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Serum Transaminase Activity in Leprosy in Relation to Skeletal Muscle Damage[1]

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Serum transaminases SGO-T and SGP-T are concentrated mainly in heart muscle and liver, but are found also in skeletal muscle, pancreas, kidney, and brain. Skeletal muscle is a rich source of transaminases, especially SGO-T. The transaminases, particularly SGO-T, are frequently raised in accident victims with widespread injury to skeletal muscle. There is a definite relationship between the amount of muscle damage and the serum enzyme level (7). SGO-T is elevated also in various neuromuscular disorders (5).

Skeletal muscle involvement in the form of atrophy with replacement fibrosis and granuloma formation is commonly found in leprosy. As skeletal muscle is a rich source of serum transaminase, especially SGO-T, it would be interesting to determine its levels in different types of leprosy and to correlate these levels with histologic changes observed in muscle.

Work now underway deals with the evaluation of transaminases SGO-T and SGP-T in all types of leprosy and correlation of their concentration with histologic changes in skeletal muscle.

MATERIALS AND METHODS

The cases for the study here reported were selected from the leprosy ward attached to the Medical College Hospital in Nagpur. The patients studied were admitted during the period August 1962 to August 1963. All were well established cases of leprosy with at least one to two years of clinical history. They were admitted either for lepra reaction or for surgical procedures in the treatment of trophic ulcers and gangrene.

A total of 51 cases were studied during this period. All of them were subjected to the following investigations:

1. Skin clipping for acid-fast bacilli and skin biopsy to determine the type of leprosy histologically (4).

2. Muscle pieces obtained by biopsy. These were fixed in 10 per cent formalin and sections from them were stained routinely with hematoxylin and eosin and with Fite-Faraco stain for acid-fast bacilli (4). The biopsy specimens were obtained from: (a) sites of gross muscular wasting, if present, and (b) calf muscle in the absence of muscular wasting.

3. Liver biopsy. Sections were stained routinely with hematoxylin and eosin and with Fite-Faraco stain for acid-fast bacilli (4).

4. SGO-T and SGP-T determinations were made by the Mohun and Cook method (8).

After through clinical study and histopathologic examination of a skin piece in every case, cases were grouped as (a) lepromatous, (b) tuberculoid, or (c) indeterminate.

The criteria followed for clinical and histopathologic differentiation were those set forth by Cochrane (1).

OBSERVATIONS

Histologic changes noted in 43 successful muscle biopsies in the present study are discussed below. Of the 43, 30 were from lepromatous, 9 from tuberculoid and 4 from indeterminate type cases. Twenty-two cases (12 lepromatous, 6 tuberculoid, and 4 indeterminate) showed atrophy of muscle fibers with fibrosis ranging from focal areas to extreme hyalinization. All these cases failed to show acid-fast bacilli by the Fite-Faraco method.

Six cases (all lepromatous) showed marked degenerative changes in muscle

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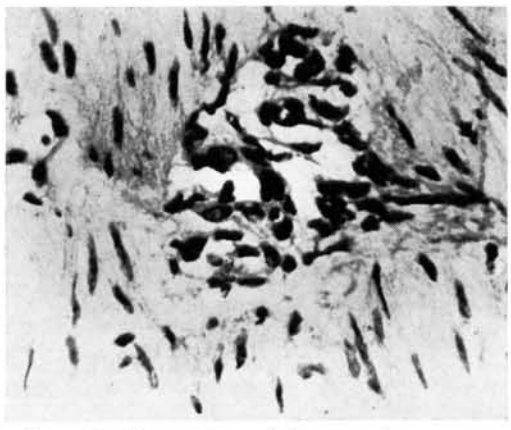

FIG. 1. Formation of lepromatous granuloma consisting of vacuolated Virchow cells between atrophic and fibrosed muscle bundles.

fibers. The muscle bundles showed shrinkage in size, fragmentation, and fatty infiltration between muscle fibers. The muscle fibers also exhibited loss of transverse striations, and some showed vacuolar degeneration. Inflammatory exudate consisting of lymphocytes and histiocytes was present between atrophied muscle fibers. In a large proportion of cases the exudate was localized around blood vessels and near the intermuscular septa. Leprosy bacilli were not detected in any of these cases.

Fifteen cases (12 lepromatous, 3 tuberculoid) showed the formation of distinct granulomas between the atrophied muscle fibers (Fig. 1). They were made up of collections of vacuolated Virchow cells surrounded by histiocytes and fibrous tissue. Most of them were formed near the blood vessels; 10 of these cases were positive for leprosy bacilli. The muscle fibers surrounding these granulomas showed all the degenerative changes described above. Bacilli were found chiefly in bundles in vacuolated Virchow cells in the form of globi (Fig. 2). In many cases they were reduced to the form of a granular mass. Single and intact bacilli were seen between the muscle fibers around the granulomas.

The relation between serum transaminase activity and various histologic changes in muscles is summarized in Table 1.

DISCUSSION

Until recently it was supposed that skeletal muscle involvement in leprosy was due to primary nerve affection. In older literature Jeanselme *et al.* ([7]) pointed out that leprotic processes can invade and destroy muscle fibers. They observed leprosy bacilli in the granular state between atrophied muscle fibers.

Ishihara ([6]), in a study of calf muscle changes in four cases of lepromatous leprosy, found various degrees of atrophy of muscle fibers, cellular infiltration, and leprosy granulomas in all four cases.

Convit *et al.* ([2]) studied muscle changes in four cases of lepromatous leprosy and found definite lepromatous granulomas in all of them. Leprosy bacilli were detected in each case.

In our study of 43 muscle biopsies granulomatous changes characteristic of leprosy were found in 15 cases, showing that primary muscle involvement is common in leprosy, especially of lepromatous type. This compares closely with the findings of other authors. The granulomatous changes were found in 12 lepromatous and three tuberculoid cases. In the lepromatous type the granulomas consisted of collections of vacuolated Virchow cells, while in the tuberculoid type they were made up of focal collections of lymphocytes and histiocytic and epithelioid cells. Definite giant cells were not detected. Ten of the cases were positive for leprosy bacilli. Degenerative

FIG. 2. Leprosy bacilli inside a Virchow cell between muscle fibers (Fite-Faraco stain).

TABLE 1. *Relation between serum transaminase activity and various histologic changes in muscle.*

Diagnosis of leprosy	Histol. changes	No. cases	No. + AFB	No. showing increased transaminase activity	SGO-T (Cabaud U.), Av. (of cases showing increased transaminase activity)	SGP-T (Cabaud U.) Av. (of cases showing increased transaminase activity)	No. showing normal liver
Lepromatous	Fibrosis	12	0	8	20	61.3	0
	Fibrosis & inflammation	0	0	4	21	62.7	0
	Granuloma	12	9	10	41	61.0	1
Tuberculoid	Fibrosis	6	0	0	—	—	0
	Granuloma	3	1	2	43	34.0	0
Indeterminate	Fibrosis	4	0	0	—	—	—

changes and fibrosis was seen in 22 cases. The degeneration was probably due to primary nerve involvement; it was observed commonly in tuberculoid and in all the indeterminate cases. None of these cases was positive for leprosy bacilli. Fibrosis, degenerative changes, and focal cellular infiltrate were observed in six cases, all lepromatous, but none was positive for leprosy bacilli.

Skeletal muscle is a rich source of serum transaminase, especially SGO-T, ranking next to heart and liver tissue. Extensive damage to skeletal muscle results in elevation of serum transaminase activity. Fleisher *et al.* ([5]) have observed marked elevation in serum transaminase levels in the majority of patients with progressive muscular atrophy (Erb's disease). The enzyme levels tend to be higher in early, active dystrophy in childhood (especially with pseudohypertrophy), whereas levels are often lower or in the normal range in the more slowly progressive adult variety or in far advanced childhood forms in which there is a great deal of muscular wasting ([10, 13]).

Elevated levels may be found also in active cases of polymyositis or in other situations in which considerable muscle necrosis occurs, e.g., myoglobinuria, and extensive muscle trauma. Normal levels are present in muscular atrophy of nervous origin, even though the muscle wasting is proceeding rapidly, and in myasthenia gravis and peroneal muscular atrophy ([3,10]).

In considering the finding noted above it was of interest to review serum transaminase activity in the light of histologic changes in muscle. The liver also is commonly involved in leprosy, and a rich source of serum transaminase. Hence it is essential to study the histology of liver in each of these cases in order to compare the effects of liver and muscle damage on transaminase activity. Hence a liver biopsy was made in every case. The detail findings of these cases are discussed elsewhere ([13]).

Ramanathan *et al.* ([11]) have estimated serum transaminase levels in patients with lepromatous leprosy and found high SGO-T levels, but have not commented on this rise in the absence of study of hepatic involve-

ment and skeletal muscle changes, and postulate that this rise may be due to extensive involvement of bones of the extremities. The histologic changes we have found in muscle and serum transaminease levels are summarized in Table 1.

When all types of leprosy are considered together, it can be seen that out of 28 cases showing fibrosis, fatty infiltration, and focal inflammatory exudate, 12 showed increased SGP-T activity. The average values for SGO-T and SGP-T in these cases were 20.5 and 62 units respectively. But it must be noted that in all these cases, there were distinct histologic changes in the liver, ranging from periportal fibrosis to distinct granuloma formation and cirrhosis. Thus it can be observed that the SGP-T rise was due mainly to liver involvement, as liver is a richer source of SGP-T than skeletal muscle.

Among 15 cases in which muscle biopsies showed distinct granuloma formation and destruction of muscle fibers, 12 showed increased transaminase activity. The mean values of SGO-T and SGP-T in these cases were 42 and 47.5 units respectively. Almost all of these cases also showed liver involvement in the form of miliary lepromas and cirrhotic change; one only showed normal histology. Thus it can be seen from the observations noted above that in cases of muscle showing active granuloma formation and destruction of muscle fibers there has been a relative increase in the mean SGO-T value as compared with cases showing fibrosis and focal inflammatory exudate. As skeletal muscle is a richer source of SGO-T than SGP-T, the increased SGO-T value observed in cases of granulomatous muscle involvement may be attributed to muscle necrosis. Thus it can be said that both hepatic and skeletal muscle damage may play a part in elevation of transaminase activity.

SUMMARY

Histologic changes in skeletal muscle obtained from 43 cases of different types of leprosy are discussed and correlated with serum transaminase levels. It was noted that the granulomatous involvement and the muscular wasting observed do not have an appreciable effect on serum transaminase levels although they may have some effect on elevation of SGO-T.

Increased transaminase activity in most of the cases was predominantly due to liver involvement.

RESUMEN

Cambios histológicos en músculos esqueléticos obtenidos de 43 enfermos de diferentes tipos de lepra se discuten y se correlacionan con los niveles de transaminasa en el suero. Se notó que el compromiso granulomatoso y el daño muscular observado no tiene un efecto apreciable en los niveles de transaminasa en el suero, aunque ellos puedan tener algún efecto en la elevación de SGO-T.

El aumento de la actividad de la transaminasa en muchos de los casos se debió predominantemente al compromiso del hígado.

RÉSUMÉ

On discute des modifications histologiques observées dans les muscles squelettiques obtenus chez 43 malades atteints de différents types de lèpre; ces modifications sont mises en relation avec les niveaux de transaminase sérique. On a noté que l'atteinte granulomateuse et la déperdition musculaire qui ont été observées n'ont pas d'effets appréciables sur les niveaux de la transaminase du sérum, encore qu'un certain effet pùisse être noté sur l'élévation de la SGO-T.

L'augmentation de l'activité de la transaminase dans la plupart des cas était surtout due à l'atteinte hépatique.

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