Hepatic morphology in Huntington's chorea

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SYNOPSIS Liver biopsy specimens from six patients with Huntington's chorea were examined locally and referred without clinical information to three colleagues abroad experienced in the interpretation of liver biopsy specimens. The minor and inconsistent abnormalities reported upon were of non-specific character. The suggested interrelation between damage to cerebral neurones and hepatocytes in Huntington's chorea was not substantiated by this study.

Since George Huntington described progressive hereditary chorea in 1872, many attempts have been made to relate the neuropathology of the basal ganglia to other and particularly more readily available tissues, but with mostly inconclusive results. However, McCaughey (1961) reported that patients with Huntington's chorea have smaller than normal livers at necropsy, and this prompted a study from Glasgow by Bolt and Lewis (1973) on 12 patients whose livers showed changes including pleomorphism, anisocytosis and increased mitosis among the hepatocytes, reticular reduplication, and increased fibrosis. We examined this question by having liver biopsies from six patients with Huntington's chorea examined independently by four experienced histopathologists of whom three were unaware of the diagnoses or any clinical details on the patients.

METHODS

PATIENTS We studied six patients consecutively referred to the Huntington's Chorea Clinic of the Department of Psychiatry, University of Melbourne. All had an unequivocal diagnosis of Huntington's chorea, and all exhibited the hyperkinetic-hypotonic type of choreiform movements. The research nature of the investigations and the procedure of needle biopsy were explained to each patient and consent was obtained from both the patient and the next of kin.

¹ Aided by a grant from the National Health and Medical Research Council of Australia.
(Accepted 29 April 1975.)

BIOCHEMICAL TESTS The patients were tested for liver function by standard tests, including serum levels of glutamic oxaloacetic transaminase, alkaline phosphatase, albumin and γ -globulin, and excretion of 5 mg per kg bromsulphthalein over 45 minutes.

LIVER BIOPSY Each patient was admitted to hospital for liver biopsy, before which all drugs were stopped for five days. Liver biopsy was performed with the Vim-Silverman needle; adequate samples were obtained and the procedure was uncomplicated in all cases. Biopsy specimens were processed by standard procedures and stained by haematoxylin eosin. The biopsy specimen was examined by one of us (P. B. Bhathal) and was referred without clinical details to three histopathologists experienced in the interpretation of liver biopsy specimens.

RESULTS

The results of biochemical investigations are shown in Table 1; all were within normal limits.

TABLE 1
BIOCHEMICAL INVESTIGATIONS

Case No.	Serum glutamic oxaloacetic transaminase (IU/l)	Alkaline phosphatase (IU/l)	Albumin (g/l)	γ -Globulin (g/l)	Bromsulphthalein excretion percent in 45 min
1	12	63	36	10	99
2	7	39	39	11	98
3	17	50	50	11	97
4	7	83	41	11	97
5	15	59	38	9	100
6	16	83	39	6	97

TABLE 2
DESCRIPTION OF BIOPSY SPECIMENS BY FOUR HISTOPATHOLOGISTS

Patient (No.)	P.B.	G.K.	R.P.	P.S.
1	Normal liver	Normal liver, moderate amount of lipofuscin in centrally located hepatocytes, well within normal limits	Normal liver	Liver with modest hydropic swelling of hepatocytes which is non-specific
2	Normal liver	Normal liver. A few scattered large fat droplets	Normal liver with some fatty change	Scanty fat droplets and lipochromic pigment in otherwise unremarkable liver biopsy
3	Normal liver	Normal liver. Many of mid-zonal and periportal hepatocytes contain small amount of fine haemosiderin granules	Normal liver, some congestion and minimal fat	Essentially normal-appearing fragment of liver
4	Normal liver with accumulation of inflammatory cells in one portal tract. Non-specific hepatitis	Normal lobular architecture. One portal triad contains moderate number of inflammatory cells, and another shows borderline increase in collagen	Normal liver, with one inflamed portal tract with some necrosis of liver cells at periphery	Liver with slight non-specific changes suggestive of older individual
5	Architecture normal. Small amount of parenchymal fat present. Slight increase in cellularity of portal areas. Very minimal fatty liver	Essentially normal liver, with small amount of central lipofuscin. Some of hepatocytes are finely granulated but show no other significant abnormalities	Normal liver with mild fatty change	Essentially normal liver
6	Normal liver	Normal liver except for one triad that shows slight increase in mononuclear inflammatory cells	Entirely normal liver	Liver biopsy showing no specific abnormalities

The reports on the liver biopsies from four observers are cited verbatim (Table 2). There were no substantial abnormalities consistently demonstrated, and the changes noted were mostly minor and non-specific, including inflammatory cells in one portal tract in one specimen, occasional fat droplets, and presence of pigment.

DISCUSSION

Liver biopsy specimens from six patients were studied to assess the claimed association (Bolt and Lewis, 1973) of hepatic abnormalities with Huntington's chorea. However, there were no consistently observed histological changes.

Our patients differed from those of Bolt and Lewis (1973) in certain respects. They were not in hospital and all lived at home with their family; patients 1, 3, and 5 were engaged in full and gainful employment, patient 2 functioned well as a housewife, while patients 4 and 6 were

not able to work gainfully because of deteriorating intellectual function. In contrast, in the patients in hospital studied by Bolt and Lewis (1973), the duration of manifest illness tended to be longer, in that in 10 the illness had lasted from 10 to 22 and in two it was present for three years and six years respectively. We suggest that patients in hospital would be receiving various drugs, and would be more likely to experience infections and possibly dietary deficiencies than patients living at home (Hunter *et al.*, 1967; Shulman 1967 a, b). Such influences could predispose to the histological changes reported by Bolt and Lewis (1973). Perhaps the minor abnormalities in the liver biopsies in our cases could be accounted for by effects of the illness on life habits of our patients.

Bolt and Lewis (1973) supported McCaughey's suggestion that the profound loss of basal ganglia cells in Huntington's chorea is shared by liver cells and that, owing to the regenerative capacity of hepatic cells, a loss of liver cell mass

would occur only late in the disease. However, in those of our patients who have had their illness for over 10 years (patients 1, 3, 4) there were no more obvious hepatic abnormalities than in the other three patients whose duration of illness was less. The mean survival time from onset of manifest illness to death has been considered to range from 13 to 16 years by various authors (Bell, 1934; Panse, 1942; Reed and Chandler, 1958; Myrianthopoulos, 1966), so that our three patients who had Huntington's chorea for 10 to 15 years could be considered to be in the later stage of this disease.

In conclusion, our study negates the hypothesis that hepatocytes participate in the histopathological processes which determine Huntington's chorea.

This study was based on the generous collaboration of Dr Gerald Klatskin, Department of Medicine, Yale University; Dr Robert L. Peters, Department of Pathology, University of Southern California; and Dr Peter J. Scheuer, Department of Morbid Anatomy, Royal Free Hospital, London. Professor B. M. Davies made the initial suggestion for this study and provided helpful

comments. Dr Graeme Symington and Dr Rodney Lambert assisted with the liver biopsies.

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