STUDY OF HISTO-FUNCTIONAL COMPLEX OF LIVER IN LEPROSY

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Summary

Seventy six cases of different types of leprosy, with varying duration of illness, were studied for their changes in liver function and hepatic lesions. Specific granulomatous lesion suggestive of lepromatous hepatitis were mainly seen in lepromatous leprosy (17 cases out of 28 cases of leprosy). Granulomata in liver were present in all types of leprosy. Some of them had progressed to stellate fibrosis (7 cases) and early cirrhotic changes (6 cases). Non-specific changes were seen in 22 cases, of which 6 (3 lepromatous) showed stellate fibrosis with attempt to incomplete lobule formation. Amyloid deposits were not seen in any of these cases.

Functional derangement has been noted mainly in lepromatous patients irrespective of the extent and duration of the disease. There was a uniform elevation of total serum protiens (6.4 9.2 gms%) mainly due to increase in serum globulin (2.2-4.0 gms%). Serum albumin was lower than normal (2.6-5.2 gms%). Thymol turbidity showed abnormal results (3-9 units) and serum cholesterol (102-206 mg%) levels were low. Other biochemical estimations were normal.

Leprosy is a chronic progressive granulomatous infection of man which in its various forms attacks mainly the superficial tissues like skin, peripheral nerves and nasal mucosa. The involvement of viscera in leprosy is well recognised and amongst the viscera, liver is the most commonly affected organ[1]. The hepatic involvement is seen in the early stage of the disease[2,3]. The most frequent lesion is the granuloma which is characteristic of the disease. Few recent reports have also described lesions mimicking cirrhosis of liver in these cases[3-5]. The studies of the functional status of liver in leprosy have revealed minimum dysfunction in tuberculoid leprosy, but marked in one test or other in lepromatous leprosy[8,10]. The present study was undertaken to assess the histo-functional complex of liver in various clinical forms of leprosy in Bundelkhand Division of Uttar Pradesh.

Material and Methods

Seventy six cases of various clinical forms of leprosy admitted to M. L. B.

Presented at the 3rd Annual Conference of Indian Association of Dermatologists, Venereologists and Leprologists, Trivandrum, January, 1975.

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Received for publication on 22—12—1975.

Medical College Hospital, Jhansi were studied. All patients were subjected to detailed clinical examination and are categorised according to various clinical types (Indian Classification)[6],[7]. Liver function tests were done by standard technique and included plasma proteins, albumin, globulin, A/G ratio, thymol turbidity, serum transaminases, alkaline phosphatase, bilirubin and cholesterol. For comparison liver function tests were estimated in 15 normal healthy individuals. Percutaneous liver biopsy was performed in 50 patients under aseptic technique with Silverman's biopsy needle. Serial sections were histologically examined staining with haematoxylin and eosin, methyl violet and congo red for amyloid. Acid fast bacilli were demonstrated by modified Zeihl Neelson's technique[8] and subsequently Fite Faraco's technique.

Observations and Results

Amongst76 patients, 37 had lepromatous, 10 dimorphous and 29 non-lepromatous types of leprosy (Table 1). Their ages varied from 10 to 81 years, the mean age being 38.4 years. Males (77.6%) predominated the series. The duration of illness varied from 21 days to 11 years with mean duration of illness of one year and 10 months.

Liver Function Tests

Alterations in liver function tests were mainly seen in lepromatous leprosy, where uniform elevation of serum proteins with lowered level of serum albumin (2.6-4.8 gms%) and raised level of serum globulin (2.6-4.0 gms%) resulted in lowering of albumin/globulin ratio (Table 2). This alteration was irrespective of the extent and duration of the disease. Abnormal results were observed in thymal turbidity with lowered level of serum cholesterol. Tests for alkaline phosphatase, serum transaminases and serum bilirubin were normal except in lepromatous leprosy. SGOT was raised in lepromatous leprosy.

TABLE 1

Age and sex distribution in various clinical forms of leprosy with duration of illness.

Clinical forms	Sex	Age groups in years					Total	Incidence
		10-20	21-30	31-40	41-50	above 50 yrs		%
1. Lepromatous leprosy	Males	2	3	12	9	3	29	38.2
	Females	1	2	4	1	—	8	10.5
2. Dimorphous leprosy	Males	—	1	4	3	—	8	10.5
	Females	—	—	—	2	—	2	2.6
3. Tuberculoid leprosy	Males	1	3	5	4	2	15	19.9
	Females	—	—	2	2	1	5	6.5
4. Polyneuritic leprosy	Males	—	1	1	1	—	3	3.9
	Females	—	—	—	—	—	—	—
5. Maculo-anesthetic leprosy	Males	—	1	2	2	—	5	6.5
	Females	—	—	1	—	—	1	1.4

Age range = 10 - 81 years.

Mean age = 38.4 years.

Duration of illness = 2 months - 11 years.

Mean duration of illness = 1 year 10 months.

TABLE 2

Liver function tests in normal healthy persons and leprosy patients

Liver function tests	Controls 15 cases	Types of leprosy patients				
		Lepromatous 37 cases	Dimorphous 10 cases	Tuberculoid 20 cases	Maculo-anaesthetic 6 cases	Polyneuritic 3 cases
1. Serum proteins (gms%)						
—range	6.6—7.8	6.8—9.2	6.4—8.3	6.4—8.0	6.6—8.0	6.8—7.9
—mean	7.4	7.9	7.6	7.2	7.4	7.4
—S.D.	+ 0.106	+ 0.088	+ 0.162	+ 0.162	+ 0.092	+ 0.480
2. Serum albumin (gms%)						
—range	4.5—6.0	2.4—6.8	3.1—5.3	4.0—5.0	3.8—4.8	4.2—4.8
—mean	4.8	3.8	4.8	4.6	4.2	4.6
—S.D.	+ 0.104	+ 0.084	+ 0.148	+ 0.136	+ 0.102	+ 0.108
3. Serum globulin (gms%)						
—range	2.1—2.8	2.6—4.0	2.2—3.2	1.8—2.9	2.2—3.8	2.6—3.8
—mean	2.3	3.8	3.0	2.4	2.8	3.2
—S.D.	+ 0.090	+ 0.086	+ 0.162	+ 0.122	+ 0.098	+ 0.86
4. Alb/Glob. ratio						
—range	1.8—3.2	1.0—1.9	1.8—3.2	1.8—3.0	1.9—3.1	2.0—3.2
—mean	2.6	1.4	2.6	2.6	2.5	2.6
—S.D.	+ 0.082	+ 0.062	+ 0.082	+ 0.082	+ 0.090	+ 0.086
5. Serum bilirubin (mg%)						
—range	0.4—1.2	0.5—1.9	1.6—2.8	1.3-2.9	1.6—2.8	1.5—2.6
—mean	0.42	0.52	0.56	0.60	0.50	0.46
—S.D.	+ 0.044	+ 0.028	+ 0.068	+ 0.092	+ 0.090	+ 0.064
6. Thymol turbidity (units)						
—range	2—5	4—9	3—8	3—7	5—8	3—7
—mean	4	6.8	5.8	4.6	6.8	4.3
—S.D.	+ 0.102	+ 0.086	+ 0.098	+ 0.092	+ 0.092	+ 0.068
7. Alkaline phosphatase (K.A. units)						
—range	5.6—14.2	5.8-18.0	5.2-16.0	6.0-18.0	6.0-15.0	7.0-15.0
—mean	8.8	10.8	12.4	14.2	11.6	10.8
—S.D.	+ 0.126	+ 0.868	+ 0.098	+ 0.462	+ 0.182	+ 0.142
8. Serum cholesterol (mg%)						
—range	116—2.18	102-208	108—205	110—206	104—200	106-210
—mean	160	148	154	152	158	168
—S.D.	+ 20.62	+06.86	+18.62	+16.25	+14.92	+15.86
9. S.G.O.T. (units/ml)						
—range	20—40	32—68	20—56	26—46	22—48	32—42
—mean	35.6	52.0	36.8	38.4	40—8	36.4
—S.D.	+ 3.24	+ 3.18	+ 4.20	+ 3.86	+ 2.92	+ 3.06
10. S.G.P.T. (Unit/ml)						
—range	18—38	28—54	20—42	19—42	18—36	24—34
—mean	28.4	38.0	36.4	34.5	28.2	26.8
—S.D.	+ 2.62	+ 2.48	+ 5.46	+ 6.02	+ 4.98	+ 4.92

N.B.: + = $\pm$

Histo-pathology

Liver biopsies could be performed in 50 cases where adequate liver tissue was obtained. The histological changes in the liver were grouped as below (Table 3) :-

1. Specific changes of granuloma suggestive of leprous hepatitis.

2. Progression of leprous hepatitis to fibrosis.

3. Changes of a non-specific nature with or without fibrosis.

TABLE 3

Histo-pathological changes in liver (50 cases.)

Changes	Types of leprosy			
	Lepromatous 24 cases	Tuberculoid 19 cases	Dimorphous 5 cases	Maculo-anesthetic 2 cases
1. Specific granulomata	16	8	2	1
(granulomata progressed to early fibrosis)	3	3	1	—
2. Progression of hepatic lesion to fibrosis	13	3	1	—
(early fibrosis-stellate)	7	2	1	—
(fibrosis resembling early cirrhosis)	6	1	—	—
3. Non-specific changes	7	11	2	—
4. Normal histology	1	—	1	1
5. Demonstration of Acid fast bacilli	21	—	3	—

Lepromatous leprosy

Liver architecture was preserved in all cases. In 16 cases characteristic granulom a of different sizes were seen in which extensive and diffuse (11 cases) as well as localised (5 cases) changes were observed. Localised granulomata were seen mainly in the peripheral portal areas which pushed aside the surrounding liver cells. The granulomata were composed of various types of cells predominantly lepra cells with scattered irregular histiocytes and rarely lymphocytes. Foamy cells were arranged in groups in most of the granulomata (Fig. 1 & 2 Page No. 246). Mycobacterium leprae were seen in 21 cases. Generally smaller granulomata were loaded with Mycobacterium leprae. Amyloid deposits were not observed in any of the cases.

Tuberculoid Leprosy

The architecture of the liver was preserved and liver cell histology practically unaltered. Changes comprised of well formed granulomata (8 cases) of different sizes and diffuse infiltration by lymphocytes, histiocytes and occasional plasma cells (Fig. 3 & 4 Page No. 246 & 247). Granulomata were seen in the peripheral parts of the liver lobules, which showed from small irregular collection of lymphocytes and histiocytes to well circumscribed compact nodes consisting of lymphocytes, histiocytes and occasional plasma cells. Proliferation of Kupffer's cells was observed in 4 cases. Sinusoids were seen with cellular infiltration of lymphocytes, neutrophils and eosinophils in 6 cases. No amyloid was seen in any of them.

Dimorphous Leprosy

The normal architecture of the liver was preserved. Granulomata (2 cases) were irregularly dispersed but mostly occupied portal area and consisted of lymphocytes and epitheloid cells (Fig. 5 Page No. 247). Mycobacterium leprae were seen in granulomata (3 cases) along with collection of foam cells and proliferation of Kupffer's cells.

Maculo-anaesthetic Leprosy

Out of 2 cases one showed presence of localised granulomata of tuberculoid leprosy type.

Discussion

Leprosy is considered to be a systemic disease because of involvement of viscera[9]. The involvement of liver especially in the lepromatous type is well known. Alteration in liver function tests were seen mainly in lepromatous leprosy. Functional abnormalities in the form of increased globulin and decreased albumin may be due to deranged hepatocyte functions and hyperplasia of reticuloendothelial cells[8,10,11]. In the present study the highest level of

serum bilirubin of 1.8 mg% was observed in 3 cases of lepromatous leprosy. Dhopte and Balkrishna[10] and Lodhe et al[11] observed high serum bilirubin in lepromatous and borderline leprosy while Monlinelli and Royer[12] and Gupta et al[8] reported normal serum bilirubin among various clinical types of leprosy. Lowered serum cholesterol level as compared to normal have been observed in the present series of cases. Similar results were obtained by other workers also[8],[13]. Present study revealed raised levels of transaminases specially S. G. O. T. in lepromatous leprosy which may be due to muscle involvement [5],[13]-[15]. No significant alterations were seen in serum alkaline phosphatase.

The present study revealed 94% incidence of pathological lesions of liver in leprosy which is in general agreement with findings of other workers[3],[8],[13],[15]. Two types of lesions were encountered i. e., granulomata specific of leprosy or non-specific collection of mono-nuclear cells in liver parenchyma or around portal area. Granuloma in liver has been described in lepromatous and tuberculoid leprosy and given the term of leprous hepatitis[4]. This has been observed by us in 27 cases (54%), of which 16 were in lepromatous leprosy patients. Both types of lesions progressed to portal scarring (hepatic fibrosis) in due course of time in 17 cases. Out of these 13 had lepromatous leprosy. The non-specific lesions progressed to fibrosis in 6 out of 20 cases. Some workers attributed this portal fibrosis to non-specific factors like drug therapy[16] or nutritional factors[4]. On the other hand it might be the end result of the disease itself[3].

Mycobacterium leprae were seen in 24 cases (48%), out of which 21 (42%) had lepromatous leprosy. These bacilli were seen along the sinusoids which suggests that the spread of infection occurs through blood stream and body tissues react to this insult by proliferation of reticulo-endothelial cells in the form of histiocytes not only in the liver but also in other organs of the body[13],[15].

No amyloid was detected in our series of cases. This may be due to shorter duration of disease in the present series. The reported incidence of amyloidosis in Western literature varies from 5.9% to 50%[17],[18] while in Indian literature only 8 cases of secondary amyloidosis have been reported so far in leprosy[18],[20].

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