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LIVER DYSFUNCTION IN LEPROSY

RESULTS OF THE BROMSULFALEIN RETENTION TEST IN 150 CASES

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Liver damage may occur in leprosy as the result of a specific granulomatous infection. A study of 50 consecutive autopsies at the leprosarium at Carville revealed lepromas in the livers in 12 instances (³). A case of hepatosplenomegaly which did not subside following an acute reactive phase was reported to have miliary lepromata on needle biopsy of the liver (⁶). Prior to the use of sulfones one of us collaborated in a study in which it was found that 138 of 200 cases had positive van den Bergh tests, the qualitative reactions being of the delayed type indicating possible early hepatic lesions (¹).

The liver is commonly involved in lepromatous leprosy by secondary amyloidosis. It has been stated that usually the bromsulfalein (BSP) test gives results within normal limits in these cases (⁶). In the series of fifty autopsies referred to, there were 17 cases of amyloidosis of the liver. The incidence in living cases is not definitely known. Amyloidosis is a major cause of death in leprosy in this institution, often following a steadily progressive course.

The cephalin-cholesterol flocculation and thymol turbidity tests and serum albumin and globulin determinations have been shown to give abnormal results in a majority of lepromatous cases (⁵). Although these findings are not proved to be related to any specific organ dysfunction, abnormal liver function is probably contributory.

It has been suggested (⁷) that, because the bromsulfalein test measures excretion by parenchymal cells, it should be one of the more useful procedures for the evaluation of liver function in leprosy, in the absence of jaundice and renal impairment. No reports regarding the results of the bromsulfalein excretion tests in leprosy were found in the literature. In attempting to determine whether liver dysfunction accompanies the liver lesions of leprosy, we are reporting the results of that test in 150 essentially unselected cases. The cephalin-cholesterol flocculation, thymol turbidity, total serum protein, albumin, globulin, and icterus index tests were performed simultaneously. The results are presented in relation to the bromsulfalein results. The clinical records of all patients showing an abnormal retention of the dye were re-

viewed for history of the use of alcohol or any other possible explanation. The type and activity of disease, age of the patient and presence or absence of clinical amyloidosis were noted in all cases.

MATERIAL AND METHODS

A total of 150 cases were studied between October 1954 and July 1956. Of the 150 cases, 140 were of the lepromatous and 10 of the tuberculoid type. Cases which were suspected of having liver disease were excluded, and 3 cases in which BSP elevations were known to result from drug effects. The mean age of all the cases was 46.3 years with a standard deviation of 17.9 years; the range was 9 to 83 years.

Approximately 15 cc. of fasting blood was drawn by vein puncture and centrifuged after clotting, the serum being analyzed on the same day. The total serum proteins, albumin, and globulin, were determined by the method of Wolfson and co-workers (8). The thymol turbidity test and the cephalin-cholesterol flocculation test were described in a previous report (5). The technique of measurement of bromsulfalein retention was that of Rosenthal and White (4). This is based on the injection of 5 mgm. of bromsulfalein per kilogram of body weight, 5 cc. of blood being drawn 45 minutes after the injection of the dye, the clear serum being used for the test. The per cent retention was read in the Coleman Jr. spectrophotometer. Less than 2 per cent retention in the serum at the end of 45 minutes is considered normal.

RESULTS

Of the 150 patients, a total of 21 (14%) showed an abnormal dye retention in the 45-minute period. Of these cases 17 were lepromatous and 4 tuberculoid. Ten of the lepromatous cases were known to be complicated by amyloid nephrosis; 2 of these showed positive dye retention. In 1 of these 2 cases miliary lepromata were found by needle biopsy of the liver. No retention of the dye was noted in the other eight cases of amyloidosis.

Table 1 shows the BSP results by type and activity (referring to bacteriologic status) of the disease. Table 2 shows the same results in relation to the patients' age. A summary of the results of the other tests including the albumin globulin ratio are presented in Table 3.

TABLE 1.—Results of the bromsulfalein test by type and bacteriologic status of the disease.^a

Results of test	Lepromatous		Tuberculoid	
	Active	Inactive	Active	Inactive
Negative	112 (88.1%)	11 (84.6%)	1 (33.3%)	5 (71.4%)
Positive	15 (11.8%)	2 (15.4%)	2 (66.7%)	2 (28.6%)
Total	127	13	3	7

^a "Active" signifies bacteriologic positivity and "inactive" signifies negativity with no implication with regard to progression or regression of the disease.

TABLE 2.—Results of the bromsulfalein test in relation to patients' age.

Age (years)	Number of cases	Positive	Negative
9-24	18	2 (11.1%)	16 (88.8%)
25-44	53	6 (11.3%)	47 (88.7%)
45-64	55	9 (16.4%)	46 (83.6%)
65-83	24	4 (16.7%)	20 (83.3%)
Total	150	21	129

TABLE 3.—Results of abnormal liver function tests by BSP in leprosy.^a

BSP results	Cases	Icteric index >7 units cases	Flocculation >2 plus cases	Turbidity >5 units cases	A/G ratio below 1.5 cases
<i>Lepromatous cases (140)</i>					
Negative	123	15	101	34	56
Positive	17	6	16	10	10
<i>Tuberculoid cases (10)</i>					
Negative	6	0	4	1	2
Positive	4	0	1	0	4

^a "Flocculation" = the cephalin-cholesterol flocculation test. "Turbidity" = the thymol turbidity test. "A/G ratio" = albumin/globulin ratio.

DISCUSSION

It is believed that, in cases in which liver disease was not suspected, the bromsulfalein test gave a correct indication of the prevalence of liver dysfunction, especially in lepromatous leprosy. While the prevalence is slightly higher in those over 45 years of age, age does not account for most of the positive cases (Table 2).

No cases of infectious hepatitis were diagnosed during this period. None of the 21 positive cases had a history of excessive alcohol intake. Powell and Swan (³) did not find an increase in cirrhosis of the liver in their fifty autopsied cases. The most plausible explanation of the positive bromsulfalein tests is liver damage from the miliary lepromata described in the literature as found at autopsy and by needle biopsy.

The positive icteric index in 13.3 per cent of negative bromsulfalein cases may indicate that liver damage is more common than can be measured by the bromsulfalein test. The similarity between the results of the cephalin-cholesterol flocculation and thymol turbidity tests is in agreement with the concept that these tests measure protein abnormalities which are systemic in nature.

An interesting case of Lucio leprosy, with marked ulcerations of the legs, was admitted to Carville prior to the study period. On admission a dye retention of 7.5 per cent was noted. Twelve months later the dye retention was 6 per cent, and after another four months the test was negative. Decreasing test results accompanied improvement in the ulcers and general condition of the patient. Another case with a negative test followed by a 5.5 per cent retention of the dye during an acute lepromatous infiltration is also suggestive of liver impairment by generalized disease.

Since the completion of this work Kinnear and Davison (2) have reported a slightly abnormal retention of bromsulfalein in 20 tuberculoid cases in Bantu patients in Africa. These workers state: "It would appear that minimal liver dysfunction exists in tuberculoid leprosy, while lepromatous leprosy is associated with gross liver dysfunction as indicated by the tests used."

SUMMARY

Blood specimens from 150 cases of leprosy, 140 lepromatous and 10 tuberculoid, were examined for bromsulfalein retention, thymol turbidity, and cephalin-cholesterol flocculation, and the albumin: globulin ratio and the icterus index were determined. The results of the liver function tests are presented in relation to the bromsulfalein retention.

Of the 150 patients, 21 (14%) had an abnormal degree of dye retention; of these cases, 17 were of the lepromatous and 4 of the tuberculoid type. No retention of the dye was noted in 8 of 10 lepromatous cases complicated with amyloid nephrosis.

A positive icteric index (13.3%) in 15 lepromatous cases, without jaundice and showing no bromsulfalein retention, may indicate that liver damage is more common than can be measured by the BSP test.

Explanation of the positive BSP test in leprosy in terms of liver damage from miliary lepromata must be considered.

RESUMEN

Ejemplares sanguíneos procedentes de 150 casos de lepra, 140 lepromatosos y 10 tuberculoideos, fueron examinados en cuanto a retención de bromsulfaleína, turbidez del timol y floculación cefalina-colesterina, determinándose además la proporción de albúmina: globulina y el índice hepática en relación con la retención de bromsulfaleína.

De los 150 enfermos, 21 (14%) mostraron un tenor anormal de retención del

colorante; de estos casos, 17 fueron de la forma lepromatosa y 4 de la tuberculoidea. No se notó retención del colorante en 8 de 10 casos lepromatosos complicados por nefrosis amiloidea.

Un índice icterico positivo (13.3%) en 15 casos lepromatosos, sin ictericia y sin revelar retención de la bromsulfaleína, puede indicar que la lesión hepática es más frecuente de lo que puede denotar la prueba de la BSF.

Hay que considerar la explicación de la prueba positiva a la BSF en términos de lesión hepática debida a lepromas granúlicos.

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