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LINER DYSFUNCTION WITH JAUNDICE IN A CASE OF SEVERE MALNUTRITION AND MALABSORPTION

K. W. HEATON, M.B. Cantab., M.R.C.P.

Medical Registrar, Royal Free Hospital, North Western Branch, London, N.W.3.*

ALTHOUGH malnutrition is accepted as a cause of liver disease in experimental animals, its role in the genesis of liver disease in man is controversial (Fernando, Medonza and Rajasuriya, 1948; Patwardhan, 1955; Higginson, Grobelaar and Walker, 1957). Protein malnutrition in children (kwashiorkor) is often associated with fatty liver, but when hepatocellular failure and jaundice occur they are usually blamed on coincidental viral hepatitis. In adults overt liver disease has seldom been convincingly attributed to malnutrition. For this reason the case is reported here of a middle-aged woman who developed jaundice and other evidence of liver-cell dysfunction in addition to fatty liver, while suffering from severe malnutrition and malabsorption.

Case Report

Miss L.M. was diagnosed in 1941, at the age of 19, as having Crohn's disease (regional enteritis). This was established at laparotomy after a two-year history of intermittent abdominal pain, vomiting and diarrhoea. Extensive bowel resection was carried out then, and by 1957 five further resections had been done for recurrences of the disease. These left her with an estimated four feet of small intestine. Steatorrhoea became apparent in 1957 and soon afterwards other symptoms of malabsorption occurred such as glossitis, oedema, paraesthesiae and a bleeding tendency. Replacement therapy was only taken spasmodically. During the first six months of 1963 her condition gradually worsened with severe anorexia, continuous diarrhoea and loss of 3 stone in weight. Shortly before admission to the Royal Free Hospital on the 19th June 1963 she began to have painful cramps of her hands and feet.

Examination at this time revealed a pale, ill and wasted woman of 41 years with a pyrexia of 99-100°F. She was faintly jaundiced and vomiting occasionally. Her stools were frequent, pale and watery, with no visible blood. Chvostek's and

Trousseau's signs were positive and at times spontaneous tetany occurred with typical carpo-pedal spasm. Pulse 120/min., regular. BP 110/65 mm. Hg. Abdomen distended, with numerous laparotomy scars, tenderness on the right side and an ill-defined mass below the right costal margin.

Investigations. Hb 11.0 g.%, film—moderate hypochromia. WBC 4,500/cu. mm. (normal differential). Prothrombin time 18 seconds (control 14 seconds). Blood urea 13 mg./100 ml. Serum potassium 1.4, sodium 140, chloride 91, bicarbonate 30 mEq/l., calcium 5.5 mg./100 ml. Plasma bilirubin 3.6 mg./100 ml., alkaline phosphatase 13 K.A. units/100 ml. Albumin 2.3, globulin 2.4 g./100 ml. ECG—generalised flattening or inversion of T waves, Q-T interval prolonged (Q-Tc = 0.65 secs.).

Progress. During the following two weeks jaundice deepened (serum bilirubin 6.5 mg./100 ml.) and features of liver-cell dysfunction appeared. These included drowsiness and euphoria, ascites, raised serum enzymes (aspartate transaminase 122 i.u./l., isocitrate dehydrogenase 11.2 i.u./l.), raised serum amino-acids (9.1 mg./100 ml.) lowered blood urea (9 mg./100 ml.) and abnormal thymol and zinc sulphate turbidities. Profuse rectal bleeding also occurred, an estimated six pints being lost and replaced. Treatment with a high-carbohydrate, protein-free diet, oral neomycin and parenteral B vitamins was ineffective, but marked improvement occurred when high-dosage corticosteroid therapy was instituted (prednisone 30 mg. 8 hourly). After a further six weeks all routine liver function tests were normal and bromsulphthalein retention was only 8% at 45 minutes. Needle liver biopsy however showed extreme fatty infiltration (also mild inflammatory cell infiltration of the portal tracts and slight periportal fibrosis not amounting to nodular cirrhosis).

Discussion

This patient presented with severe malnutrition and an exceptional degree of electrolyte depletion and was found to have increasing jaundice and evidence of liver cell dysfunction amounting almost to hepatic precoma. No cause could be found for her hepatocellular failure apart from

* Present address: Department of Medicine, Royal Infirmary, Bristol, 2.

her nutritional and metabolic state. This in turn was clearly related to malabsorption from repeated bowel resections which had left her with only four feet of small intestine. Continuing activity of her Crohn's disease (manifested by abdominal pain and tenderness, fever and a persistent leucocytosis) no doubt contributed to her anorexia and diarrhoea, if not to her malabsorption.

In spite of the well-known association between protein under-nutrition and liver pathology in experimental animals, a similar association in adult man remains poorly documented. In children protein under-nutrition leads to the kwashiorkor syndrome, an integral part of which is fatty infiltration of the liver. Jaundice and other evidence of liver cell dysfunction are however uncommon and never severe (Trowell, Davies and Dean, 1954; Edozien, 1961). Evidence of hepatic dysfunction has been sought by studies of serum transaminases and raised levels have sometimes been found (Baron, 1960; Edozien, 1961; but see Smith, 1962). In adult malnutrition the situation is less clear. Fatty liver is of course well-known in alcoholics, and in poorly nourished individuals acute hepato-cellular failure may occur (Popper, Szanto and Parthasarathy, 1955). Apart from alcoholics however there are very few published reports of nutritional liver disease. Detailed studies of the livers of malnourished men with hunger oedema in Germany immediately after the war (Sherlock and Walshe, 1951) showed normal liver function and generally normal histology. In particular, fatty infiltration was not seen. However in these cases the undernutrition involved calories to the same extent as protein whereas a relative deficiency of protein is thought to be the main factor in the aetiology of kwashiorkor. Sepulveda, de la Portilla, Rojas and Macias (1957), reporting a study of 80 patients with primary malnutrition in Mexico City, found evidence of mild liver cell dysfunction in about 40% of cases and fatty infiltration in 74%, but frank hepatic coma only occurred in one patient. A study of patients with cirrhosis in Ceylon (Fernando, and others, 1948) showed that in general they ate a diet less adequate than that of other patients and that an excessive proportion belonged to a vegetarian racial group.

Malabsorption syndrome alone rarely causes hepatic disease. Badenoch (1960) recorded a series of 163 patients with steatorrhoea in which two deaths were attributed to liver failure. At least one of the two cases however was considered to have serum hepatitis. Arends, Nieweg and Engelhardt (1954) described 9 cases of liver disease associated with steatorrhoea, the pathology being severe fatty infiltration in 4 patients, one of whom died in hepatic coma.

The case described here would appear to be one of nutritional liver disease in which extreme fatty infiltration was associated with jaundice and hepatocellular failure. It is not possible to say

with certainty why the liver was so seriously affected but two points may be made. Firstly, it must be very exceptional for a patient to survive with biochemical disturbances as severe as in this case (serum potassium of 1.4 mEq/l in particular is not usually regarded as compatible with life) and these may have conditioned her for liver cell failure. Secondly, continuing activity of her Crohn's disease may have led to a liver-damaging portal toxæmia (analogous to the portal bacteraemia that has been demonstrated in ulcerative colitis, Brooke, Dykes and Walker, 1961). It is suggested that the combined effect of these two factors precipitated hepatocellular failure in this case.

Summary

The case is described of a woman with severe malnutrition and malabsorption following multiple small bowel resections for Crohn's disease, who developed jaundice and hepatocellular failure as well as extreme fatty liver. It is suggested that this is a case of true nutritional liver disease, and the association between malnutrition and human liver disease in general is briefly discussed.

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