A TUBERCULOID-LIKE REACTION IN LEPROMATOUS LEPROSY

A REACTIONAL REVERSAL PHENOMENON

Not yet, it would seem, have we reached the end of distinguishing previously unrecognized features of leprosy. To the anguish of those who wish to keep classification simple, the forms, varieties, and reactional phases of the disease that must be recognized are becoming more numerous. The "good old days" of comfortable simplicity are gone; our present-day ignorance is less thorough-going, and less comfortable.

With respect to tuberculoid leprosy, de Souza Campos began at least ten years ago[1] to insist that the original concept of lepra reaction in that type of the disease[2] really comprises two different things: (1) an acute aggravation or activation of existing tuberculoid lesions, "tuberculoid reactivation (tuberculoid lepra reaction)"; and (2) a relatively spectacular condition of abrupt onset and often startling appearance, sometimes occurring in persons with only simple lesions or none at all, which he

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[1] [II CONFERENCIA PANAMERICANA] Relatório da Comisão de Classificação. II. Conf. Panamericana de Lepra, Rio de Janeiro, Oct. 1946; Rio de Janeiro, 1947, Vol. **3**, pp. 176-189.

[2] WADE, H. W. Tuberculoid changes in leprosy. II. Lepra reaction in tuberculoid leprosy. Internat. J. Leprosy **2** (1934) 279-292.

called "reactional tuberculoid leprosy."[3] The latter, presumably, is the one which in Japan has long been known as *"akuter Schub."*

It now appears that some Japanese leprologists are making a distinction among the reactions that may occur in lepromatous leprosy—apart from erythema nodosum leprosum—somewhat similar to that of de Souza Campos in tuberculoid leprosy. This is recent, because at the Leonard Wood Memorial Working Clinical Conference held in Japan in 1952[4] only a single condition was considered, it being called "acute lepromatous infiltration." To some if not most of the foreign participants, its description was decidedly less than satisfying. Now, however, comes Tajiri in this issue of THE JOURNAL with an article (a combined translation of two previous ones [5, 6]) in which is made a distinction between (1) "acute lepromatous infiltration" (in place of which term he has accepted "acute lepromatous activation"), which is basically an acute activation and aggravation of the existing lepromatous condition; and (2) "acute infiltration" (the term avowedly used for lack of a more satisfactory one) which in appearance and otherwise is much like the *akuter Schub* of tuberculoid leprosy.[7] The resemblance goes so far that, besides morphological similarities, the lepromin reaction becomes positive, the histology of the characteristic lesions are of epithelioid (tuberculoid) rather than lepra cell (lepromatous) nature, and the bacilli in them are much fewer than in actual lepromatous lesions although more than in the typical *akuter Schub* lesions of tuberculoid cases.

Development of tuberculoid characteristics in lepromatous leprosy as a result of sulfone treatment has been reported before. In 1948, Davey[8] told of an advanced lepromatous case receiving sulphetrone which developed a papular exanthem histologically of atypical tuberculoid nature, while the lepromin reaction turned from negative to strongly positive. If there have been other such reports they have been overlooked.[9]

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[3] SOUZA CAMPOS, N. and RATH DE SOUZA, P. Reactional states in leprosy. Lepra reaction, tuberculoid reactivation (tuberculoid lepra reaction), reactional tuberculoid leprosy, borderline (limitantes) lesions. Internat. J. Leprosy **22** (1954) 259-272.

[4] [MEMORIAL CONFERENCE] The Leonard Wood Memorial Working Clinical Conference, held in Japan, Sept. 15-27, 1952. Internat. J. Leprosy **20** (1952) 385-392 (news).

[5] TAJIRI, I. On Mitsuda's reaction in cases of acute infiltration of lepromatous leprosy. La Lepro **23** (1954) 119-121 (in Japanese; English abst. p. 119).

[6] TAJIRI, I. On acute infiltration of the lepromatous type of leprosy. La Lepro **23** (1954) 261-269 (in Japanese; English abst. p. 261).

[7] Abstracts of Tajiri's previous articles on the subject appeared in our last issue. Also in that issue were three Letters to the Editor on the subject, by Tajiri, Kitamura, and Rodriguez.

[8] DAVEY, T. F. The treatment of leprosy with sulphetrone. Leprosy Rep. **19** (1948) 55-61.

[9] In the next year de Faria wrote about a lepromatous case that was supposed to have become tuberculoid, but the report does not indicate when, how or why that happened.

Twice, de Souza Lima[10, 11] has written of a "pseudoexacerbation" phenomenon occurring in lepromatous cases under sulfone treatment, and in this issue of THE JOURNAL there is a translation of the second of these reports. The condition he describes seems to be basically similar to Tajiri's "acute infiltration," although there are differences. It happens that the writer personally had the opportunity, in 1948, of seeing in São Paulo some of de Souza Lima's cases and sections from their lesions. The condition was definitely not ordinary lepromatous lepra reaction, but was basically of tuberculoid nature—albeit histologically atypical, as lesions of "reactional tuberculoid leprosy" cases and borderlines are liable to be.

As for the differences between the descriptions from Japan and Brazil, the condition in de Souza Lima's cases usually occurred early in sulfone treatment, in Tajiri's cases late. The Brazilian cases remained negative to lepromin.[12] The bacilli in their lesions were found to be modified; Tajiri remarks especially that they were not so in his cases. Both authors say much the same thing about the numbers of bacilli and their location.

Rodriguez[13] wrote of similar observations in the Philippines, saying that it was borderline cases that had "developed some of the typical characteristics of the lepromatous type" which are liable to develop "pseudoreactivation" under sulfone treatment. "These drugs seem to have the capacity of stirring up the tuberculoid portion of the dual nature of these cases."

This suggestion is important. It is an understandable explanation of a phenomenon which otherwise would be most difficult even to accept as possible. Souza Lima, in response to a personal inquiry, has agreed that the condition probably occurs in secondary lepromatous cases that have evolved to that state from borderline, and that—although almost anything can happen in leprosy—it is unlikely that the phenomenon could occur in cases lepromatous from the outset. Tajiri, in an addendum resulting from correspondence, discusses borderline cases but does not say that the lepromatous cases that develop the acute infiltration were once of that kind. However, in two places he speaks of "transition to the lepromatous type" from the original form—whatever that may have been. He says only that the acute infiltration is a process contrary to the change from borderline to lepromatous, but that the lepromatous cases that have this peculiar reaction do not become borderline as a result of it.

About terminology, the use of "acute lepromatous infiltration" for

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[10] DE SOUZA LIMA, L. and RATH DE SOUZA, P. Pseudo exacerbação da lepra pelas di-amino-di-phenyl sulfones. V. Congr. Internac. Lepra, Havana 1948; Havana 1949, pp. 205-206; *also* Internat. J. Leprosy **17** (1949) 19-21 (in English).

[11] DE SOUZA LIMA, L. Estados reacionais da lepra "pseudo exacerbação." Mem. Terc. Conf. Panamericana Leprol., [Buenos Aires, 1951], Vol. **1**, 1953, pp. 184-188.

[12] Dharmendra's antigen was used at first, but later regular lepromin was used (personal communication).

[13] RODRIGUEZ, J. N. "Pseudoexacerbation" and "borderline" cases. Internat. J. Leprosy **18** (1950) 95.

one kind of reaction in lepromatous leprosy and "acute infiltration" for another is decidedly confusing. For the former kind "acute lepromatization" seems no more helpful for cases already lepromatous, because it suggests a process of change to lepromatous from another form. "Acute lepromatous activation," proposed by us and accepted by Tajiri, is at least different and not readily subject to confusion.

For the latter kind of reaction, "pseudoexacerbation" is hardly more informative than "acute infiltration." Souza Lima says that Rabello has suggested "induced tuberculoid," which would at least be better. We suggest, however, the introduction of the idea of a *reversal* phenomenon, an attempt to return from the (presumably secondary) lepromatous condition in which this kind of reaction occurs toward a more resistant form or stage; and for that "reversal reaction" in lepromatous leprosy might serve.

Be that as is may, there is here a form of reaction in cases necessarily classified as lepromatous, occurring at some time during sulfone treatment, that few leprologists have recognized. It follows that wherever and whenever the condition is encountered, there should be careful inquiry into the previous history of the case, thorough search for significant stigmata, and adequate follow-up afterward. Clinicians would do well to watch for cases of this kind, and enlist the cooperation of pathologists in the study of them, to fill an apparent gap in our understanding of the disease.

—H. W. WADE