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Case report

Primary biliary cirrhosis in early childhood – A rare case report

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ABSTRACT

Introduction and importance: Primary biliary cirrhosis (PBC) is a chronic and progressive autoimmune liver disease with no known etiology. This disease is mainly characterized by granulomatous destruction of intrahepatic biliary ducts, severe peri-portal inflammation, and ultimate progress to liver fibrosis and cirrhosis. Here, we report a five-year-old girl diagnosed with PBC, presented to us with end-stage liver disease for liver transplantation. Our patient successfully underwent liver transplantation with an uneventful recovery. This case highlights the need for awareness to report further PBC cases in the pediatric age group.

Case presentation: A five-year old female child presented with a 6 months history of progressive jaundice. She had multiple admissions for hepatic encephalopathy and this time she was admitted for hepatic transplantation. On examination, she was icteric and had hepatomegaly. After thorough workup, she underwent successful hepatic transplantation and was alright post-operatively. At 6 months follow up, she is doing well.

Conclusion: PBC is rare in childhood. The natural history and exact incidence of PBC in childhood are not known. Hence, there is a need for awareness to report further PBC cases in the pediatric age group.

1. Introduction

Primary biliary cirrhosis (PBC) is a chronic and progressive autoimmune hepatic disease with no known etiology, and usually has positive anti-mitochondrial antibodies (AMA) in approximately 90% of cases [1], but those with negative AMA, typical histopathologic features on biopsy have a key role in the diagnosis of the disease [2].

This disease starts with autoimmune granulomatous destruction of intrahepatic biliary ducts and severe peri-portal inflammation, and ultimate progress to hepatic fibrosis and cirrhosis [1].

The incidence of PBC is 2.7–3.5 cases per 10,0000 people per year, and predominantly affects middle aged women between 30 and 50 years of age [3].

PBC at a young age has very rarely been reported in the literature. Invernizzi et al. published a case report of AMA positive PBC in a three-year-old girl [4] and also, another case was published in the literature of a 12 years old young female [5].

Here, we report AMA positive PBC case in a five-year-old female kid presented to our unit with end-stage liver disease for liver transplantation.

This work has been reported in line with the SCARE 2020 criteria [6].

2. Case presentation

A five-year old female child presented with symptoms of progressive jaundice, body aches, and history of multiple hospital admissions for hepatic encephalopathy for six months. On examination, she was pale, icteric, and had enlarged liver on abdominal palpation.

Her routine blood tests revealed hemoglobin level of 9.6 g/dl. Liver function tests showed raised serum bilirubin (17.2 mg/dl) with a high level of direct bilirubin. Alkaline Phosphatase level was raised 5 times that of normal value and serum Gamma Glutamyl Transpeptidase (GGT) was also elevated (Table 1). The auto-immune profile showed positive PBC-specific Anti-nuclear antibodies (ANA) and positive AMA. Other serological markers like anti-smooth muscle Antibodies were negative. Alpha-fetoprotein level was also elevated with a value of 467.7 ng/ml. Serum Copper, Ceruloplasmin level, urinary copper, and Alpha-1 Anti-trypsin were all normal. Viral markers for Hepatitis B and Hepatitis C virus were not detected.

Fibro scan showed F4 Fibrosis. While Tri-phasic CT abdomen revealed irregular liver having size of 12.3 cm, with caudate and left lobe hypertrophy. Small progressive enhancing areas were also found in both lobes of the liver likely to be focal fat sparing areas. Spleen size was 8.0 cm and Portal vein was patent (Fig. 1).

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Table 1
Showing routine laboratory findings.

Laboratory	Result	Reference range
WBC (cells/mm^3)	8420	4000-11,000
Hemoglobin (g/dl)	9.6	11.5-15
Platelet count (cells/mm^3)	203 × 10^9	150-400*10^9
Albumin (g/dl)	2.4	3.4-5
Total bilirubin (mg/dl)	17.2	1.2-2
Direct bilirubin (mg/dl)	12.5	
Aspartate aminotransferase (U/L)	593	<45
Alanine aminotransferase (U/L)	440	9.4 to 36
Alkaline phosphatase (U/L)	1496	65-306
Gamma GT (U/L)	320	7-31.5
International normalized ratio	3.18	1-5

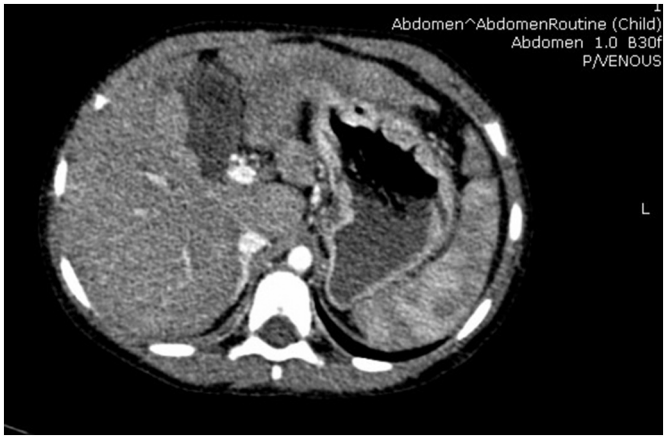

Fig. 1. CT scan of abdomen showing irregular enlarged liver.

She was planned for liver Transplantation (Living Donor). The donor was his brother. She underwent surgery with a left lobe graft (Graft weight was 314 g and GRWR of 1.9). A single Left Hepatic Artery, Left Portal Vein, and Left Hepatic duct were implanted with no per and post-operative complications. Explant liver histopathology report showed inflamed biliary duct epithelium with cytoplasmic vacuolization, nuclear disarray, and infiltration by inflammatory infiltrates (Fig. 2). The portal tracts were surrounded by moderate mixed inflammatory infiltrates, predominantly comprising lymphocytes, few neutrophils, and plasma cells (Fig. 3). The hepatocytes showed prominent irregular cirrhotic nodules (biliary type cirrhosis) with lymphocytic interface activity (Fig. 4). Areas of cholestasis were also found. No evidence of malignancy was found. Overall features were suggestive of primary biliary cirrhosis.

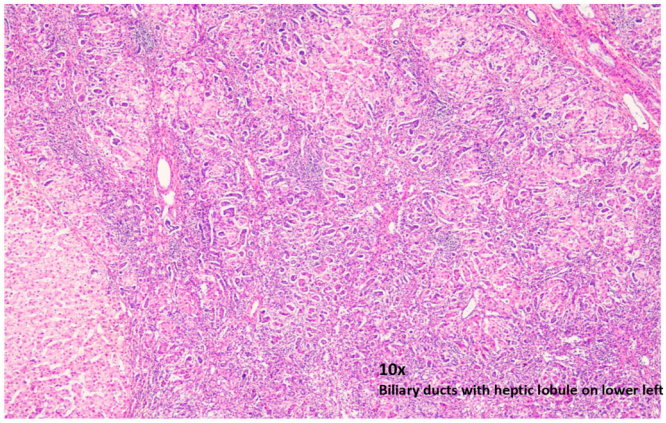

Fig. 2. Showing inflamed biliary ducts with hepatic lobule.

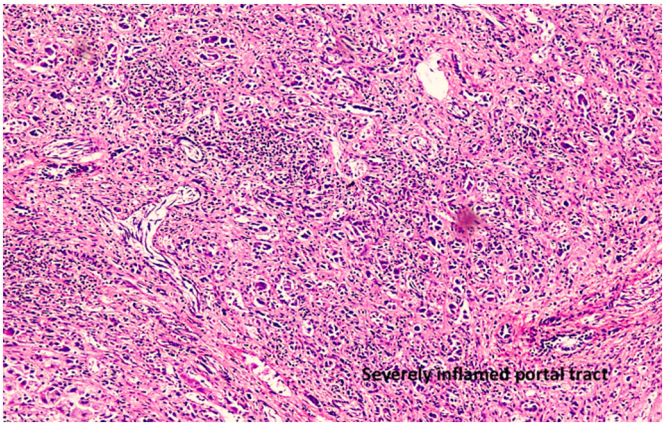

Fig. 3. Showing severely inflamed portal tract.

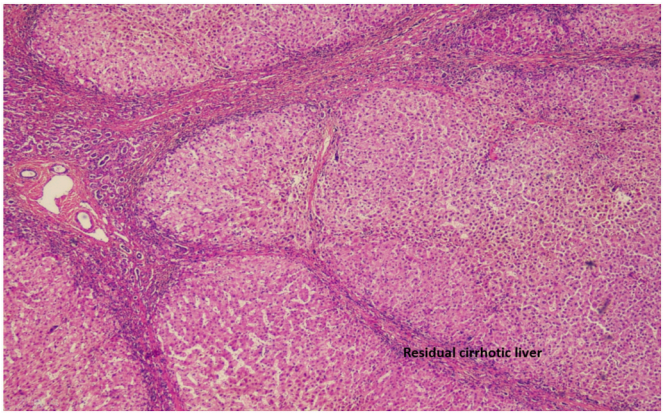

Fig. 4. Showing cirrhotic changes.

At 6 months initial follow up, she is fine.

3. Clinical discussion

Almost 60% of PBC cases remain asymptomatic, usually for ten to twenty years, and are incidentally diagnosed [7]. Common Symptoms of PBC are pruritus, fatigue, jaundice. Systemic manifestations of this disease include rheumatoid arthritis, thyroid disorders, scleroderma, systemic lupus erythematosus, glomerulonephritis, and polymyositis. Dividing the disease into pre-cirrhotic and cirrhotic phases is essential for management [1].

The serologic hallmark of PBC is AMA in 90% of cases, which is having a rare association with other diseases. Titers of >1: 40 are usually found in PBC [1]. Also, PBC negative AMA is possible [2]. Other laboratory markers include high serum alkaline phosphatase level and elevated serum GGT levels. Magnetic resonance cholangiopancreatography and computed tomography are done in suspected cases to exclude other differentials. Biopsy of the liver is not mandatory as needle biopsy in majority of cases may not be representative of the true disease [1].

Rubin et al. defined four successive patho-morphologic stages of this disease, i.e., portal, peri-portal inflammation, septal scarring, and finally the fibrotic cirrhotic stage [8]. In PBC often different grades of severity is seen in various areas of the liver, hence staging with a needle biopsy will be rarely helpful. Occasionally all four stages can be present in explant liver specimens. Hallmark histologic finding includes epithelioid cell granulomas with damaged bile ducts [9].

Criteria defined by American Association for the Study of Liver Diseases (AASLD) for patients with suspicion of PBC should have two of the following three parameters: high alkaline phosphatase level, positive

AMA serology, and liver biopsy showing non-suppurative intrahepatic biliary duct destruction [10]. Our patient was having increased alkaline phosphatase and GGT levels, positive AMA and supportive biopsy features making the diagnosis of PBC in a non-usual age presentation.

Regarding treatment, uptill now no specific medical therapy/treatment is available. The Food and Drug Administration (FDA) has approved Ursodeoxycholic acid for PBC patients, with a dose of 15 mg/kg/day. In the advanced stage of the disease, treatment combinations of prednisolone or azathioprine can be considered with Ursodeoxycholic acid. Liver transplantation is the treatment of choice for PBC patients with end-stage liver disease [11]. Our patient was also having decompensated liver disease, so she underwent a liver transplantation procedure. The hepatobiliary consultant performed the procedure. PBC has a rare presentation in the younger age group. However, other autoimmune diseases e.g., autoimmune hepatitis, are well-known causes of chronic liver disease in childhood [3].

Our patient was having favorable histopathology findings, raised serum alkaline phosphatase and bilirubin levels, and positive AMA. All these pieces of evidence supported the diagnosis of PBC according to the AASLD guidelines.

4. Conclusion

The natural history and exact incidence of PBC in childhood are not known. And there is a need for more awareness to report further PBC cases in the pediatric age group. So, these cases can be diagnosed and managed on time.

5. Patient perspective

My daughter was suffering from yellow discoloration of my eyes and the itching was a misery. I took her to the hospital on multiple occasions and she was treated momentarily. But when her disease condition worsened, we took her to the organ transplant center where she was managed in expert hands and so she underwent a liver transplant. My son donated her this gift of life. We were quite satisfied by the level of care she received, and she is feeling quite well now.

Ethical approval

Pir Abdul Qadir Shah Jeelani Institute of Medical SCIENCES, Gambat, Sindh, Ethical Committee.

Sources of funding

N/A.

Author contribution

Kaleem Ullah: Study conception and design.
Shams Uddin: Acquisition of data.
Abdul Wahab Dogar: Performed the procedure, critical revision and overall supervision.
Zaka Ullah Jan: Drafting of manuscript.
Syed Hasnain Abbas: Review of discussion.

Guarantor

Kaleem Ullah.

Registration of research studies

N/A.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

None declared.

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