

A CLINICAL AND HISTOLOGICAL STUDY OF CUTANEOUS LEISHMANIASIS

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Abstract. Sixty-five cases of proved cutaneous Leishmaniasis have been studied on clinical, histological and laboratory grounds. A new histological classification is proposed and emphasis is given to specific histological changes and their correspondence to distinct clinical signs.

Cutaneous Leishmaniasis (Old World dermal Leishmaniasis), endemic in many countries of the Middle East, around the Mediterranean Sea, in Africa and Central Asia, is a chronic infection caused by *Leishmania tropica*. This protozoon of the family Trypanosomidae, exists in two forms, the *Leishmania* (amastigote) and the *leptomonas* (promastigote).

There are two known strains of *Leishmania* responsible for the disease: *L. type major* and *L. type minor* (6, 10).

Leishmaniasis of the Old World is transmitted by sand flies (insect vectors) of two genera, *Phlebotomus* and *Sergentomyia* (2, 5, 8, 11).

In certain regions of Greece the disease is endemic. These areas are: the island of Crete where the Leishman lesion is known under the names Chaniotico and Loubini, certain Ionian and Aegean islands and areas of Peloponnesus, and Euboea where the lesion is locally recognized under the name Mavro. *Paraphlebotomus Alexandrii* has been identified as the main insect vector in Greece, in Cyprus, North Africa and India (1, 9).

The clinical manifestations of cutaneous Leishmaniasis may be classified as follows:

1. Acute Leishmaniasis: localized or generalized.
2. Chronic Leishmaniasis: localized or generalized.
3. Leishmaniasis recidivans.

The ordinary lesion begins as a papule, becoming a firm nodule, which then ulcerates to leave finally a disfiguring scar.

Cutaneous Leishmaniasis ordinarily appears as a single lesion. Multiple lesions are the result of several infective bites by the sand fly.

Whereas the usual course of the disease lasts approximately one year, it may assume a chronic course of several years. In this case the lesion is usually of the nodular type, it rarely ulcerates and is found predominantly on the face of adult patients.

Leishmaniasis recidivans is a rare form of the disease. The clinical picture consists of fresh lesions in or around existing scars of previously healed lesions. It is supposed that a change of the local immunity causes reactivation of the intracellular organisms. Its incidence is in the range of 3-10% (7). It develops when there is a disturbance of the immunity acquired after the primary lesion.

The disseminated forms of cutaneous Leishmaniasis (acute and chronic) are considered to be the result of a defect in cellular immunity response of the host as to give a negative leishmanin skin test (3, 4).

MATERIAL AND METHODS

Sixty-five patients, 39 women and 26 men, with cutaneous Leishmaniasis, have been studied at the Department of Dermatology of the Andreas Sygros Hospital (University of Athens).

More than one biopsy and direct smear examination with Giemsa stain was carried out on each patient.

The diagnosis was made after a comparative study of the clinical signs, the histological picture and the follow-up of the patient.

The existence of the Leishman organisms was proved by: 1) direct smear stained with Giemsa stain; 2) demonstration of the Leishman bodies in tissue sections; or 3) a combination of these two.

The biopsy specimens were fixed in formaldehyde solution (formalin) and processed in the usual manner. Sections were stained with haematoxylin eosin and Giemsa.

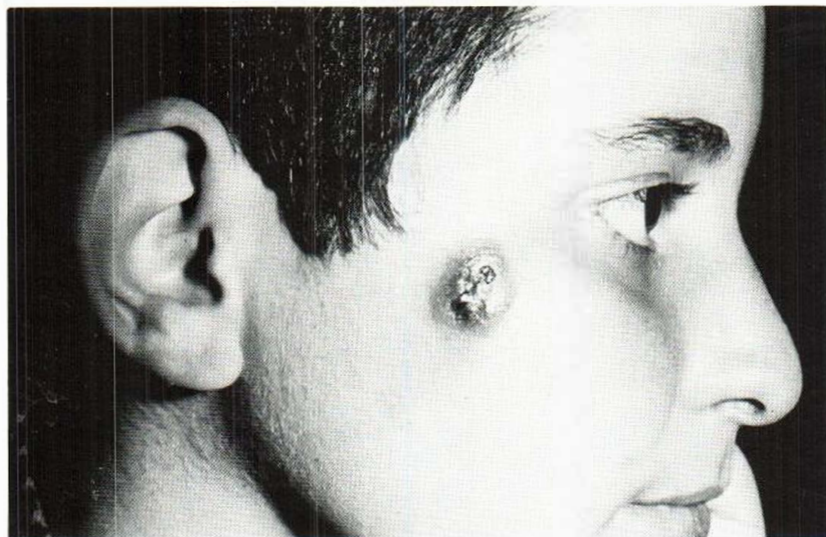


Fig. 1. Cutaneous Leishmaniasis. Single lesion appearing as an ulcerated nodule on a 9-year-old male patient.

All patients were submitted to Leishmanin skin tests (the antigen for which was prepared from cultures of the organisms) which were interpreted after 24 and 72 hours.

RESULTS

A. Clinical and Epidemiological Findings

The patients came from many parts of Greece. The Ionian islands seem to have the greatest preponderance of the disease. In some cases, more than one member of the same family was infected in 6 years, which would seem to indicate the endemic nature of the disease.

The ages of the patients ranged from 3 to 92 (average 37.7) years. Only 3 patients were under 5 years of age.

The lesion was single in almost all patients, except in two cases, where 3 and 10 lesions could be counted.

The lesions were most commonly located on the face and the exposed parts of the body.

Fourteen cases were of the chronic type of Leishmaniasis, non-ulcerated, sometimes covered with scaly nodules, with little inflammatory reaction. It could also assume occasionally the picture of an indurated plaque with more than one nodules.

Five cases were of the recidivans type of Leishmaniasis.

B. Laboratory Findings

Direct smear examination revealed Leishmaniae in 70% of the cases.

The Leishmanin skin test was found positive in 50% of the cases. It was never positive in cases of a duration shorter than 3 months. The chronic form of the disease as well as the recidivans form have yielded most of the positive results.

C. Histopathological Findings

Epidermis. The most frequent change was hyperkeratosis and acanthosis. In 62 (87.32%) out of 71 specimens examined, hyperkeratosis was found and in 48 (67.6%), acanthosis. In a small number of cases parakeratosis and atrophy of the malpighian layer were also observed. Occasionally, acanthosis and atrophy of the prickle cell layer coexisted.

Exocytosis and liquefaction degeneration of the basal cell layer were common findings. The latter was almost always in the presence of a dense contiguous infiltrate.

Pseudocarcinomatous hyperplasia was noted in 16 (22.53%) of the specimens. Epidermal cell masses and strands with occasional horn pearl formation invaded the dermis and sometimes extended below the level of the sweat glands. However, although dyskeratosis was usually evident and individual cell keratinization was often noted, mitotic figures and hypertrophic and hyperchromatic nuclei were rare findings. Pseudocarcinomatous hyperplasia prevailed in patients with long-standing granulomatous lesions and was evidently due to the chronic inflammatory reaction. This epidermal abnormality regressed to normal after therapy and

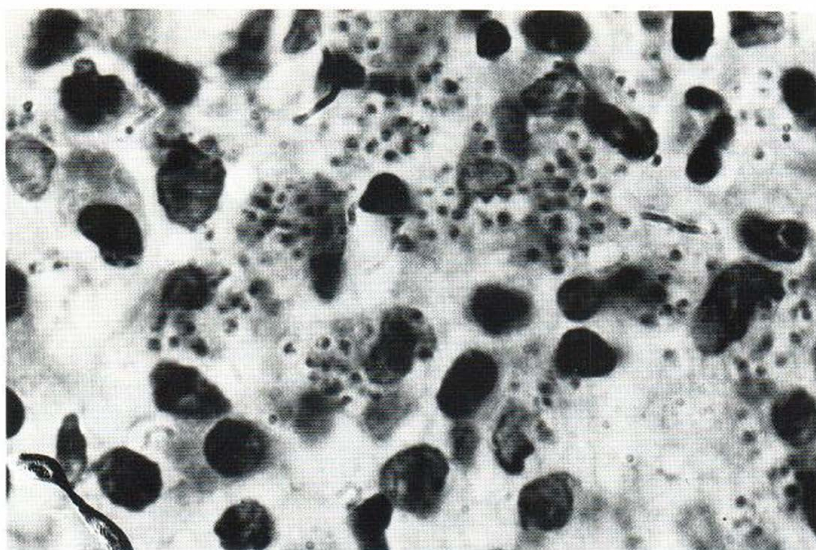


Fig. 2. Cutaneous Leishmaniasis. High magnification. Granulomatous phase. Numerous Leishmaniae within histiocytes. Hematoxylin-Eosin 1×40 .

was analogous to the one seen in the granulomatous mycoses. In one case only the histological criteria were in favour of squamous cell carcinoma and the tumour behaved as such and metastasized.

Intra-epidermal abscesses were seen in 7 cases. They contained neutrophils and lymphocytes and were more frequent in specimens with pseudocarcinomatous hyperplasia.

Other epidermal changes were ulceration (experienced in 17 cases) and the presence of Leishman bodies in the epidermal cells (5 cases). The latter was always accompanied by numerous Leishmaniae in the vicinity of the basal cell layer.

Dermis. The changes in the dermis appeared to be more distinct and were related to the duration of the disease.

In the acute phase or granulomatous phase the dermis was occupied by a massive and diffuse cellular infiltrate which extended into the lower layers of the corium and was composed of histiocytes, lymphocytes and a varying number of plasma cells and neutrophils. Eosinophils were rarely found. The histiocytes—mainly those in the upper layers of the dermis—contained many Leishman bodies; when numerous, they were also seen extracellularly. The bodies can be clearly demonstrated, with either haematoxylin-eosin stain or Giemsa stain. The blood vessels were dilated and extravasated erythrocytes could occasionally be found throughout the corium.

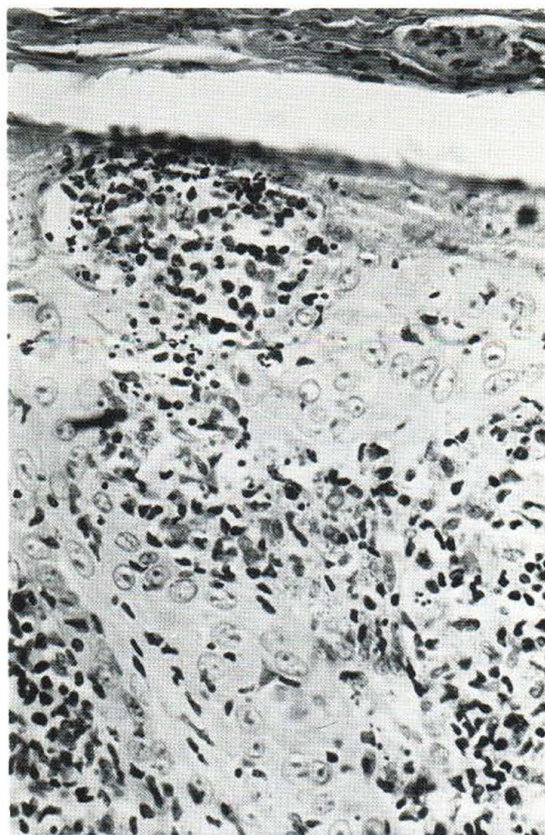


Fig. 3. Cutaneous Leishmaniasis. Granulomatous phase. Pseudocarcinomatous hyperplasia. An intraepidermal abscess is also present. Hematoxylin-Eosin 1×25 .

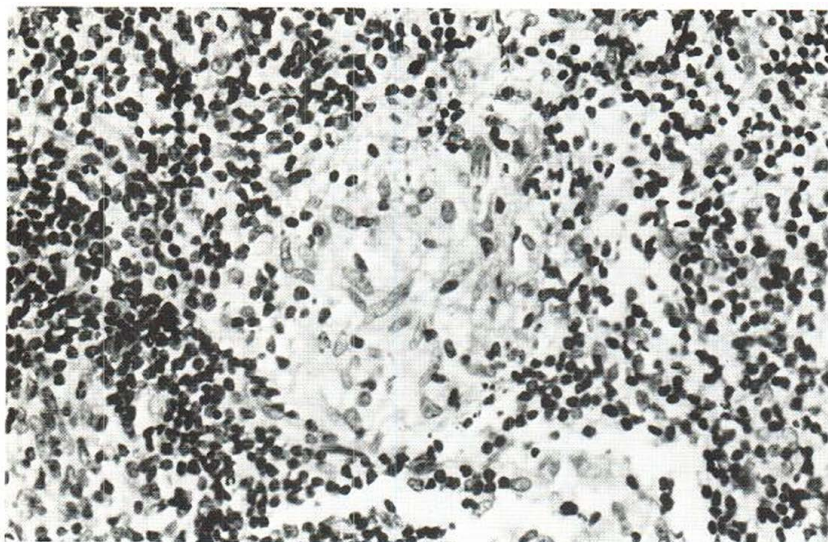


Fig. 4. Cutaneous Leishmaniasis. Microtubercloid phase. Minute tubercloid structures in the dermis, surrounded by an intense cellular infiltrate. Hematoxylin-Eosin 1×40.

In the chronic or microtubercloid phase there was a characteristic pathognomonic histologic picture which consisted of varying numbers of very small tubercloid structures which consisted of a comparatively small number of epithelioid cells. Giant cells were absent and the microtubercles were surrounded by a more or less intense cellular infiltrate consisting mainly of lymphocytes and histiocytes. Histiocytes were less numerous than in the granulomatous phase and the epidermis showed minute changes. As a rule, Leishman bodies could

not be found except in borderline cases which in some areas of the specimens showed remnants of the granulomatous reaction.

In the recidivans or late phase the histologic changes were almost identical with those found in lupus vulgaris. The dermis was occupied by tubercles which were surrounded by an intense zone of cellular infiltrate of lymphocytes and histiocytes. The tubercles consisted of epithelioid cells and giant cells. Areas of necrosis were absent and plasma cells were sparse.



Fig. 5. Cutaneous Leishmaniasis. Recidivans phase. The lesion shows papules dispersed around a pre-existing scar.

DISCUSSION

Clinical and histological observations and long-term follow-up rendered possible the classification of the disease into three histological phases which corresponded to more or less distinct clinical pictures.

The *granulomatous phase* persists for almost a year and is characterized by a granulomatous infiltrate in the dermis. A pseudocarcinomatous hyperplasia of the epidermis is a common finding in this phase and is of special interest because in chronic neglected cases a possible development into a squamous cell carcinoma cannot be excluded.

The granulomatous phase corresponds clinically to the papule-nodule ulcerated lesion accompanied by an intense inflammatory reaction (Figs. 1, 2, 3).

The *microtuberculoid phase* is characterized by the demonstration of a variable number of minute tuberculoid structures without giant cells, areas of necrosis and plasma cells. Leishmaniae are absent, as a rule (Fig. 4).

This phase corresponds clinically to a non-ulcerated, sometimes scaly nodule with little inflammatory reaction.

The *recidivans or late phase* is characterized by a histologic picture similar to lupus vulgaris and corresponds clinically to papules dispersed around a pre-existing scar of a cured Leishmaniasis lesion (Fig. 5).

The most effective schedule of treatment has been considered the intramuscular injection of pentavalent antimonial methylglucamine antimoniate (Glucantime) in daily doses of 0.1 g/kg for 10 days. No side reactions have been seen. Combination with topical treatment in the form of intralesional corticosteroid injections has given better results. Neglected chronic cases respond

satisfactorily to diathermy or cryotherapy or even to surgical excision.

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