

A PROBLEM IN LEPROSY CLASSIFICATION

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SUMMARY: *Type I reactions are one of the greatest problems in the classification of leprosy, and the evolution of its concept is analysed since pre-sulphone era.*

*These reactions occur in established tuberculoid and borderline cases and can suddenly occur, being the only manifestation of the disease. On the other hand they can occur before, during and after treatment. In the opinion of the author, all of them are the expression of the same phenomenon, that is, a delayed type of hypersensitivity to antigens released by destruction of multiplying *M.leprae*.*

Based in discussion of these facts it is proposed a new classification of the disease, in which each clinical form is imutable and there is no shift in the immunity.

Key words: *Reversal reaction, Type I Reaction, Pseudo-exacerbation, Classification*

One of the most challenging problems in the classification of leprosy is the Type I reaction (Jopling). To study this phenomenon it is important to take into account the accurate description that some investigators reported during the period when no effective treatment was available and the natural story of the disease could be followed without the interference of modifying factors.

Undoubtedly, Wade, in 1930, was the first author to recognize reactions in tuberculoid cases. At that time, the study of tuberculoid leprosy was at its beginning. He said: "Manifestations of lepra reaction in cases of tuberculoid leprosy or in individual tuberculoid lesions have not been described as such. Evidence of its occurrence would doubtless be found in the literature if it were searched diligently bearing in mind the fact that tuberculoid lesions are usually not recognized for what they are."

Soon after many other authors presented their own observations on this issue.

In the 40's there was already a consensus

in relation to the clinical characteristics of these acute manifestations. They could occur in established cases of tuberculoid leprosy where previous lesions became more erythematous and edematous and often new lesions could appear. Nerves could either be involved or not. After the regression of the reactional episode the patient could show a higher number of lesions than before. The episodes could follow one another. The general condition of the patients was preserved. Skin smears were negative. Lepromin test was positive and the histopathology showed tuberculoid granuloma with signs of acute inflammation.

There were also reactional episodes with disseminated lesions which occurred in cases that showed initially, only anaesthetic patch or indeterminate macules or even a tuberculoid plaque or macule. After acutization of the early lesions, several erythematous plaques, nodules and papules with clear-cut edges appeared all over the body with a unique localizations around

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the mouth and eyes at the face, and also at the palms and soles. Reactional lesions became the only manifestations of the disease in these cases.

These cases are referred as Reactional Tuberculoid cases by South-American authors and as Akuter Shub by Japanese investigators. They are the cause of the controversy concerning the characteristics and the progression of reactional cases which still remains.

Before Dapsone's era, leprosy workers already noted several different characteristics in these generalized reactional cases. Some of them showed smear negative or weakly positive lesions and the lepromin was positive and sometimes strongly positive. Whereas others showed more edematous lesions, with marked edema of the limbs and were more prone to develop nerve damage. Skin smears were ever positive and Lepromin test was weakly positive or negative. The episodes tended also to be repetitive.

Among others, Cochrane did not agree to include these cases as reactional tuberculoids. He considered the reactional tuberculoid cases as acute manifestations of the major tuberculoid leprosy and he could not accept a tuberculoid case with a negative lepromin test. He referred these cases as indeterminate, and declared in 1940: "A negative lepromin test in major tuberculoid leprosy is a contradiction."

A few years later Souza Lima presented the following results of lepromin test out of 264 tuberculoid reactional cases: strongly positive (+++), 51; positive (++) , 85; fairly positive (+), 60; negative (-), 59; doubtful, 9. In relation to the 25% of negative cases he states: "We should consider, however, that in our cases it seems that some influence of the negative result should have occurred since these cases are found mainly among those with anomalous evolution, that is, those that evolved to lepromatous leprosy".

Then, we can assume that in that period there was already some suspicion of the existence of reactional cases that were different in its behavior regarding reaction against *M. leprae*.

Many authors have mentioned this transformation in some of these cases to lepromatous form but, to our knowledge, there is not any accurate description of this phenomenon. Wade, who introduced the concept of borderline

leprosy, although recognized this possibility, could not well document a single case. One of the cases he described in 1940 as borderline tuberculoid deserves some additional comments. This case evolved with acute manifestations for 10 years, showing marked modifications in the original aspect of the lesions and finally presented a bullous reactional episode even though he did not become a lepromatous case. Ryrie in Malaysia had a reasonable experience in the follow up of reactional cases with bulla and ulcers and he also claimed that these cases would finally evolve to become lepromatous. Wade, while visiting Ryrie, could not see any of those cases undergoing such transformation.

Based in the experience of these authors and others, we can conclude that many reactional cases may show modifications in the aspect of their skin lesions, but those that really undergo lepromatous transformation are a few, if so.

The Madrid Congress in 1953 just considered the reactional cases as acute manifestations of the disease, although they recognized the existence of a reactional tuberculoid and a reactional borderline. Unfortunately, the Congress did not give an accurate definition of them. It was included in the definition of reactional tuberculoid those cases that should be considered as intermediate or borderline. In addition the Congress also stated that a borderline case may arise from a reactional tuberculoid one, after successive reactional episodes. Unfortunately from these facts arose a broad and wrong concept that reactional tuberculoid cases with repetitive episodes could become lepromatous through a borderline transformation.

Furthermore, the Committee of Classification in the Madrid Congress, while defining reactional borderline cases, only refers to one of its particular forms. It did not mention the existence of borderline cases with chronic evolution which could develop reactions in the same way that the tuberculoid cases.

At that time, Dapsone was already the treatment for leprosy and the patients could not anymore be studied under the light of the natural history of the untreated disease. Therefore, many of the statements about reactions made afterwards did not take into account the early observations of previous authors.

To our understanding, the reactions in tuberculoid and borderline cases of chronic evolution and the reactional and borderline reactional cases are the same phenomenon, although many authors consider the former as special features of the disease. Tajiri says that: "reaction in established tuberculoid cases, which is simply an activation of pre-existing lesions of that type, perhaps with the development of new ones, a condition not given special status by Japanese workers; .."

Indeed, much importance was not given to reactions in tuberculoid and borderline cases as a whole. In this regard, in the International Congress that was held in Rio de Janeiro in 1963, the panel on leprosy reactions declares: "leprologists are aware of the damage left by reactions in other forms of leprosy but consider as more frequent and important acute and subacute episodes in lepromatous leprosy."

However, old concepts are still valuable although using new names and including new aspects not previously described. In this sense, Cochrane in 1964 described his low resistance tuberculoid leprosy. According to this author, in this form, the lesions have all the features of tuberculoid leprosy but with two atypical aspects: the lesions are in a greater number and have symmetrical distribution although retaining the clear-cut edge feature of tuberculoid leprosy. In these cases the lepromin test is always positive, sometimes markedly, and the histopathology is similar to tuberculoid leprosy. As regards the evolution, Cochrane declared that he never saw a case with lepromatous transformation but recognized that some cases can last for many years retaining the same clinical aspect.

In the other hand, Leiker, in the same year, studied a group of patients with a form of the disease which he also called "low resistance tuberculoid leprosy". According to his description this form seems to be reactional tuberculoid cases with less obvious acute manifestations, with important neural involvement, skin smears frequently negative but sometimes weakly positive, the lepromin test doubtful or weakly positive, and the histopathology shows "small epithelioid foci". As regards the evolution the author says that no deterioration to borderline-lepromatous leprosy was observed. He was indeed

convinced of the tuberculoid nature of these cases. He also suggested to include the reactional tuberculoid cases in the low-resistance tuberculoid group and tried to divide this group in low - resistance major tuberculoid and low- resistance minor tuberculoid variety which would include his cases.

In 1966, Ridley and Jopling presented their classification of leprosy for research purposes. In this classification reactions are not considered although the photo of a BT case that illustrates their original article seems to be a reactional case.

In 1969, Ridley specifically studies reactions. He divides those reactions occurring in borderline cases (according to this classification) in downgrading and reversal reactions and asserts that these reactions were previously and clearly recognized by Tajiri in 1955.

As a matter of fact, Tajiri described a clinical condition that he called "acute infiltration" that occurred in lepromatous leprosy in those cases with a long period of regression and reabsorption of the disease, which were becoming more common with dapsone therapy. This condition had a sudden presentation, was intensely inflammatory, raised and often presented an erysipela-like appearance. Sometimes it was similar to a tuberculoid macule or plaque with raised edges and resembling a lesion of a reactional tuberculoid case, the ones that Japanese authors were used to call "akuter shub", although less intense. Fever, neuritis and joint pain could be present. Histologically the lesions were like those of reactional tuberculoid leprosy with more bacilli than in pure reactional tuberculoid lesions. Lepromin test was positive. Although a high proportion of positives, the reactional grade was lesser than in tuberculoid cases, specially in the so-called "akuter shub". Tajiri concludes his article saying that borderline form is a transitional stage in a progression from tuberculoid to lepromatous, a malign development in a benign type. The acute infiltration he described should be the opposite process. It was a benign evolution in the malign lepromatous type.

A few years before this article, in 1946, Souza Lima described an acute condition very similar to the one described by Tajiri in lepromatous patients treated with sulphone. Souza Lima called this condition as "pseudo exacerbation".

This issue deserved an editorial in the "International Journal of Leprosy" by Wade. He concluded that, although the differences among the observations of the authors, such as the positivity of lepromin test in the acute infiltration of Tajiri and the presence of solid stained bacilli, which contrasted with the findings of Souza Lima, these conditions "seems to be basically similar". Wade was whom proposed the name of reversal reactions to this kind of reaction.

Davey also described a similar condition in one patient treated with sulphone, and Rodrigues, while describing this reaction in patients from the Philippines considered that "it was borderline cases that had developed some of the typical characteristics of the lepromatous type which are liable to develop pseudo-reactivation under sulphone treatment".

In this way, it is easy to understand why Ridley classified reactions under the statement of: "the movement towards lepromatous leprosy is associated with a clinical and histological disturbance that makes up the downgrading reaction, whereas the movement towards tuberculoid leprosy is associated with the features of reversal reaction". He continues later: "downgrading reactions are associated with a decline of immunity and a corresponding increase in the number of bacilli and extension of infection in the neartubercu-

loid and borderline patients. Reversal reactions are the opposite. They occur in nearlepromatous and borderline patients when the bacterial load is diminished as a result of treatment; and they are associated with a corresponding increase of immunity".

It is clear that he did not consider the untreated reactional tuberculoid cases with negative skin smears that remains in this situation even in the occurrence of new episodes and with a lepromin test above 8 mm. He also did not consider the fact that in many reactional cases with positive skin smears before treatment, bacilli disappears while the episode subsides and reappears in the next reactional episode, as we can conclude from cases described by Wade. Moreover, Ridley did not present sufficient elements to make a distinction between the two reactions, neither clinically nor histopathologically. He says that: "reactions have very similar clinical features; there is erythema and swelling of the skin lesions, which may proceed to ulceration; severe cases develop fever and often there is nerve involvement. New lesions can appear; in a reversal reaction they may present a tuberculoid appearance." He just forgot to mention that not only reversal reaction may show these features, but all reaction, even without treatment.

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