FULMINANT HEPATIC FAILURE AND SHIGELLA BACTEREMIA

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SUMMARY

A three and a half year old boy with shigellosis developed fulminant hepatic failure. The hepatic derangements rapidly improved over a period of two weeks after treatment of the shigellosis with parenteral gentamicin. We believe this is the first documented report of fulminant hepatic failure due to shigella sepsis.

INTRODUCTION

Although shigellosis is primarily an intestinal disease, extraintestinal manifestations do occur. These rarely include hepatitis, first reported in 1910 [1] and more recently in 1976, [2] the latter with a cholestatic component.

The present report describes the first case of fulminant hepatic failure associated with shigellosis.

CASE HISTORY

A previously healthy 3½ years old Chinese boy was hospitalised after two days of fever, vomiting and bloody diarrhoea. There was no history of contact with any jaundiced persons and no history of ingestion of any hepatotoxic drugs. There was no family history of liver disease.

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On examination, he was drowsy, disorientated, acidotic, and jaundiced. The liver was palpable 4 cm below the right costal margin, but there was no splenomegaly.

Investigations showed the haemoglobin to be 12 gm/dl, leucocyte count of 22,000 with 60% polymorphs, 40% lymphocytes, and platelets 105,000/mm ^{3}. Blood urea was 2.6 mmol/l, glucose 0.8 mmol/l, serum sodium 110 mmol/l, potassium 5.3 mmol/l. The prothrombin time was 10% of normal and serum bilirubin 104 umol/l (conjugated 30 umol/l). The aspartete and alanine aminotransferases were 550 IU/l and 590 IU/l respectively.

Following correction of fluid and electrolyte imbalances he was maintained on an infusion of 10% dextrose, intravenous vitamin K, oral neomycin and oral lactulose.

Over the next 24 hours, he became more drowsy, more confused and more jaundiced. The liver edge could not be palpated now. The serum bilirubin had increased to 316 umol/l and the blood ammonia was 500 umol/l. There were further elevations of the aspartate and alanine aminotransferases to 2,000 IU/l and 800 IU/l respectively.

As the blood glucose remained persistently low, hypertonic glucose solutions were infused through a central venous catheter.

The stool and blood cultures performed on three separate occasions grew *Shigella flexneri* type 2a. Serology for hepatitis B, typhoid, paratyphoid and leptospirosis were negative, as was the indirect hemagglutination test for *Entamoeba histolytica*. Serum ceruloplasmin was also normal.

He was started on intravenous gentamicin, which was the only non hepatotoxic antibiotic the shigella

was sensitive to, and this was continued for fourteen days. He made significant clinical and biochemical improvement and his liver became palpable again. On the tenth day of the illness, a liver biopsy showed regenerating hepatocytes with individual cell necrosis and mild lymphocytic infiltration. His liver function tests came back to normal on the fourteenth day of the illness.

One week later, he developed an intermittent pyrexia associated with a leucocytosis of 16,000 with 60% polymorphs. Clinical examination did not provide any clues for the fever and repeated cultures of his throat, trach 1 secretions, urine and blood were negative. Viral studies were also non informative. Liver function test showed a bilirubin of 36 umol/l and normal aminotransferases. A liver scan showed a rounded filling defect over the right hepatic lobe, suggesting a liver abscess. A second course of parenteral gentamicin lead to defervescence and a repeat scan two weeks later showed complete resolution of the abscess.

The levels of serum immunoglobulins G, M and A were normal, but low levels of C_3 and C_4 during the acute stage returned to normal levels three weeks later.

DISCUSSION

A patient is in fulminant hepatic failure (FHF) when the deterioration in liver function is so rapid and severe that encephalopathy follows within eight weeks of the onset of liver disease. [3] Our patient fits into this category. In a series from the King's College Hospital London, FHF carried a mortality of 72 percent. [4] The causes of FHF include infections due to hepatitis A or B, paracetamol overdosage, halothane toxicity, and drug hypersensitivity. Our patient had no history of drug ingestion likely to cause hepatic damage. Hepatitis B antigen was negative. There was no clinical or epidemiological evidence of hepatitis A infection in this child, and the acute history with absence of any prodromal symtoms is not suggestive of hepatitis A infection. However there was a clear temporal association between the onset of his bacillary dysentery and the hepatitis. *Shigella flexneri* was isolated on three separate occasions, from the stools as well as from the blood. There was also a return to normality of the liver function with specific treatment of the shigellosis. It is therefore reasonable to implicate shigellosis as contributing to the FHF.

Following initial improvement, there was a recurrence of fever due to a liver abscess. *Entamoeba histolytica* is one of the common causes of liver abscess in this region, and is associated with high serological titres of antibodies against the protozoa. In this case the titres were negative. It would appear then that the abscess was due to the persistence of the shigella in the liver.

Tissue invasion by shigella is an uncommon phenomena and the possibility of immunodeficiency was considered, but this was not borne out by the results of the tests performed.

Extraintestinal manifestation of shigellosis are protean and have included involvement of the central nervous system, respiratory system, eyes, joints and the urinary tract. An extensive review by Barrett-Connor and Connor [6] did not include hepatic involvement among the many diverse and unusual complications they described. The few reports in the literature of hepatic involvement by shigellosis described fatty liver [1], focal necrosis [7], and cholestatic jaundice. [2] To date, the association of shigellosis and fulminant hepatic failure have not been documented.

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