

Serum Proteins and Immunoglobulins in Leprosy¹

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Seibert and Nelson (19) observed that in advanced cases of leprosy total serum proteins were higher than normal, albumin decreased and the alpha and gamma globulin fractions were markedly raised. Similar observations were made by other workers (4, 6, 11, 14, 17, 20).

Bergot *et al* (1) first observed that the increase in globulin concentration in leprosy was due to a simultaneous increase of IgM (β_2M) and gamma globulins in lepromatous and indeterminate leprosy. In the tuberculoid form the reaction was more heterogeneous. Lim and Fusaro (12) observed an elevation of IgA (β_2A) and IgM (β_2M) in the lepromatous type but not in tuberculoid leprosy. Sheagren *et al* (2) noted increased levels of IgG and IgA in lepromatous leprosy while IgM levels were normal in all groups. Similar observations were made by Jha *et al* (10).

In the present work, the changes in serum proteins and immunoglobulins in different types of leprosy have been studied.

MATERIALS AND METHODS

Two hundred patients from inpatient and outpatient departments of the Leprosy Mission Hospital, Naini, Allahabad (U.P.), India suffering from various clinical forms of leprosy were studied. The patients were classified according to the criterion of Ridley and Jopling in 1962. All cases were subjected to clinical examination, bacteriologic examination of skin and nasal mucosa, lep-

romin test and skin biopsy. Only three dimorphous (BB) cases were encountered and all had varied results, hence, these were excluded from the present study. Only cases of tuberculoid (TT), lepromatous (LL), borderline tuberculoid (BT), and borderline lepromatous (BL) leprosy were included in this study. Of these, 85 were suffering from TT, 75 from LL, and 20 each from BT and BL leprosy. All of the subjects were male. Only those patients whose hemoglobin was more than 10 gm% were included in the study. Blood samples for analysis were taken from fasting patients. Urine examinations were done in all patients to detect any renal disease. Cases having albuminuria were not included in this study. Stool examination was done in all cases to exclude the possibility of any parasitic infestation.

Total serum protein was estimated by the biuret method (24). Paper electrophoresis of the serum protein was carried out on a horizontal electrophoresis apparatus using veronal buffer, pH 8.6, ionic strength 0.05, at 150 volts for eight to ten hours. The scanning of the strips was done with a Photovolt electronic densitometer.

The quantitative estimation of different immunoglobulins could be done in only 60 leprosy patients; 20 each of TT and LL, and 10 each of BT and BL types. The estimation was done by the single radial diffusion technique (8) using monospecific antisera from Behringwerke (West Germany) and WHO reference serum No. 67/97 as controls. The concentration of IgG, IgM and IgA in the reference serum was 10 mg, 0.8 mg and 2.25 mg per ml, respectively.

RESULTS

The total serum protein and its different fractions in healthy individuals and in different types of leprosy are given in Table 1. Total serum proteins were found to be elevated in all forms of leprosy. The increase varied according to the severity of the disease. The cases who had either longer dura-

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TABLE 1. Mean values (gm%) of total serum protein and its different fractions in normal healthy individuals and in different types of leprosy.

No. of cases	Total protein	Albumin	Globulins			
			Alpha-1	Alpha-2	Beta	Gamma
Normal (25)	8.15	4.26	0.34	0.57	0.89	2.10
S.D.	0.45	0.36	0.10	0.15	0.10	0.45
Tuberculoid (85)	8.62	3.89	0.30	0.58	0.94	2.91
S.D.	0.95	0.27	0.10	0.10	0.20	0.23
p value	<0.01	<0.001	>0.05	>0.05	>0.05	<0.001
Borderline-tuberculoid (20)	8.34	3.97	0.29	0.38	1.12	2.58
S.D.	0.62	0.35	0.10	0.10	0.10	0.20
p value	>0.05	>0.05	>0.05	<0.001	<0.001	<0.001
Borderline-lepromatous (20)	8.70	3.55	0.30	0.56	0.76	3.53
S.D.	0.94	0.20	0.10	0.10	0.10	0.83
p value	<0.01	<0.001	>0.05	>0.05	<0.01	<0.001
Lepromatous (75)	8.90	3.25	0.36	0.75	0.82	3.72
S.D.	0.95	0.40	0.10	0.10	0.15	0.50
p value	<0.001	<0.001	>0.05	<0.001	>0.05	<0.001

TABLE 2. Mean value (mg%) of different immunoglobulins in normal healthy individuals and in different types of leprosy.

Immuno-globulin	Leprosy type	No. of cases	Mean value	\pm	Range	p value
IgM	Control		1675.5		344.80	
	TT	20	1584.0		315.57	>0.05
	BT	10	1660.0		305.29	>0.05
	BL	10	2026.0		504.39	<0.01
	LL	20	2598.0		364.22	<0.001
IgG	Control		149.50		55.45	
	TT	20	245.00		68.38	<0.001
	BT	10	215.00		45.00	<0.001
	BL	10	210.50		48.30	<0.01
	LL	20	297.25		90.29	<0.001
IgA	Control		278.40		86.20	
	TT	20	295.00		96.88	>0.05
	BT	10	250.00		35.00	>0.05
	BL	10	283.00		86.15	>0.05
	LL	20	393.00		86.50	<0.001

tion of illness or in whom the extent of lesions were more extensive, showed greater alteration of serum proteins and immunoglobulins. The authors agree, however, that there is no separate data to support this. The elevation was not significant in BT ($p > 0.05$), significant in TT and BL ($p < 0.01$),

and highly significant ($p < 0.001$) in LL. Albumin was significantly decreased in the BL, LL and TT types ($p < 0.001$), but the decrease in BT was not significant.

Alpha-1-globulin showed no significant alteration in any form of leprosy. Alpha-2-globulin was found to be decreased in BT

and increased in LL; the change was highly significant ($p < 0.001$). In TT and BL the alterations were not significant. Beta-globulin did not show any significant deviation from the normal in TT and LL, whereas the decrease in BL and an increase in BT types were significant. Gamma globulin was found to be significantly increased in all types of leprosy ($p < 0.001$).

In TT the alteration of IgG and IgA was statistically not significant (Table 2). The elevation of IgM was highly significant ($p < 0.001$). In LL the rise in all three immunoglobulins, IgG, IgM and IgA, was highly significant ($p < 0.001$). The cases of BT showed a highly significant increase of IgM alone, whereas in BL both IgM and IgG were found to be increased (Table 2).

DISCUSSION

Tuberculoid leprosy. Eighty-five cases of tuberculoid leprosy were studied. Total serum protein was found to be significantly increased. Electrophoretic studies showed a highly significant decrease of albumin and an increase in the globulin fraction. No significant alteration was observed in alpha-1, alpha-2 and beta globulins. The increase in total serum protein in these cases was primarily due to an increase in serum gamma globulin. Similar results were obtained by others (5, 11, 17, 20).

Muelling *et al* (15) studied the sera from patients with active and inactive tuberculoid lesions and noted slightly increased levels of total proteins. In their studies albumin was normal, beta globulin was more elevated than gamma globulin and elevation of alpha globulin was rarely observed. Other workers did not find any dysproteinemia in the tuberculoid type of leprosy (2, 3, 9).

Dhople and Magar (7) observed a decrease in alpha globulin and an increase in beta globulin in nonlepromatous leprosy. No variation in total protein and gamma globulin levels was noted since the results were expressed in relative percentage of different fractions of serum proteins and not the absolute values. In the present series, the decreased value in relative percentage of alpha-1-globulin in tuberculoid cases is in conformity with the observations of these workers. No significant alteration in the relative percentage of beta globulin was observed. There was no alteration in the absolute amount of alpha-1-globulin. The

observations of the present study vary from those of Thomas and Anantchari (22) who studied serum proteins in 15 cases of tuberculoid leprosy and noted a slight increase in the beta globulin fraction only.

Immunologic studies in tuberculoid leprosy were carried out in 20 cases. There was a significant elevation of IgM, IgG and IgA were found to be within normal limits. Lim and Fusaro (13) reported an increase in both IgA and IgM in tuberculoid leprosy. Saha *et al* (18) found an increase of IgG and IgA whereas IgM was found to be normal.

Lepromatous leprosy. Seventy-five cases were studied. Total serum protein in these cases varied from 7.4 to 11.5 gm% with a mean of 8.9 gm%. The mean values of albumin and alpha-1, alpha-2, beta and gamma globulins were 3.25, 0.36, 0.75, 0.82 and 3.72 gm%, respectively. The increase in total serum proteins, alpha-2 and gamma globulins and decrease in albumin fraction were highly significant. The alpha-1 and beta globulins were found to be either within normal limits or insignificantly decreased. Jardin and Beytont (9) attributed the increase of the gamma fraction in leprosy patients to a decrease of other fractions such as albumin and alpha and beta globulins. They suggested that the other changes in serum protein pattern sometimes found in leprosy patients (alpha and beta globulins, gluco- and lipoproteins) were not attributable to leprosy itself but were due to secondary and concomitant affections like tuberculosis, nephritis or nephrosis and, in particular, to amyloidosis.

In lepromatous cases, all three immunoglobulins (IgG, IgM and IgA) were found to be significantly raised. Similar values have been observed by others (10, 13, 18, 21). Lim and Fusaro (12) reported a consistent increase in the IgA level in all types of leprosy, greatest in tuberculoid and least in lepromatous. Nath *et al* (16) observed a twofold increase of B cells in the circulation in lepromatous leprosy patients. These cells are the precursors of antibody producing cells and are responsible for the increased immunoglobulin levels in lepromatous leprosy. This increase of B cells in lepromatous leprosy was reflected in the lymph nodes as evidenced by fluorescent antibody technic (23). Lymphocytes bearing Ig fluorescence were found to be 42.3% of total lymphocytes in lepromatous leprosy whereas their proportion in normal nodes was 23.4%.

Borderline tuberculoid and borderline lepromatous leprosy. No report of separate studies on serum proteins in BT and BL types of leprosy are available because most workers have classified their cases only in two broad groups, i.e., lepromatous and non-lepromatous types. In the nonlepromatous type they have included both the tuberculoid and borderline forms of leprosy. In the present series, ten cases each of BT and BL were studied. In BT cases there was a significant increase of beta and gamma globulins whereas alpha-2-globulin was significantly decreased. Total serum protein, albumin and alpha-1-globulin were found to be within normal limits. In contrast, in BL cases there was a significant increase of total serum protein and gamma globulin whereas albumin and beta globulin showed a significant decrease. No change in alpha-1 and alpha-2 globulins was seen in BL cases. Immunoglobulin studies showed a highly significant rise of IgM alone in cases of BT, while in BL cases both IgM and IgG were found to be significantly increased. The rise in IgG levels in LL and BL was found to be consistent with the findings of others (10, 13, 21).

The alteration in the total serum protein and its different fractions in different clinical forms of leprosy does not seem to be of diagnostic importance. The significant increase of different immunoglobulins in leprosy, especially in the lepromatous type, suggests a humoral response which is directly proportional to the severity of the lesion.

SUMMARY

Serum proteins and immunoglobulins were studied in patients suffering from various types of leprosy. A significant increase in total protein and decrease in albumin was found in all types of leprosy except borderline-tuberculoid. Gamma globulin was found to be increased in all types. An increase of alpha-2-globulin in lepromatous, a decrease of beta globulin in borderline-lepromatous, and a decrease of alpha-2 and increase of beta globulin in borderline-tuberculoid were observed. These changes do not seem to be of diagnostic importance.

A statistically significant increase of IgG in borderline-lepromatous and lepromatous, IgM in all types of leprosy and IgA only in lepromatous was found. The increase of different immunoglobulins in leprosy, especially the lepromatous type, suggests a hu-

moral response which was found to be directly proportional to the severity of the lesion.

RESUMEN

Se estudiaron los niveles de las proteínas séricas y de las inmunoglobulinas en pacientes con lepra de diversos tipos. En todos los tipos de lepra, excepto en el cercano al tuberculoide (borderline-tuberculoide), se encontró un aumento significativo en las proteínas totales y una disminución en la albúmina. En todos los tipos de lepra hubo hipergammaglobulinemia. Se observó un aumento de las alfa-2-globulinas en los lepromatosos, una disminución de las beta-globulinas en los cercanos al extremo lepromatoso (borderline-lepromatosos) y una disminución de las alfa-2 con aumento de las beta-globulinas en los borderline-tuberculoideos. Estos cambios no parecen ser de importancia diagnóstica.

Se encontró un aumento, estadísticamente significativo, de la IgG en los borderline-lepromatosos y en los lepromatosos, de IgM en todos los tipos de lepra y de IgA sólo en los lepromatosos. El aumento de las diferentes inmunoglobulinas en lepra, especialmente en el tipo lepromatoso, sugiere una respuesta humoral que es directamente proporcional a la severidad de la enfermedad.

RÉSUMÉ

Chez des malades souffrant de divers types de lèpre, on a étudié les protéines du sérum et les immunoglobulines. On a observé une augmentation significative des protéines totales et une diminution de l'albumine, dans tous les types de lèpre, excepté la forme borderline-tuberculoide. Dans tous les types, on a relevé une augmentation des gamma globulines. On a également observé une augmentation de l'alpha-2-globuline dans la lèpre lépromateuse, une diminution des beta globulines dans la lèpre borderline-lépromateuse, et une diminution de l'alpha-2 et une augmentation des beta-globulines dans la lèpre borderline-tuberculoide. Ces modifications ne paraissent pas avoir d'importance diagnostique.

Une augmentation statistiquement significative des IgG dans la lèpre borderline-lépromateuse et dans la lèpre lépromateuse, de même qu'une augmentation des IgM dans tous les types de lèpre et des IgA dans la lèpre lépromateuse uniquement, ont été observées. L'accroissement des différentes immunoglobulines dans la lèpre, spécialement dans la lèpre lépromateuse, suggère qu'il existe une réponse humorale directement proportionnelle à la gravité des lésions.

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