PATHOLOGICAL QUIZ

(Liver Biopsy in a Case of Jaundice)

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A seven years old male child came to medical attention after sustaining a fracture of the left radius bone. During preanaesthetic assessment, he was detected to have icterus. Parents on questioning informed that the boy had yellowish discoloration of the eyes since the age of eight months. There had been three episodes of exaggerated jaundice prior to the present admission. The child was otherwise asymptomatic. He had achieved normal developmental mile stones. There was no history of consanguinity and other siblings and parents were asymptomatic.

On examination there was icterus and mild pallor.

Abdominal examination showed hepatomegaly of 5 cms (span 9 cms) and splenomegaly of 2 cms. The gall bladder was not palpable and there was no ascites. Other systems were normal on clinical examination. Hemogram suggested a mild anaemia of folic acid deficiency. Urine was positive for bile pigments. Liver function tests showed a conjugated hyperbilirubinemia (10.3 mg/dl). The transaminase and alkaline phosphatase levels were within normal limits. Serological markers for liver disease were negative. USG abdomen confirmed hepatomegaly with no intrahepatic biliary radical dilatation and a normal gall bladder. A liver biopsy was done. (Fig 1)

Fig. 1 : Liver biopsy

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ANSWER TO THE PATHOLOGICAL QUIZ

Microscopic Examination Report

The liver biopsy specimen was slate gray in colour. On microscopic study the lobular architecture of the liver was maintained. The hepatocytes contained abundant granular, dark brown intracytoplasmic pigment concentrated along the canalicular border. The pigment was most prominent in perivenular hepatocytes. The portal tracts were unremarkable and no necrotic or inflammatory changes were seen within the hepatic parenchyma. There was no Kupffer cell hyperplasia.

Pathological Diagnosis

Based upon the characteristic histopathological findings a diagnosis of Dubin Johnson Syndrome was made.

Discussion

Liver disease is most often suspected in a child because of the discovery of jaundice, hepatomegaly, or the serendipitous detection of abnormal liver function tests. However, in certain inherited disorders of the liver, the clinical findings may be minimal and these come to medical attention for reasons other than the primary problem. In general, the presence of conjugated hyperbilirubinemia implies underlying significant hepatobiliary disease. In the absence of normal liver function or signs of cholestasis, inherited disorders must be suspected. Specific autosomal recessive disorders of bilirubin metabolism, characterized by conjugated hyperbilirubinemia in the absence of abnormal liver function tests or signs of cholestasis, include Dubin Johnson and Rotor syndrome. In both disorders, hepatic transport of anions such as bilirubin is deficient. Both syndromes are recognized in late childhood or early adolescence, and only occasionally in infancy [1]. Serum bilirubin levels, which are only

mildly elevated, may get exaggerated by infection. The three episodes of 'jaundice' in the present case recognized by parents could have occurred due to intercurrent infection.

The Dubin Johnson syndrome is most likely caused by a congenital impairment of an ATP-dependent transport system specific for a variety of multivalent organic anions, including bilirubin diglucuronide. Bilirubin is thus conjugated but inefficiently secreted into bile. The symptoms are mild, possibly due to the presence of residual transport activity in the membrane catalyzed by separate transport proteins. The dark discoloration of the liver is due to deposition of a pigment formed from products of amino acid catabolism that cannot be secreted into bile [2]. In another elegant study, the workers have identified the membrane protein mediating the adenosine triphosphate (ATP)-dependent transport of glutathione and glucuronate conjugates as a multidrug resistance protein (MRP) and localized it to the canalicular as well as to the lateral hepatocyte plasma membrane. Using double-label immunofluorescence and confocal laser scanning microscopy with antibodies directed against MRP, the workers demonstrated the selective absence of the canalicular isoform of MRP (cMRP) from the hepatocytes in patient with Dubin Johnson syndrome [3].

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