Hepatitis - A induced Non Infantile Giant Cell Hepatitis

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Introduction

Giant cell hepatitis is seen frequently in neonates, but it is rare thereafter. Various conditions and diseases associated with post-infantile giant cell hepatitis (PIGCH) have been described, but the pathogenesis remains unknown. Such cases have been attributed to autoimmune disease, hepatotropic viruses, drugs, and recently to paramyxovirus infection [1]. Histopathology of liver tissue reveals giant cell formation with up to 20 nuclei in 20-70% of all hepatocytes. Prognosis is variable with majority of cases presenting with chronic liver disease and histopathological features ranging from mild fibrosis to established cirrhosis [2]. We report a case of fatal fulminant hepatic failure following infection with hepatitis- A showing giant cell hepatitis on histopathology in a five year old child which has been rarely reported.

Case Report

A five year old male child was brought with history of anorexia, low-grade fever and progressively increasing jaundice over the preceding eight days followed by abnormal behaviour, hematemesis and coma for the last 24 hours. There was no significant past history of jaundice, blood transfusion or injections other than routine immunization. Examination revealed tachycardia, tachypnoea, fever, deep icterus, oedema and pallor. Systemic examination revealed a comatose child with stage III hepatic encephalopathy, bilateral lung crepitations and normal sized liver. On investigations haemoglobin was 8.5gm%, total leucocyte count 12,400/cumm (polymorhs 49%, lymphocytes 30%, eosinophils 20%, and monocytes 1%), platelet count 1.9 lac/cumm, serum bilirubin 20.0 mg% (conjugated 18.2, unconjugated 1.8), aspartate aminotransferase 406 IU/L, alanine aminotransferase 220 IU/L, blood urea 18 mg %, serum creatinine 0.7mg%, serum sodium/potassium-137/3.8meq/L, random blood sugar 65mg%, prothrombin time-94.80 seconds (control 13.4 second), ammonia 201mcg/dl, arterial blood gases pH-7.49, pCO₂-29.2, pO₂-78, HCO₃-22.3, base excess (extra cellular fluid) - 1mmol/L. HBsAg, HEV- IgM and HCV- IgM antibodies were negative. HAV-IgM antibodies were positive. IgM for leptospira,

antinuclear antibody and coomb's test were negative. Serum ceruloplasmin was within normal limits (38mg/dl).

The child was managed for fulminant hepatic failure with hepatic encephalopathy (stage III) and coagulopathy. He was started on oxygen, intravenous fluids, broad spectrum antibiotics (cefotaxime and sodium penicillin), vit K, H₂ blockers, lactulose, enema and fresh frozen plasma followed by mechanical ventilation. The child continued to deteriorate with stage IV encephalopathy and refractory upper gastrointestinal bleed. He died within 15 hours of admission. The parents did not consent for a postmortem, but agreed for a liver biopsy, which was done within 20 minutes of death.

The biopsy tissue was greyish brown in colour. On histopathology the haematoxylin and eosin stained slide showed disorganization of normal hepatocyte architecture (lobular disarray). Many scattered multinucleated hepatocytes ("giant cells") with upto 20 nuclei were seen. There was a characteristic minimal lymphocytic infiltrate seen in periportal area. Focal neutrophilic infiltrate around degenerating giant cells was seen. No bile duct proliferation or portal fibrosis was seen. Variable degree of cholestasis, and acidophil cells were seen. No areas of fibrosis were seen. "Activated" perisinusoidal cells were present, especially in relation to areas of inflammation and necrosis (Fig. 1).

Fig. 1 : Numerous syncytial giant cells seen (H&E stain-400X).

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Discussion

The occurrence of plasmodial giant cells in the liver is probably a morphological reaction pattern with the most diverse causes. In babies and infants, these changes occur particularly in neonatal hepatitis and intra/extrahepatic bile duct atresia. PIGCH has been associated with viral infections (HAV, HBV, HCV, HIV, paramyxovirus) and/or autoimmune reactions and is rare as compared to neonatal giant cell hepatitis with only about 100 cases reported in the last 20 years [3,4]. Paramyxoviral infection has been increasingly linked to post-infantile giant cell hepatitis. It has been visualized under electron microscope as pleomorphic particles of 150 - 250 microns, filamentous strands, and particles of 14 - 17 nm with peripherally disposed spikes [5,6]. Autoimmune causes account for approximately 40% of PIGCH, which commonly presents as chronic liver disease while 25% cases have an acute presentation [5]. The pathogenesis is probably linked with altered immunoreactivity to a variety of agents [7].

Only two cases have been reported earlier, in which hepatitis A infection could be demonstrated serologically. One had raised antinuclear antibody (ANA) [4], and the other had hypereosinophilia of obscure aetiology [8,9]. Our case had eosinophilia apart from positive serological evidence of HAV. We presume that eosinophilia could have been due to a drug reaction (child was on local treatment for jaundice in the village). This was a rare case of fatal post-infantile giant cell hepatitis with eosinophilia, associated with HAV infection which suggests that PIGCH is a morphological reaction pattern with the diverse causes resulting from an immunoreactivity to a variety of agents some of which may be coexistent.

The clinical picture of post infantile giant cell hepatitis varies from mild chronic liver disease to subacute hepatic failure. Liver biopsy is diagnostic which shows giant cells as the common pathological finding. Other biopsy findings are periportal lymphocytic infiltrate (T lymphocytes), piecemeal necrosis, "activated" perisinusoidal cells, bilirubinostasis, Mallory bodies, often

associated with neutrophilic infiltrate and severe fibrosis [10].

The treatment is symptomatic and patients having autoimmune origin of hepatitis respond to steroids and ursodeoxycholic acid. In fulminant cases, liver transplantation is the only option. Non-infantile giant cell hepatitis resolves in few, but progress to chronic active hepatitis, hepatic fibrosis, cirrhosis or fulminant hepatic failure in others.

Conflicts of Interest

None identified

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