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TUBERCULOID RELAPSE IN A HEALED LEPROMATOUS (L3) CASE

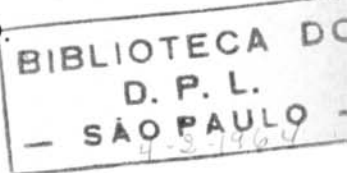
ENRIQUE D. L. JONQUIERES, M. D.

*Central Dispensary of Dermatology
Buenos Aires, Argentina*

ALBERTO J. MELAMED, M. D.

AND RICARDO O. MANZI, M. D.

*Sanatorio Baldomero Sommer
Buenos Aires, Argentina*



The concept of "polarity" of the types of leprosy includes, by definition approved by the Madrid Congress held in 1953, the idea of marked stability and the mutual incompatibility of the lepromatous and tuberculoid forms. This schematization is undoubtedly acceptable, and should be maintained for practical and teaching purposes. Biologically, however, it must be admitted that no disease entirely respects the efforts to devise complete and permanent schemes of classification. Leprosy, with many questions regarding its pathogenesis still unanswered, is no exception to this rule.

Thus, occasionally, authentic "mutations" of the polar types have been reported. Tuberculoid cases have transformed to lepromatous, according to reports of, among others, Schujman⁽¹⁰⁾, Mariano⁽⁷⁾, and Masanti and Jonquieres⁽⁸⁾. On the other hand, it seems that, with increasing frequency since the beginning of the sulfone era, there has been observed the phenomenon of "conversion" of intermediate forms toward the polar types.

Although this phenomenon has been described under terms which may lead one to think of a "mutation," we firmly believe that it is not correct to identify this process of conversion with true mutation. Thus, neither the "pseudoexacerbation" of tuberculoid type in lepromatous cases under sulfone treatment described by Souza Lima^(11, 12, 13), nor the "acute infiltration" studied since 1931 by Tajiri^(15, 16, 17), can properly be regarded as a mutation of type from lepromatous to tuberculoid. Both Rodriguez⁽⁹⁾ and Tajiri⁽¹⁶⁾ are of the opinion that the tuberculoid pseudoexacerbation and the acute infiltration pertain to the phenomena of conversion occurring in the borderline group.

Wade (18) has suggested the term "reversal reaction" for this acute phenomenon. We have observed (5) that in borderline cases submitted to sulfone therapy the conversion to tuberculoid, more or less reactional in nature, occurs in 54 per cent of the cases, through a phenomenon similar to or identical with the "acute infiltration" reaction.

Nor, inversely, can the lepromatous transformation of a reactional tuberculoid case be accepted as a mutation of the polar type because, as can be gathered from the descriptions of the cases, the phenomenon concerns the "borderline" form, which is prone to undergo that transformation.

But there is another aspect rarely observed in the evolution of the disease which we wish to emphasize, and which is the subject of this report. We refer to an apparently actual mutation of lepromatous patients, long treated and cured, toward the tuberculoid type. An apparently typical case is that reported by Davey (3).

REPORT OF CASE

CASE No. 5279 (D.C.D.).—Nidia F. de V., Argentinian, a white female aged 31 years, admitted to the Sommer Sanatorium in November 1943. A native of Tandil, she resided in Corrientes for 6 years, from her 3rd to 9th years. When she was 8 years old (about 1920), cyanotic spots appeared on the external surface of the lower third of the right leg. She was treated with chaulmoogra from 1928 to 1943 (but irregularly, she admitted), during which time the disease progressed to an advanced nodular lepromatous stage, with leonine facies, deformation and sinking of the nasal ridge, and a profusion of spots and lepromas of the trunk and limbs (L3 grade).

From the time of her internment in the Baldomero Sommer Sanatorium in 1943, she was continued under chaulmoogra treatment with little improvement until 1946. From then until 1957, a period of 11 years, she received the regular sulfone treatment (with, secondarily, thiosemicarbazone). The response was so favorable that in 1957 she was declared clinically cured, although she had had numerous and severe lepromatous reactions up to 1956. At the time she was declared cured she exhibited many residual cicatrices, typical facies because of the sunken nasal ridge (boxer's face), alopecia of the eyebrows and eyelashes, and gerodermic and telangiectatic skin. Bacteriologically, rare bacilli were found (3 smears of 11 examined). The Mitsuda reaction was, for the first time, recorded as weakly positive. All specific treatment was suspended because of the appearance of hyperthyroidism. Later she developed carcinoma of the cervix of the uterus, for which she received the Regaud radium therapy, and finally, in 1961, she underwent operation.

Beginning in 1959, there appeared eruptions on the trunk of circinate elements which had a tendency to subside under ACTH treatment without completely disappearing. A biopsy of one of the lesions showed a simple chronic, indeterminate infiltration more exuberant than usual. On the thorax there were large geographic bordered areas and several rounded plaques. All of these elements were well-defined and elevated, grossly resembling the centrifugal annular erythema of Darier. The face appeared as an erythematous mask, with edema of the upper lip. Up to 1961 she had several such outbreaks or exacerbations which she stated lasted for 2 to 3 months, after which the eruption subsided until it almost disappeared. She was not able to tell if the present lesions appeared in the same places that had been affected previously.

Present condition (November 15, 1961).—The patient is in fairly good general condition, and is mentally sound. Actually 48 years old, she has had leprosy for 40 years. She has the characteristic face of an advanced lepromatous case in the residual stage.

The skin of the face is gerodermic and erythematotelangiectatic. Nasal deformity due to the sunken ridge. Alopecia of the eyebrows and eyelashes. Numerous cicatricial lesions on the extremities and buttocks; large areas of marked skin atrophy. Sequelae of leprosy panniculitis with sclerotic marmorization on the limbs. Bilateral cubital clawing. On the neck, chest, mammae, and the back down to the waist (Fig. 1), and on the upper extremities, are numerous annular and oval lesions, some confluent, of copper-orange color, the centers slightly hypochromic, the borders clear-cut and distinctly infiltrated and easily palpable. These lesions are anesthetic.

Bacteriology: negative. Lepromin reaction: Fernandez and Mitsuda reactions weakly positive, the latter producing small nodules 3 mm. in diameter. A biopsy specimen (No. 3303, Central Dispensary, reported by Dr. J. Abulafia) shows, under an unchanged epidermis, abundant dermal infiltrates which run down deep around the adnexa and the communicating vessels, reaching the interstitiae of the sweat glands. These infiltrates consist of rounded collections of epithelioid cells with some giant cells of the Langhans' type, surrounded by mantles of lymphocytes. Ziehl-Neelsen staining: no acid-fast bacilli. Sudan IV staining: negative for lipids (Fig 2).

In a previous biopsy specimen (No. 5555, Sanatorio Sommer) the structure was found to be that of the reactional tuberculoid type, with edematous epithelioid cells and without giant cells. In addition, in the proximity of these infiltrates, and occasionally centering lymphocytic infiltrates, there are observed small accumulations of cells of the Virchow type, mostly without bacilli; only one long granular form and several acid-fast granules were found inside of one of these cells.

The histologic examination of the Mitsuda reaction nodule (No. 5728, Sanatorio Sommer) reveals circumscribed cellular infiltrations in the skin, in two sectors distinctly different from each other. The upper level, near the papillary dermis, is composed of a cellular infiltrate of epithelioid type, with fibroblasts and multinuclear cellular patterns without the typical characteristics of the Langhans' cell. There is no tendency to form definite follicles, although the cells tend vaguely to arrange themselves in rounded formations without lymphocytic mantles. In the immediate proximity of this sector, but deeper in the dermis, is observed an infiltrate composed of vacuolated cells, many of them with nuclei pushed to the side, with the characteristics of the uninhabited Virchow cells.

DISCUSSION

The case here described exhibited certain particularities worthy of analysis: (1) The previous condition of the patient was unquestionably lepromatous. (2) The last episodes—clearly tuberculoid clinically, histologically and immunologically — appeared coincidentally with the clinical and bacteriologic clearing-up of the preexisting lesions. (3) The histology of the tuberculoid lesions, as well as that of the nodule of the Mitsuda test performed in the neighborhood of a residual lepromatous lesion, denotes the coexistence of follicular structures and granulomas that were not differentiable from the lepromatous condition, notwithstanding the negativity of Sudan IV staining and the very great reduction of the bacillary content.

This situation can be explained synthetically by admitting the coexistence of a *residual* lepromatous granuloma with another of the follicular type. Nevertheless, the diagnosis of borderline cannot be entertained as there were no lepromatous lesions in activity (with easily demonstrable bacilli).

What, then, can have been the pathogenesis of the episodes under discussion? An explanation is attempted based on certain known facts. It is recalled, in the first place, that the bacillary lipids of *M. leprae*⁽⁴⁾, as well as those of the Koch bacillus⁽¹⁴⁾, may cause the production of follicular structures; that in our case the histologic picture of the tuberculoid plaques and of the nodule of the Mitsuda reaction (due to intervention of the bacilli) are similar; and that the lesions of the patient contained very small numbers of bacilli. For these reasons it seems logical to believe that the tuberculoid plaques and the follicular structures had appeared in the vicinity of the preexisting residual lepromatous granuloma at the expense of the bacillary fractions (lipids) liberated by the rupture of the Virchow cells.

The possibility that the lepromatous case in the residual period may produce tuberculoid granulomas in the presence of the Hansen bacillus constitutes an immunologic fact of great significance, and is seemingly well established by the study of Azulay and collaborators⁽¹⁾. Since the situation became apparent after the bacilli had disappeared from the lesions, or at least when their numbers had been greatly reduced, it seems evident that the body could control the development of the bacilli and cause their destruction. In connection

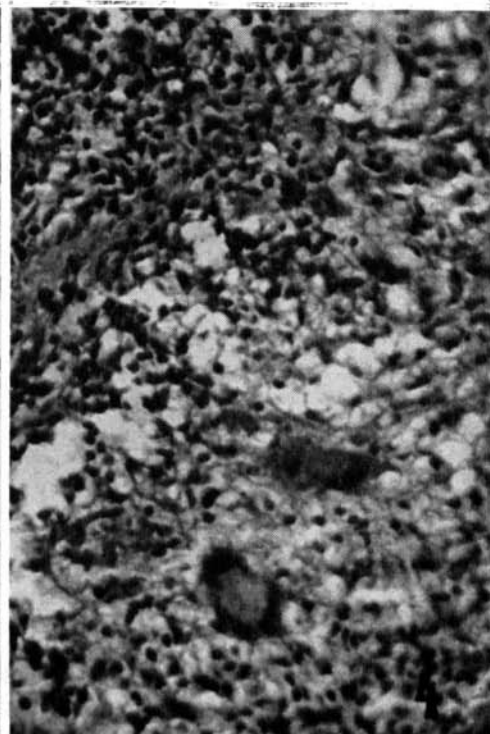
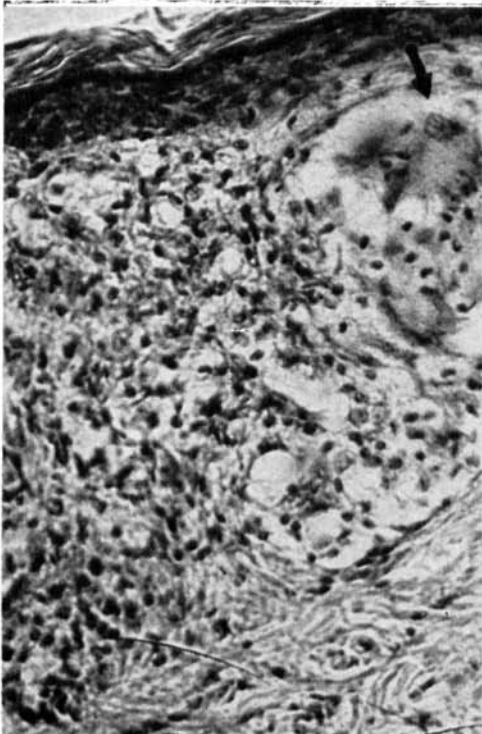
DESCRIPTION OF PLATE

FIG. 1. Reactional lesions on the back of the patient concerned in this report, of the major tuberculoid aspect.

FIG. 2. Photomicrograph of a granulomatous cord of follicular structure. Sudan IV stains, negative for fats.

FIG. 3. Langhans' giant cell (arrow) in a follicle in the papillary layer of the dermis, showing atrophy of the epidermis.

FIG. 4.—Langhans' giant cells centering a lesion follicle. The edema of the epithelial cells reveals the reactional histologic character of the infiltrate.



with these ideas we may cite the fact that tuberculosis of rabbits provoked by mammalian bacilli shows at the beginning a granuloma very similar to that of lepromatous leprosy (⁶), which later shows follicular structures coincident with the appearance of sensitization and the destruction of many of the preexisting bacilli. Also worthy of mention is the study of Canetti (²), which proved that in tuberculosis no epithelioid metaplasia can be seen in the caseous foci, because necrosis of the macrophages prevents their conversion into epithelioid cells. These citations and reflections lead hypothetically to the following conclusions:

(1) The Virchow cell is a consequence of the rapid proliferation of the Hansen bacillus, and it presents degeneration phenomena which prevent it from converting into the epithelioid cell. This state coincides with a lack of capability of destroying the bacilli by immunologic means (negative Mitsuda reaction) and it gives the picture of a state of immuno-tolerance.

(2) The acquisition of resistance, early or late, against the bacillus in the healed lepromatous case implies the ability to control the growth of the bacillus and to provoke its rapid destruction, with in consequence the conversion of the macrophages into epithelioid cells. Nevertheless, the preexisting Virchow cells, affected by degenerative phenomena, will persist as such until their destruction as a result of having lost the ability of conversion shown by the normal macrophage.

These concepts of pathogenesis may justify, in the case reported, the coexistence of the follicular granuloma with the bacillus-negative lepromatous picture.

SUMMARY

This is a report of a lepromatous case of 40 years duration and 26 years of treatment, which during the first 15 years had been treated with chaulmoogra which did not prevent the disease from progressing to an advanced (L3) state, and later for 11 years had been treated with the sulfone medicaments and had cleared up clinically and bacteriologically. At that time the patient began to present tuberculoid outbreaks, clinically, histologically and immunologically authentic.

The coexistence in histologic sections of tuberculoid follicles and residual lepromatous structures in which granular bacillary debris was found seems to indicate that the lipids of this debris were responsible for the tuberculoid response, induced by the resistance or immunity acquired by the tissues. This, we hold, is an authentic case of mutation of type.

RESUMEN

Se comunica el caso de una paciente lepromatosa con 40 años de tratamiento, de los cuales los primeros quince en que recibió chaulmoogra fueron inefectivos

progresando la enfermedad hasta la forma L3, y que luego blanqueó clínica y baciloscópicamente con tratamiento sulfónico llevado durante once años. En este momento la enferma comienza a presentar brotes tuberculoideos, clínica, histológica e inmunológicamente auténticos. La coexistencia histológica de folículos tuberculoideos con estructuras lepromatosas residuales en las que se encuentran restos bacilares granulados, hace suponer que los lípidos de estos restos son los responsables de la respuesta tuberculoide, inducida por la resistencia o inmunidad alcanzada por los tejidos. Se trataría de un caso de auténtica mutación de tipo.

RESUMÉ

Ce rapport relate le cas d'un malade atteint de la lèpre lépromateuse depuis 40 ans, qui fut traité durant 26 ans. Le chaulmoogra fut d'abord employé pendant 15 ans, et cela n'empêcha pas l'affection de progresser vers un état avancé (L 3); plus tard, et pour 11 ans, le malade fut soigné par des médications sulfonées avec comme résultat un nettoyage clinique et bactériologique. A ce moment, le sujet commença à présenter des épisodes tuberculoïdes, authentifiés du point de vue clinique, histologique et immunologique.

La coexistence dans les coupes histologiques de follicules tuberculoïdes et de structures lépromateuses résiduelles parmi lesquelles des débris bacillaires granuleux pouvaient encore être mis en évidence semble indiquer que les lipides de ces débris sont responsables de la réponse tuberculoïde, qui serait suscitée par la résistance ou par l'immunité acquises par les tissus: Nous soutenons que ce cas constitue une réelle mutation d'un type à l'autre.

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