical signs of the disease after treatment, the intradermal injection of old tuberculin or PPD resulted in the development of persistent dermal lesions. These lesions were indistinguishable from true lepromata, both clinically and histologically.

RESÚMEN

Se presentan dos casos en los cuales se desarrollaron nódulos de carácter lepromatoso luego de inyectar tuberculina en dichos pacientes leproso y los cuales aparentaban estar clínicamente libres de actividad leprosa. Estudios histopatológicos en dichos nódulos demostraron células típicas de verdaderos nódulos lepromatoso incluso el hallazgo de bacilos ácido-resistentes en uno de los casos y gránulos ácido-resistentes en el otro. Las lesiones así producidas no se podían distinguir de verdaderos nódulos lepromatosos, tanto clínica como histopatológicamente.

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DESCRIPTION OF PLATE

PLATE 16.

FIG. 1. Case 1. A large granulomatous lesion, occupying the whole thickness of the dermis. Smaller foci of infiltrations are scattered in the surrounding dermis. (Hematoxylin-eosin, 44 \times .)

FIG. 2. The same lesion as in Fig. 1, under higher magnification (85 \times). Showing the subepidermal zone, free of infiltration.

FIG. 3. The same section as in Fig. 2. (400 \times). Histiocytic cells predominate, showing elongate nuclei and a poorly defined cytoplasm filled with large sudanophilic vacuoles.

FIG. 4. Another part of the same section (same magnification), in which histiocytes with many small vacuoles in the cytoplasm predominate. Lymphocytes, fibroblasts and fibrocytes are more numerous.

FIG. 5. The persistent skin lesion at the site of the tuberculin test 6 months after the injection in Case 1. Several small, brownish-red nodules are present around the original papule, which resembles a flat leproma.

FIG. 6. The clinical appearance of the tuberculin reaction in Case 2 3 months following the test. A brownish-red, deep infiltrate is seen, which persisted for 11 months.

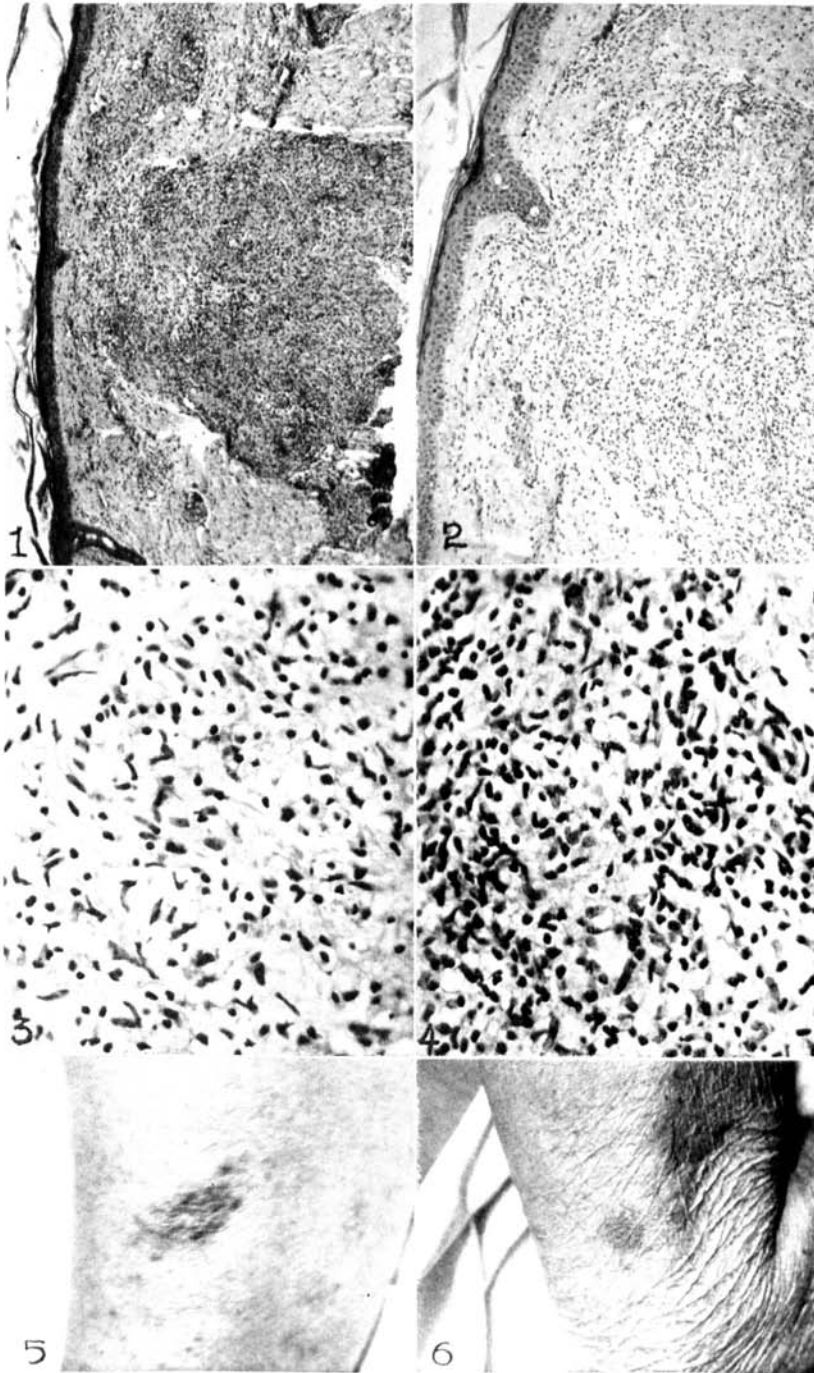


PLATE 16.