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CONGENITAL HEPATIC FIBROSIS IN A FOUR MONTH CHILD: CASE REPORT WITH REVIEW OF LITERATURE.

Pathology

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ABSTRACT

Congenital hepatic fibrosis (CHF) is a rare autosomal recessive disease because of defective formation of ductal plate of liver in the intrauterine life. This is therefore also known as ductal plate malformation. It is invariably associated with polycystic kidney disease. However, isolated forms do occur. CHF can be found as a part of many hepatobiliary syndromes. The prognosis is generally good but the disease may worsen if complicated by portal hypertension or cholangitis. The diagnosis of CHF depends on the combined approach of radiological and appropriate histopathological interpretations in the context of clinical presentation. We present here a case of CHF in an infant with characteristic histopathological features along with a review of the literature.

KEYWORDS

Congenital Hepatic Fibrosis, Ductal Plate Malformation, Liver Fibrosis, Caroli Disease, Polycystic

INTRODUCTION

Congenital hepatic fibrosis (CHF) is a rare autosomal recessive disorder. It was first described by Dobbs in 1960 and later elaborated by Kerr et al. (Janowski et al., 2017)The detection rate for this entity has increased recently, owing to the development of noninvasive diagnostic tools such as ultrasonography (USG), Computed Tomography (CT), and Magnetic Resonance Imaging (MRI) (Gunay-Aygun et al., 2013). The prevalence of this disease is approximately 1/10000–20000 (Zhu et al., 2020). The anatomic and pathological examination of liver biopsy is considered gold standard for the diagnosis of CHF.

Pathogenesis of CHF is based on ductal plate malformation (DPM), namely, ciliopathy or fibrocystic liver disease (Zhu et al., 2020). CHF is most commonly associated with Autosomal recessive polycystic kidney disease (ARPKD) but can be seen with other disorders such as Caroli's disease, von Meyenburg complex, and choledochal cyst (Desmet, 1992). Many other syndromes have been associated with morphological abnormalities of CHF (Landing et al., 1980; Wright et al., 1994). We present here a case of CHF with a choledochal cyst in a neonate patient.

CASE REPORT

A four-month-old female child was brought to the emergency department with fever, respiratory distress, and unconsciousness for one day. On general physical examination, she was lethargic and had icterus. The abdomen was soft, mildly distended and an external drainage catheter was already placed in the abdomen. The patient's attendants gave a history of treatment from some peripheral hospital for two days. The patient was referred to a higher center, as her condition did not improve.

Routine laboratory investigations revealed increased serum levels of direct and indirect bilirubin, liver enzymes, and creatinine. Complete blood counts were within normal limits. Viral profile screening was done and all were non-reactive. Prothrombin time was normal. However, the International Normalized ration (INR) was slightly raised. Abdominal USG showed mild intrahepatic biliary radical dilatation and a 2.2x2.3 cm sized cystic lesion in porta hepatis which communicated to the common bile duct. A choledochal cyst, Type 4a was suggested.

An urgent contrast-enhanced CT scan of the abdomen was done subsequently, which revealed cystic dilatation of extrahepatic common bile duct along with mild dilatation of common hepatic and right hepatic duct. No renal lesions were detected. After proper stabilization of the patient, a percutaneous liver biopsy was done.

The histopathological evaluation demonstrated extensive Porto-portal fibrosis leading to incomplete to complete nodule formation (Fig. 1A). Focal preserved central veins were identified. Extrahepatic cholestasis and bile plugs were evident (Fig. 1B, center of image). PAS stain highlighted the normal hepatocytes present within the nodules. No accumulations of PAS positive extra or intracellular material were seen. The expanded fibrous septae showed marked proliferation of nascent bile ductules having angulation and irregular branching (arrowheads, Fig. 1C). Reticulin stain demonstrated Grade II reticulin fibrosis along the fibrous septae (Figure1D).

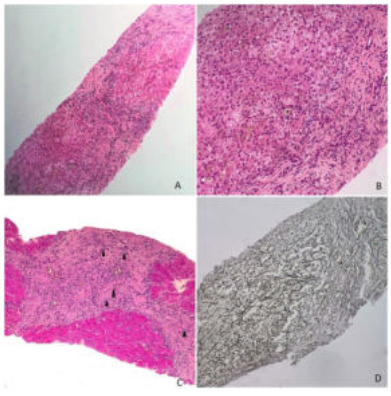

Figure 1A-D (1A, B: Hematoxylin & Eosin stain, 100x and 400x magnification respectively): Trucut biopsy of liver showing extensive fibrosis with residual nodules of hepatocytes. Darker center shows proliferating biliary channels (A). Multiple bile plugs can be seen (B, brownish dark blobs). The nodules of hepatocytes are clearly visible as well as the nascent biliary radicals (arrowheads) along with interspersed chronic inflammatory cells (C, PAS stain). Reticulin stain highlighted the peri-hepatocellular and also the marked porto-portal fibrosis (D).

DISCUSSION

CHF is a fibrocystic disease that mainly affects the kidneys and liver. There are fusiform dilatations of the renal collecting duct along with ductal plate malformation of the liver. The incidence of this disease is approximately 1:20,000 live births (Hasbaoui et al., 2021). Mutations in the PKHD1 gene are present in most cases. PKHD1 encodes for fibrocystin/ polycystin, which is expressed by the renal and biliary epithelium and is responsible for maintaining the three-dimensional tubular architecture (Blyth & Ockenden, 1971; Hasbaoui et al., 2021).

Lack of remodeling at around the 12th week of intrauterine life in

ductal plate configuration of the liver leads to the persistence of an excess of embryologic bile duct structures called DPM. This is considered a basic lesion in all variants of fibrocystic liver diseases. DPM is often associated with progressive destruction of immature intrahepatic bile ducts by a nonspecific necro-inflammatory process, which gives rise to anatomical-clinical entities known as CHF and Caroli's syndrome (Desmet, 1992).

Congenital hepatic fibrosis was first reported by Bristowe in 1856. In 1961, the varied clinical findings of CHF were elaborated by Kerr et al. which comprised of hepatosplenomegaly, hematemesis, and melena among 13 patients. The median and mean age of diagnosis were 2 and 11.2 years, respectively (Hasbaoui et al., 2021). However, our case was younger, being just four months old. The clinical symptoms and signs depend on various forms of CHF. Portal Hypertensive (PH) and mixed CHF are the two most common forms of CHF in childhood. Splenomegaly and liver cirrhosis occur more often in children with CHF. Fever, jaundice, and hepatomegaly are more frequently seen in children with mixed CHF than in those with PH CHF (Wu et al., 2016). Some rare cases may present with episodes of cholangitis (Guerra et al., 2018). However, some of the patients remain asymptomatic because of which some cases are detected in adulthood (Hasbaoui et al., 2021). In many cases CHF is seen associated with Caroli disease. But now it is believed that CHF involves the arrest of small interlobular bile ducts maturation, while in Caroli it is the medium intrahepatic bile ducts that are defective.

White blood cell counts, platelet counts, mean platelet volume, serum levels of alanine transaminase, aspartate transaminase, alkaline phosphatase, γ-glutamyl transferase, leucine aminopeptidase, and total bile acids are found to be raised in children with mixed CHF than those with PH CHF (Wu et al., 2016).

Imaging modalities are very useful and it has increased the detection rate to a great extent.

Ultrasound evaluation is employed first and foremost and the most common findings include hypertrophy of the left lateral and caudate hepatic segments, right segment atrophy, splenomegaly, intra- and extrahepatic biliary dilatation with concomitant cystic and solid lesions (regeneration nodules), periportal thickening, hepatic and renal cysts. Computed tomography (CT) provides a better image of the gross morphology of the liver with accurate volume measurements and imaging of liver vasculature, as well as demonstrating any changes in the biliary tree. However, nuclear magnetic resonance imaging (MRI) with cholangioresonance has emerged as an important diagnostic alternative because of no radiation exposure and detailed evaluation of the biliary tree (Hasbaoui et al., 2021).

A liver biopsy usually helps in confirming the diagnosis and distinguishing between portal hypertensive, cholangitic and mixed hypertensive-cholangitic type (Alsomali et al., 2020). CHF is easily confused with liver cirrhosis. However, biopsy helps in the exclusion of cirrhotic changes and confirms hepatic fibrosis with signs of hepatoportal sclerosis.

No treatment has been proven till now, to stop or reverse the process of congenital hepatic fibrosis. Symptomatic therapy can be given, which depends on the type of CHF. In portal hypertensive form, management of varices and bleeding is warranted with sclerotherapy or EVL and in some beta-blockers can be beneficial (Mazigh et al., 2006). Rawat et al. (Rawat et al., 2013) concluded in their study that early (neonatal) presentation is the best predictor for the need for a transplant.

CONCLUSION

Congenital hepatic fibrosis (CHF) is a rare autosomal recessive disorder presenting in childhood with features of hepatic fibrosis and portal hypertension. It usually occurs in association with other fibrocystic diseases. Pure/ isolated CHF is very rare. Clinical presentation and laboratory parameters depend on the four clinical forms of CHF.

Screening imaging modalities and liver biopsy confirms the diagnosis. CHF generally favors a good prognosis with preserved liver function when detected and managed at early stage, before getting complicated with portal hypertension and cholangitis. Interpretation of liver biopsy accompanied by appropriate special stains and a knowledge of the clinical setting helps in correct diagnosis and an early intervention.

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