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Immunoglobulins in Leprosy [1]

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Dysproteinemia associated with hypergammaglobulinemia ([4]) and persistent variable increases in IgG and IgM levels in lepromatous leprosy ([14]) remain intriguing problems in pathogenesis. The present study was undertaken to evaluate serum levels of immunoglobulins G, A and M in different clinicohistopathologic groups of leprosy patients belonging to Eastern Uttar Pradesh, a poor and backward region of India.

MATERIALS AND METHODS

Sera of 81 adult male leprosy patients, 32 of whom were suffering from tuberculoid leprosy (TT), 28 from lepromatous leprosy (LL), and 21 borderline cases (belonging to both BT and BL subgroups) were studied. Sera of 50 normal healthy adult males belonging to a similar low socioeconomic class served as controls ([6]). The patients were residents of the districts of Allahabad or Varanasi. Ridley and Jopling's classification ([10]) was followed.

Total serum protein (TP) was estimated by the biuret method ([16]) while paper electrophoretic patterns of serum proteins were studied by transmitted light densitometry ([12]). Immunoglobulins were quantitated by single radial diffusion technic as described previously ([3]). WHO serum No. 67/97 was used as control and monospecific anti-IgG, IgA and IgM sera were obtained from Behringe Werke, West Germany. Student's "t" test was applied for statistical analysis of the data.

RESULTS

Table 1. Total serum protein was significantly lowered in LL patients. Paper electrophoresis revealed a significant fall in albumin along with rises in beta and gamma globulins. In TT patients, though there was no significant fall in total serum proteins, albumin was relatively reduced along with an increase in beta globulins. In BB patients no variation was noted either in total proteins or their electrophoretic profile.

Table 2. Comparing immunoglobulins in leprosy patients with the controls, significantly raised IgG levels were observed in LL patients ($p < .001$) and significantly low IgA levels in the BT subgroup ($p < .001$). Serum IgM levels were uniformly raised in the TT, BT and LL subgroups ($p < .001$).

Table 3. A comparative analysis of immunoglobulins G, A and M levels in various subgroups of leprosy patients showed a significant increase in IgG level ($p < .001$) in LL patients only. Serum IgA and IgM levels were comparable in all of the groups except for the BT subgroup where significant lowering of IgA was observed ($p < .01$).

DISCUSSION

Immunoglobulins G, A and M are antibody proteins which migrate in beta and gamma regions on paper electrophoresis. Significant dysproteinemia characterized by raised beta and gammaglobulins observed in LL patients is well substantiated by the significantly raised IgM and IgG levels observed in these patients. The IgA level was also raised in LL patients, though statistically the rise was not significant. Reduction in total protein (TP) and albumin values could perhaps be attributed to the chronic destructive nature of the disease and liver involvement ([2]).

Significant and variable increases in mean IgG, IgA and IgM levels observed in LL patients in the present study is well substantiated in the literature ([7,8]) (Table 4). However, the significance of hyperimmunoglobulinemia in these patients remains a matter of conjecture since the raised immunoglobulin levels appear to have little protective role. It is interesting to note that even in *erythema nodosum leprosum* (ENL), a reactive stage characterized by the Arthus type of reaction resulting in acute vasculitis, very

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TABLE 1. *Serum protein electrophoretic pattern in leprosy.*

Groups	TP	% of Total Protein				
		Albumin	Alpha-1	Alpha-2	Beta	Gamma globulin
TT	6.7 ±0.76	41.0[a] ±0.47	6.0 ± 0.84	11.62 ± 2.44	16.0[a] ± 2.56	25.37 ± 4.71
BT & BL	6.87 ± 0.25	41.75 ± 4.57	5.5 ± 1.73	11.0 ± 2.0	16.75 ± 0.95	25.0 ± 3.39
LL	6.55[a] ± 0.8	43.80[a] ± 5.7	5.0 ± 0.8	10.66 ± 2.25	15.16[a] ± 3.18	25.33[a] ± 6.47
Control	7.13 ± 0.86	50.0 ± 6.88	5.8 ± 2.5	9.0 ± 3.9	13.2 ± 2.48	21.9 ± 4.92

[a]Significant variation compared to control (> ± 2 S.D.).

TABLE 2. *Immunoglobulins G, A and M in leprosy.*

Groups[a]	Immunoglobulins in mgm% mean ± S.D.		
	IgG	IgA	IgM
TT (24)	1667.5 ± 626.48 + 0.0585 p > 0.9	277.91 ± 128.7 + 0.003 p > 0.9	266.33 ± 110.28 + 4.801 p < 0.001
BT (9)	2008.88 ± 674.91 + 1.448 p > 0.1	182.22 ± 51.81 + 4.585 p < 0.001	316.66 ± 139.1 + 3.975 p < 0.001
BL (8)	1837.5 ± 616.21 + 0.726 p > 0.4	313.75 ± 124.31 + 0.784 p > 0.4	205.00 ± 110.32 + 1.408 p > 0.1
LL (22)	2241.81 ± 715.91 + 3.537 p < 0.001	338.63 ± 135.86 + 0.656 p > 0.5	242.5 ± 110.17 + 3.75 p < 0.001
Control (50)	1675.5 ± 344.80	278.00 ± 86.20	149.00 ± 55.45

[a]Number of patients in parentheses.

TABLE 3. *Comparative evaluation of immunoglobulins in various subgroups of leprosy.*

Group	IgG	IgA	IgM
TT vs BT	t 1.319	3.005	1.13
	p > .02	< .01	> .2
TT vs LL	t 2.884	1.55	0.631
	p < .01	> .1	> .6
TT vs BL	t 0.773	0.70	1.295
	p > .4	> .4	> .2
BT vs LL	t 0.856	3.598	1.556
	p > .4	< .01	> .1
BT vs BL	t 0.5472	2.79	1.96
	p > .6	< .02	> .05
LL vs BL	t 1.519	0.472	0.823
	p > .1	> .7	> .2

little variation in IgG level is reported ([11, 15]).

It appears that persistent increases in IgG, IgA and IgM levels observed in LL cases is caused by loss of homeostatic control of suppressor T cells controlling the immunoglobulin synthesis which are known to require macrophage collaboration for their regulatory function ([13]). It is plausible that the simple process of macrophage blockade resulting from bacterial overload is responsible for the loss of homeostatic control in LL patients. Prolonged antileprosy treatment for more than 24 months resulting in a fall in bacterial overload is reported to be associated with a fall in antibody titer ([9]).

TABLE 4. *Reported immunoglobulin G, A, and M levels in lepromatous leprosy patients.*

Reference	Type of disease	mgm% IgG	IgA	IgM
1. Gupta *et al* (present study, India)	Without ENL	2241.81 ± 715.91	338.63 ± 135.86	242.5 ± 110.17
2. Sheagren *et al* *(1969, U.S.A.)*	With ENL	1350	390	170
	Without ENL	1510	360	130
3. Bullock *et al* (1970, Taiwan) Treated for 12 months	With ENL	2370	460	130
	Without ENL	2520	470	130
4. Bullock *et al* [1] (1970, Taiwan) Treated for more than 24 months	With ENL	2860	710	110
	Without ENL	2540	350	110
5. Waters *et al* (1971, Malaysia)	With ENL	2350	500	220
	Without ENL	2380	500	280
6. Jha *et al* [5] (1971, India)	Without ENL	1435 ± 50	276 ± 5.0	123 ± 3.0

SUMMARY

Serum immunoglobulins IgG, IgA and IgM were estimated in 22 lepromatous (LL) patients, 28 tuberculoid (TT), 9 borderline tuberculoid (BT), and 8 borderline lepromatous (BL), and compared with 50 normal healthy adult males belonging to a low socio-economic class. Immunoglobulin IgM was invariably significantly raised in TT, BT and LL subgroups of leprosy patients compared to the control but variation among different subgroups was statistically insignificant.

Mean serum IgA levels were also raised in TT, BL and LL subgroups but statistically the rise was not significant. In the BT subgroup, significantly low IgA levels were observed both compared to the control and the other leprosy subgroups. Immunoglobulin G levels were significantly raised only in the LL subgroups compared to the control and the other subgroups of leprosy patients.

It is proposed that persistently raised gamma globulins and immunoglobulin G, A and M levels observed in lepromatous leprosy patients could be caused by macrophage blockade hindering the suppressor T-cell mediated homeostatic control for immunoglobulins.

RESUMEN

Se midieron los niveles de las inmunoglobulinas séricas IgG, IgA e IgM, en 22 pacientes lepromatosos (LL), 28 tuberculoides (TT), 9 tuberculoides subpolares (borderline, BT) y 8 lepromatosos subpolares (borderline, BL). Los resultados se compararon con los encontrados en 50 hombres sanos de bajo nivel socioeconómico. En comparación con los controles sanos, los niveles de la IgM estuvieron invariablemente y significativamente elevados en los pacientes de los subgrupos TT, BL y LL, pero la variación entre los diferentes subgrupos fue estadísticamente insignificante. Los niveles promedio de la IgA sérica también estuvieron elevados en los subgrupos TT, BL y LL, pero la elevación no fue estadísticamente significativa. En el subgrupo BT se observaron niveles de IgA significativamente bajos en comparación con el grupo control y con los otros subgrupos de lepra.

Se propone que la persistente elevación en los niveles de las gamma-globulinas y de las inmunoglobulinas IgG, IgA e IgM, en los pacientes con lepra, podría ser causada por el bloqueo de los macrófagos, lo cual impediría el control homeostásico de las inmunoglobulinas mediado por las células T supresoras.

RÉSUMÉ

Chez 22 malades atteints de lèpra lépromа-

teuse (LL), 28 tuberculoïdes (TT), 9 tuberculoïdes borderline (BT) et 8 lépromateux borderline (BL), on a déterminé les taux d'immunoglobulines sériques IgG, IgA et IgM; les valeurs ont été alors comparées avec celles observées chez 50 sujets normaux en bonne santé, de sexe masculin, et appartenant à une classe socio-économique défavorisée. L'immunoglobuline IgM était toujours élevée de façon significative dans les groupes TT, BT et LL de malades de la lèpre, par rapport aux valeurs observées chez les témoins; néanmoins, les variations observées entre ces différents sous-groupes étaient statistiquement non significatives. Les taux moyens d'IgA sériques étaient également élevés dans les sous-groupes TT, BL et LL, mais statistiquement cette élévation n'etait pas significative. Dans le sous-groupe BT, un niveau significativement faible d'IgA a été observé tant par rapport aux témoins que par rapport aux autres sous-groupes atteints de lèpre. Les taux d'immunoglobulines G étaient significativement augmentés dans le sous-groupe LL seulement, comparés aux témoins ainsi qu'aux autres sous-groupes des malades de la lèpre.

L'explication proposée suggère que l'élévation régulière des taux de gammaglobulines et d'immunoglobulines G, A et M, observée chez les malades atteints de lèpre lépromateuse, pourrait être causée par un blocage des macrophages qui entraveraient le contrôle homéostatique des immunoglobulines effectué par les cellules suppressives T.

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