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LOW-RESISTANT TUBERCULOID LEPROSY[1]

D. L. LEIKER, M.D.

Ministry of Health
Jos, Northern Nigeria

Tuberculoid lesions are characterized, according to the last three International Congresses of Leprology ([2, 3, 4]), by an asymmetric distribution of lesions, a clear definition of the margins, and, often, central healing in lesions. The superficial varieties may present a rough and dry surface (macular variety) or a papular surface or a raised papular margin (minor variety).

In West Africa, but also in other countries, a fairly high proportion of the tuberculoid cases do not present these typical features, or such features occur only faintly in part of the lesions. Such cases are classified, according to the background of the examiner, as macular tuberculoid, atypical tuberculoid, maculo-anesthetic, dimorphous or borderline macular, or even as indeterminate. They belong to what Davey ([5]) has called the "macular series," ranging from nearly typical tuberculoid to nearly lepromatous.

In this article a group of cases at the tuberculoid end of the spectrum is discussed. The author is of the opinion that this subgroup deserves a special designation. Although the cases present sufficient tuberculoid features to include them in the tuberculoid group, there is evidence of a lower resistance as compared with typical tuberculoid cases. The prognosis is, on the average, much more serious, and special care is needed in the treatment.

The cases are intermediate between typical tuberculoid and borderline-lepromatous. Apart from the disadvantage of introducing new designations, such as "dimorphous," which have not met general agreement in the international congresses, the cases are so much on the tuberculoid side of the spectrum that creation of a special group is not necessary. Because of clinical, immunologic, bacteriologic, histologic, and prognostic aspects, it is suggested that these cases be included in a subgroup of tuberculoid leprosy, called "low-resistant tuberculoid leprosy."

Onset.—The first lesion is usually a macular or maculoid, rather

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well defined, moderately hypopigmented patch. The surface is rather dry and rough. Often the definition of the lesion, the degree of hypopigmentation, and the surface texture, point to a tuberculoid development. In other cases the lesion is not characteristic and has to be classified as indeterminate.

In other cases the first lesion or lesions are macular tuberculoid, or even resemble typical minor tuberculoid. They differ usually from typical tuberculoid lesions by a broad, spreading micropapular edge. Satellite lesions are common. In most lesions central healing is slow, inconspicuous or absent.

Progress.—The first lesion or lesions may grow in size during several months, but then the growth stops spontaneously. Lesions that were somewhat raised become flat. After a few months, or later, however, several new lesions appear. They are seen usually in the first year after the first lesion has appeared, but may be seen after a longer interval. The initial lesion often does not show reactivity while new lesions appear and has apparently become an immune area. In other cases only part of the first lesion shows reactivity.

Some of the new lesions are rather typical tuberculoid. They are well defined and markedly hypopigmented, and central healing is evident. Other lesions are less well defined and less hypopigmented, and central healing is not evident. Some lesions are macular tuberculoid. Others resemble minor tuberculoid lesions, but the micropapular edge is very broad, the papules are minute, and satellite lesions near an active spreading edge are common. Several lesions may coalesce and cover large areas of skin.

In this active stage most lesions are slightly raised, but not so much so as reactional tuberculoid lesions. Hypesthesia is present in most lesions or parts of lesions, but is less marked as compared with typical tuberculoid lesions. Loss of perspiration may be only slight and the hairs are not completely lost in this active stage.

After weeks or months the lesions become flat, the hypopigmentation becomes less marked, edges of lesions become less well defined, and the patches resemble indeterminate lesions. Often the lesions gradually almost disappear. A somewhat dry, shiny area may be the only indication left from a formerly conspicuous lesion. As compared with typical tuberculoid cases, healing is slow.

Distribution of lesions.—In a large proportion of patients a typical distribution of lesions is seen. Lesions in the face are common. Often several lesions coalesce and form a large lesion in the center of the face, covering cheeks, nose and part of the forehead. Unlike typical tuberculoid lesions the distribution is symmetric.

Many patients also present numerous lesions on both arms and legs. Here too several lesions may coalesce and a large part of the extremities may be affected. Lesions on both elbows, both knees, and the

hands and feet are common. The distribution is rather symmetric.

The lesions on the back are often more typically tuberculoid. They are asymmetrically distributed, but in cases with many lesions a tendency to symmetry is seen.

Generally speaking, the periphery is more affected than the trunk. Lesions on the palms of the hands, on the soles of the feet, and around the ears, sometimes partially covering them, are fairly common. Not infrequently lesions are found on the scalp. Occasionally lesions are found on the penis or scrotum.

Nerve involvement.—In typical tuberculoid cases usually only one nerve or a few nerves are affected. The distribution is asymmetric. The nerves are nodularly enlarged. Deformity, particularly contractures, appear in an early stage. In many tuberculoid cases nerves are not seriously affected.

A much larger proportion of the low-resistant tuberculoid cases show serious nerve involvement. Bilateral paralysis of the face is common. In the extremities most, if not all, larger nerves are affected. The nerves are diffusely enlarged over a great length. Bilateral peroneal paralysis is common.

The deformity, which is symmetrically distributed, develops more slowly as compared with that in typical tuberculoid cases. Shortening of all fingers and toes is more marked than contractures. Often the deformity develops long after the skin lesions have become quiescent.

A very high proportion of the very disfigured beggars in West Africa and elsewhere are burnt-out low-resistant tuberculoid cases. One could speak of the "beggar type" of deformity.

Bacteriology.—Routine smears are often negative. As compared with typical tuberculoid leprosy, they are more often positive, usually weakly so, but occasionally moderately so. They remain positive longer than in typical tuberculoid cases. Globi have never been found. Occasionally a positive smear may be obtained from nasal mucosa or from ear lobes. Usually, but not always, an inconspicuous lesion is found at these sites.

Immunology.—The lepromin reaction is doubtful to weakly positive. Most patients show reactions 3-7 mm. in diameter with standard Mitsuda-Wade antigen. Cases presenting a larger reaction to lepromin are more typically tuberculoid. The lesions are more raised and can be classified adequately as reactional tuberculoid.

Histology.—In active lesions foci of perivascular and perineural histiocytes, round cells and epithelioid cells are seen. The epithelioid tuberculoid foci are usually small. The distribution of the infiltrate is less limited to the upper part of the dermis. Papillary spaces are often free from infiltrate. An interrupted free subepidermal zone is often present. The nerves, although usually affected, are less rapidly destroyed than in typical tuberculoid cases.

The shape of infiltration is less like that of tuberculoid cases. Star and stripe appearance is more common. The sweat glands are less damaged than in typical tuberculoid cases.

Bacilli, if present, are found within nerve twigs. They are present in only a minority of the cases, but more often than in typical tuberculoid cases.

Prognosis.—Most cases become arrested spontaneously. Activity in the nerves may be found long after the skin lesions have become arrested. A high proportion of the cases develop serious bilateral deformity. In a minority of cases relapses with new skin lesions are seen. This may happen many years after apparent arrest. Lepromatous deterioration has not been observed.

Differential diagnosis.—Clinically, immunologically, and histologically the low resistant tuberculoid variety shows features that lie between typical tuberculoid and lepromatous character. It is not possible at present, however, to include the cases in the borderline group. The lesions are less infiltrated, more hypopigmented, more predominantly tuberculoid, better defined, and not dome-shaped. Some show a tendency to central healing and a micropapular edge. Smears are less often positive. Deterioration toward lepromatous leprosy is not seen. Unless a subgroup of borderline leprosy toward the tuberculoid side of the spectrum is created, it is more nearly correct to include these cases in the tuberculoid group.

Something could be said for inclusion of the cases in the reactional tuberculoid variety. A sudden crop of new lesions, sometimes followed by more crops is seen. The lesions are raised in the active stage of the disease.

Typical reactional tuberculoid cases, however, evolve from major tuberculoid lesions. The new lesions are also more infiltrated. Consequently they leave more hypopigmentation and atrophy. Histologically a dense, extensive tuberculoid infiltrate without a free or partly free subepidermal zone is seen.

Unless the reactional tuberculoid group is extended to a greater range of clinical symptoms, inclusion in this group is not satisfactory.

It is a common mistake to classify low-resistant tuberculoid cases as indeterminate. This often happens when a patient is first seen some time after the active stage. The lesions have become flat, less hypopigmented and even less well defined, thus resembling indeterminate lesions. Histologically the lesions also have become similar to indeterminate. However, the fact that the lesions have been raised and that tuberculoid foci are present in the active stage excludes an indeterminate classification.

The course of maculo-anesthetic leprosy is essentially benign. The majority of cases with one or a few lesions seem to fit into the macular tuberculoid variety. In a minority of the cases, however, numerous lesions are seen, and in such cases the development of polyneuritic

symptoms is common. It is not unlikely that such cases are similar to low-resistant tuberculoid leprosy with slight elevation (maculoid) only.

A large proportion of the cases classified as macular dimorphous, particularly those at the tuberculoid end of the spectrum, fit into the low-resistant tuberculoid group. It is not so important to agree whether this variety should be included in an already existing subgroup or in a new subgroup, as it is to recognize its place in the spectrum, i.e., at the borderline side of tuberculoid leprosy, or at the tuberculoid side of a wider intermediate, dimorphous or borderline group.

Treatment.—The treatment of low-resistant tuberculoid leprosy is at least as great a problem as the treatment of lepromatous cases presenting repeated reactions. The reactions in low-resistant tuberculoid leprosy are more disabling to the patient than reactions in any other type of leprosy.

There is no doubt that a high proportion of low-resistant tuberculoid patients become crippled without treatment with antileprosy drugs. Many more patients become more seriously crippled by routine treatment.

Tuberculoid leprosy is comparable with a fire than burns high and rapidly burns out. Low-resistant tuberculoid leprosy is more like a smouldering fire. It is tempting to add some fuel to shorten the time of combustion. There is little indication for treating typical tuberculoid cases in the active stage of the disease. There is no indication to treat such cases in a reactive stage of the disease with antileprosy drugs.

The decision is less easy in low-resistant tuberculoid cases. It is a more chronic process, the tissue resistance is not strong enough to destroy the bacilli rapidly, and the chance for dissemination of bacilli that may reach the larger nerves remains high as long as the disease is active. It is desirable to destroy the bacilli as rapidly as possible. However, as soon as bacilli have already entered larger nerves, any active antileprosy treatment becomes dangerous. Nerve reactions in low-resistant tuberculoid leprosy are much more likely to cause life-long crippling deformity than reactions in cases more on the lepromatous side.

Until a year ago tuberculoid cases in Nigeria received an initial dose of 100 mgm. of DDS per week routinely. After six weeks the dosage was increased by 100 mgm. Thereafter the weekly dosage was increased by 100 mgm. every four weeks, until a maximum dosage of 400 mgm. weekly was reached. In some of the cases this maximum dosage was raised to 600 mgm. weekly.

The treatment of lepromatous cases was more conservative. An initial dose of 50 mgm. was given for six weeks, followed by an increase of 100 mgm. per week every six weeks until a maximum dose of 400 mgm. was reached, or in some of the cases until 600 mgm. was given.

At present all cases are treated according to the latter scheme, and

the maximum dose seldom exceeds 400 mgm. It was felt that typical tuberculoid cases do not need a more rapid increase in dosage than lepromatous cases, and in view of the high incidence of low-resistant tuberculoid cases the most conservative regimen is to be preferred.

The incidence of reactions in low-resistant tuberculoid cases has decreased after introduction of this regimen. The incidence is still too high, however, and probably an even more conservative treatment program is indicated.

In a number of cases receiving only 50 mgm. of DDS during the first half year of treatment, i.e., the most critical period, the incidence of reactions was lower again.

In our opinion low-resistant tuberculoid cases in reaction, or with thickened, tender nerves, should not receive antileprosy treatment before the reaction has subsided. Such cases should receive steroids. After the reaction has subsided, a very low dose of an antileprosy drug should be given under coverage of steroids for one to two months. The dosage should not exceed 50 mgm. DDS. Thereafter the steroids can be withdrawn, but the patient should be kept on 50 mgm. DDS for some months. After about three months the dosage is increased to 100 mgm. weekly. After another three months 200 mgm. may be tolerated. There appears to be no reason to increase further in the first year of treatment. Treatment with DPT (Ciba 1906) is to be preferred to sulfone treatment, at least in the first half year.

The reactions usually do not respond well to antimony compounds or other drugs used against reactions. Although steroid treatment in leprosy has disadvantages, it is felt that it is the only drug known that may prevent deformities in low-resistant tuberculoid leprosy. The dosage should be high enough to suppress reactions in the nerves rapidly, and the administration should be continued sufficiently long. The maintenance dosage needed usually does not exceed the equivalent of 100-150 mgm. of cortisone.

It is not practical to administer steroids locally, along or within nerve sheaths, because the number of nerves affected is too large, and they are involved over a great length. Surgical decompression of nerves is not advocated as a routine measure for the same reason. Although it may relieve pain, the infiltration in the nerves is so diffuse that extensive surgery is needed for complete decompression. The risk of damaging nerve fibers becomes great.

Generally speaking, all low-resistant tuberculoid cases that are still active should be admitted temporarily to leprosy settlements or specialized hospitals. In mass treatment campaigns effort should be made to admit patients before nerves are seriously affected or reactions appear. After 4-6 months most patients can be further treated in outpatient treatment centers again. Once the nerves are seriously affected, it is difficult, even with great care, to prevent the development of deformities.

Usually attention is focused on lepromatous leprosy. Low-resistant tuberculoid leprosy is regarded as more important from the socio-economic point of view and deserves equal if not more attention.

DISCUSSION

In "Leprosy in Theory and Practice," by Cochrane and Davey (1) use of the designation low-resistant tuberculoid leprosy instead of reactional tuberculoid is advocated. Much can be said for another designation for reactional tuberculoid disease. It is often confused with tuberculoid in reaction. However, for most leprologists the designation reactional tuberculoid means cases with a sudden outbreak of major tuberculoid or at least markedly infiltrated lesions, often "lying as tablets on the skin." After repeated "reactions" a development toward borderline-lepromatous may be seen. The cases described in this article never show markedly infiltrated lesions, and deterioration toward borderline-lepromatous disease has not been seen.

It seems possible, however, to include the reactional tuberculoid cases in the low-resistant tuberculoid group, and to divide the group into (1) cases with flat, maculoid and slightly raised lesions, as described in this article and (2) cases with markedly infiltrated lesions, usually called reactional tuberculoid. Paralleling the division of mild tuberculoid leprosy into a minor and a major variety, the low-resistant group could also be divided into a low-resistant major tuberculoid and a low-resistant minor tuberculoid variety.

The difficulty is, however, that in contrast to reactional tuberculoid leprosy the low-resistant minor tuberculoid variety seldom if ever deteriorates toward borderline-lepromatous disease. I have often wondered if the explanation is not to be sought in our failure to recognize less conspicuous clinical differences between the large proportion of reactional tuberculoid cases that heal spontaneously (although often with serious deformity) and the smaller number of cases that deteriorate. I have noted deterioration frequently in those major tuberculoid cases that show only a weak response to lepromin and are somewhat less well defined, sometimes showing a slightly pale halo around the lesion. I have not seen the development of borderline-lepromatous disease in any typical reactional tuberculoid cases with a frankly positive (2+) lepromin reaction. I am inclined to believe that the former cases have been borderline already in the early, "major tuberculoid" stage.

Indian authors have often mentioned that a small proportion of maculo-anesthetic cases present multiple lesions and that these cases may show serious multiple nerve involvement. In conformity with suggestions made above such cases could be classified as low-resistant macular tuberculoid leprosy. I am fully aware of the objection that the histologic structure of maculo-anesthetic cases is not typically tuberculoid. However, in the active stage, small epithelioid tuberculoid foci are usually found. Probably they would always be found in serial sec-

tions. The fact that these minute tuberculoid structures are not clinically visible, as in minor and major tuberculoid disease, seems to me of lesser importance than the fact that the simple maculo-anesthetic cases do fit in, immunologically (lepromin reaction) and bacteriologically (negative smears), as well as prognostically (spontaneous healing) in the same part of the spectrum of leprosy as the benign minor and major tuberculoid cases. Similarly the maculo-anesthetic cases with multiple lesions fit in the same place in the spectrum as the low-resistant tuberculoid cases. This seems to be of greater importance than the terminology.

"Tuberculoid" may not be a satisfactory designation, just as use of the designation "macular" for lesions that are not completely flat, is not satisfactory. I fear, however, that a complete change of terminology would cause so much confusion that the average field worker would prefer to leave classification to those who are convinced that a classification of leprosy cannot be restricted simply to two or at most three groups.

SUMMARY

Low-resistant tuberculoid leprosy is a variety of tuberculoid leprosy on the borderline side, which differs from typical tuberculoid leprosy in its lesser degree of hypopigmentation, the absence of a papular margin (there may be a very broad micropapular edge), the absence of central healing in many lesions, the presence of symmetric lesions on the extremities, a tendency to symmetry on the trunk, and symmetric nerve involvement of all larger nerves. The lepromin reaction is not strongly positive. Bacilli are found more often than in typical tuberculoid cases. Histologically the epithelioid tuberculoid foci are relatively small, and widely disseminated in the dermis, and often there is some indication of an interrupted free subepidermal zone. Nerves are less rapidly destroyed. Loss of perspiration and loss of hairs are less marked and appear later than in typical tuberculoid cases.

The recognition of low-resistant tuberculoid leprosy is important because special precautions must be taken in the treatment. Even moderate dosage of sulfones may precipitate reactions that often cripple the patient. A very conservative dosage scheme is advocated, and in case of nerve reactions steroids are the drugs of choice. Many patients can best be cared for in settlements in the first half year of treatment, which is the most critical period of treatment.

From the socio-economic point of view low-resistant tuberculoid leprosy is as important as lepromatous leprosy, if not more so.

RESUMEN

La lepra tuberculoide de baja resistencia es una variedad de lepra tuberculoide en la zona límite, la que difiere de la típica lepra tuberculoide en el menor grado de hipopigmentación, la ausencia de un margen papular (puede haber un borde ancho micropapular),

la ausencia de cicatrización central en muchas lesiones, la presencia de lesiones simétricas en las extremidades, una tendencia a la simetría en el tronco, y el envolvimiento nervioso simétrico de todos los grandes nervios. La reacción de la lepromina no es fuertemente positiva. Los bacilos se encuentran mas a menudo que en los casos tuberculoides típicos. Histológicamente los focos tuberculoides epitelioides son relativamente pequeños y ampliamente diseminados en el dermis, y frecuentemente hay alguna indicación de una zona subepidermica libre interrupta. Los nervios estan menos rápidamente destruídos. Pérdida de la perspiración y pérdida de cabellos están menos marcadas y aparecen mas tardíamente que en los casos tuberculoides tipicos.

El reconocimiento de la lepra tuberculoide de baja resistencia es importante porque deben ser tomadas precauciones especiales en su tratamiento. Aún moderadas dosis de sulfonas pueden precipitar reacciones que frecuentemente invalidan al enfermo. Se preconiza un esquema muy conservador en dosis, y en el caso de reacciones nerviosas, los esteroides son las drogas de elección. Muchos pacientes pueden ser tratados en establecimientos en la primera mitad del año de tratamiento, el cual es período mas crítico de su tratamiento.

Desde el punto de vista socio-económico la lepra tuberculoide de baja resistencia es tan importante como la lepra lepromatosa, si no lo es mas.

RÉSUMÉ

La lèpre tuberculoïde à résistance faible est une variété de lèpre tuberculoïde proche du "border-line," qui se distingue de la lèpre tuberculoïde typique par son moindre degré de pigmentation, l'absence de bords papuleux (il peut y avoir un très large bord micropapuleux), l'absence de guérison central dans beaucoup de lésions, la présence de lésions symétriques sur les extrémités, une tendance à la symétrie sur le tronc, et une atteinte nerveuse symétrique de tous les nerfs les plus gros. La réaction á la lépromine n'est pas fortement positive. On trouve plus souvent des bacilles que dans les cas tuberculoïdes typiques. Histologiquement les foyers épithélioides tuberculoïdes sont relativement petits et largement disséminés dans le derme; souvent il n'y a pas de trace d'une zone sous-épidermique fragmentée. Les nerfs sont moins rapidement détruits. La perte de la transpiration et la perte des poils sont moins marquées et apparaissent plus tardivement que dans les cas tuberculoïdes typiques.

Il est important de reconnaître la lèpre tuberculoïde à résistance faible car des précautions spéciales doivent être prises quant au traitement. Des doses même modérées de sulfones peuvent entraîner des réactions qui souvent rendent le malade invalide. Une posologie très basse est recommandée, et lors des réactions touchant les nerfs les stéroïdes constituent la médication de choix. Durant les six premiers mois de traitement, qui représentent la période la plus critique pour la thérapeutique, c'est dans des institutions spéciales que les malades peuvent être le mieux surveillés.

D'un point de vue socio-économique, la lèpre tuberculoïde à résistance faible est aussi importante que la lèpre lépromateuse, sinon davantage.

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