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PRIMARY BILIARY CHOLANGITIS- CAN IT BE A FUTURE OBSTETRIC CHALLENGE?

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ABSTRACT
Background: Primary biliary cholangitis (PBC) is an autoimmune mediated liver disease which can progress to fatal cholestatic disease. The peak incidence occurs in fifth decade, and it is uncommon in persons under 25 years of age. We report our experience with diagnosis of primary biliary cholangitis in a young woman and discuss her possible obstetric outcome.
Case presentation: A 24-year-old unmarried girl was evaluated for abdominal pain, abdominal distension, and jaundice. Haematological, biochemical, autoimmune investigations and imaging done. She was diagnosed with hyperbilirubinemia, moderate anaemia and a large ovarian cyst and splenomegaly. Anaemia improved with Vitamin B12 supplementation. The patient underwent ovarian cystectomy along with liver biopsy. Histopathology of liver biopsy showed evidence of primary biliary cholangitis and that of ovarian cyst was suggestive of serous cystadenoma. The patient was started on ursodeoxycholic acid. A multidisciplinary approach to the patient and an opportunity for liver biopsy led to the diagnosis.
Conclusion: This case is unique in nature of presentation as it is diagnosed in a woman of 24 years even before childbearing. Literature review showed that PBC is well tolerated in pregnancy, except in cases with oesophageal varices. Ursodeoxycholic acid offers hepatoprotection in pregnancy although it will not reduce serum level of bile acids.

***Keywords*:** *Primary Biliary Cirrhosis, Jaundice, Pregnancy, Chronic Liver Disease*

INTRODUCTION

Primary biliary cholangitis is a chronic, progressive, and often fatal cholestatic liver disease, characterized by the destruction of small intrahepatic bile ducts along with portal inflammation and scarring, and the eventual development of cirrhosis and liver failure (Campbell & Faust, 2006). Its peak incidence occurs in the fifth decade of life and is uncommon in persons under 25 years of age **(**Kaplan, 1987**).** We report a case that involved a benign ovarian cyst and moderate anaemia which we encountered and was a diagnostic challenge.

CASE

A 24-year-old unmarried female patient presented to the OPD with a history of abdominal pain. She was asymptomatic for one week before presenting for which ultrasound abdomen and pelvis was advised and it showed a large cystic abdominopelvic mass arising from left ovary. Other than the above symptom, patient did not have any further complaints. Physical examination revealed mild icterus and mild pallor. Abdominal distension was noted with no shifting dullness.

Investigations

Laboratory data revealed hemoglobin of 8 gm%. Total leukocyte count- 7200/mm3, platelet count- 3.54lakhs/mm3. Reticulocyte count is-10.2%. Serum LDH- 532 U/L. Red cell indices showed increased MCV, which was confirmed by macroovalocytes in the peripheral smear along with few ovalocytes and tear drop cells. Polychromasia was also noted. WBCs and platelets were normal. Vitamin B12 level was measured, which was reduced to -222 pg/mL. Both direct and indirect Coomb's tests were positive, and ANA was negative. She was treated with parenteral Vitamin B12, and anaemia improved.

The biochemical parameters showed total bilirubin5.13 mg/dL. The indirect fraction of bilirubin was measured to be 3.96 mg/dL. The transaminases- ALT and AST were 86 U/L and 78U/L respectively. Total protein in serum was 7.1 g/dL and albumin- 3.9 g/dL. Alkaline phosphatase levels were 140 U/L. Serology for hepatotropic viruses (A to E) was negative.

Ultrasound of abdomen and pelvis showed a large cystic lesion in central abdominal cavity extending from pelvis to epigastric region of 25 x 18 cm. Splenomegaly was present. CA-125 and CEA levels were 7.35 IU/mL and < 0.5 IU/mL respectively. CT abdomen and pelvis showed large cystic mass lesion arising from left ovary suggestive of benign ovarian neoplasm along with splenomegaly. Mild intrahepatic bile duct dilatation was also noted.

Autoimmune hepatitis profile was done because of the transaminitis with IHBRD. Antimitochondrial antibody (M2) was positive. As the patient's LFT did not show any improvement with supportive therapy during the waiting period for surgery- it was decided to perform liver biopsy intraoperatively. She underwent laparotomy (Figure 1) with para ovarian cystectomy and intraoperative liver biopsy. The frozen section of the cyst showed serous cystadenoma and HPE revealed benign serous cystadenoma of the left ovary.

Liver biopsy (Figure 2) showed maintained architecture of liver parenchyma; subcapsular scattered neutrophils were noted. Bile duct reduced in number with ductulitis, few ducts showing infiltration by lymphocytes. The Periportal region shows moderated chronic inflammation with lymphocytes and plasma cells. Lymphoid follicles are also seen, with few with germinal centres. The periportal region showed increased fibrosis which is confirmed by Retic stain (Figure 3). Focal intrahepatic cholestasis was also seen without any evidence of granuloma or malignancy.

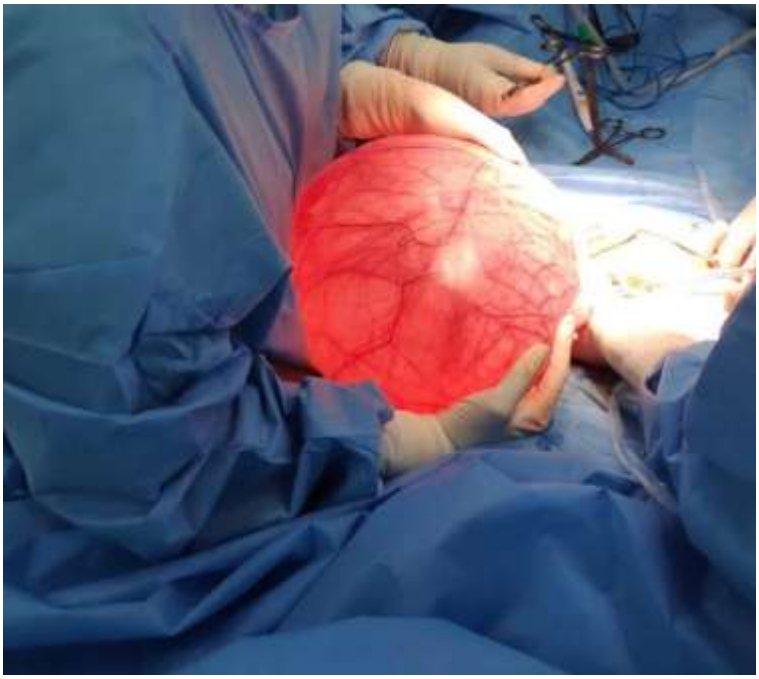

Figure 1: Intraoperative image showing delivery of the large ovarian cyst

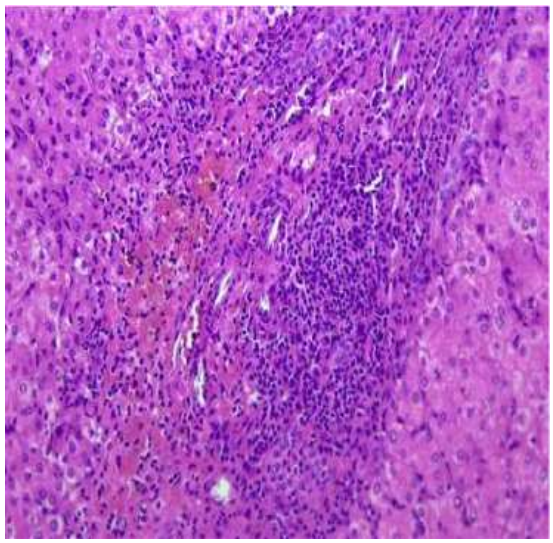

Figure 2: Lymphocytic infiltration of bile ducts

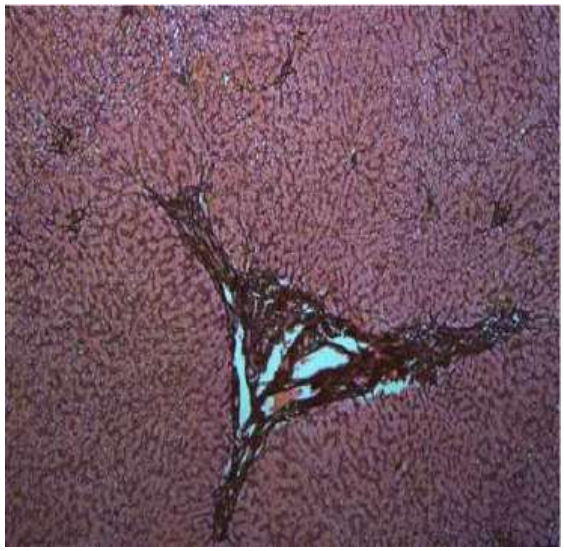

Figure 3: Retic stain showing dense fibrosis of periportal region

DISCUSSION

Primary biliary cholangitis (PBC; previously mentioned as primary biliary cirrhosis) is described by a T-lymphocyte-mediated attack on small bile ducts within the lobules of liver (Poupon, 2021). This may occur at different rates and with varying degrees of severity in different patients. The loss of bile ducts leads to reduced bile secretion and the retention of toxic substances within the liver, causing further hepatic damage, fibrosis, cirrhosis, and eventually, liver failure (Kaplan,1987). This disease is a cause for chronic illness and disability.

The disorder and its natural history has been more correctly described after the term was changed to primary biliary cholangitis (Beuers *et al.*, 2015). The reported prevalence varies from 19 to 402 cases per million persons (Kim *et al.*, 2000), (Sood *et al.*, 2004).

Most of the patients (90 to 95 per cent) are women, and majority them are diagnosed between the ages of 30 and 65 years (often in their 40s or 50s), though the disease has been reported in women as young as 15 years and as old as 93 years (Kaplan,1987), (Dahlan *et al.*, 2003), (Lleo *et al*, 2008) . Around 60 per cent

of patients with PBC are without any notable symptoms at diagnosis and are encountered due to abnormal liver function tests collected for other reasons (Prince *et al.,* 2003).

Fatigue and pruritus are the most prevalent symptoms. Right upper quadrant discomfort and malabsorption are less common manifestations. Skin findings such as hyperpigmentation, excoriations, xanthelasmas, and jaundice are common. Jaundice is a later manifestation of the disease but can be seen at presentation in some patients. Hepatomegaly and splenomegaly are common as the disease progresses, and the late is a sign of portal hypertension (Poupon, 2021).

Common laboratory test abnormalities in patients with PBC include elevated alkaline phosphatase, antimitochondrial antibodies (AMA), antinuclear antibodies (ANA), and hyperlipidemia. It may also include mild elevations in the aminotransferases and an elevated bilirubin level (Poupon, 2021).The common complications of PBC are cirrhosis, hepatocellular carcinoma and metabolic bone diseases.

A diagnosis of PBC (Lindor *et al.,* 2019) is established if there's no extrahepatic biliary obstruction, no comorbidity affecting the liver, and a minimum of two of the subsequent are present:

● An alkaline phosphatase a minimum of 1.5 times the upper limit of normal

● Presence of antimitochondrial antibodies (AMA) at a minimum titre of 1:40 (or presence of other PBC specific autoantibodies [sp100 or gp210], if AMA is negative)

● Histopathological confirmation of PBC (destructive cholangitis without suppuration and destruction of interlobular bile ducts)

Histologic findings in PBC are put on a scale of zero to four (Ludwig *et al.,* 1978)

Stage 0: Normal liver

Stage 1: Inflammation and/or abnormal connective tissue limited to the portal areas

Stage 2: Inflammation and/or fibrosis restricted to portal and periportal areas

Stage 3: Bridging fibrosis

Stage 4: Cirrhosis

Treatment with Ursodeoxycholic acid (UDCA) is associated with improved outcomes and quality of life in patients with PBC. Factors associated with a worse prognosis include the presence of symptoms at the time of diagnosis, elevated alkaline phosphatase and bilirubin levels, more advanced histologic stage, presence of antinuclear antibodies, cigarette smoking, and certain genetic polymorphisms (Poupon, 2021)

As an unmarried girl of the reproductive age group, the concern would be regarding its impact on her future obstetric outcome and maternity care. Literature reviews show that pregnancy with primary biliary cholangitis is well tolerated. Women are likely to have favourable outcomes as per studies (Cauldwell *et al.,* 2020), (Trivedi *et al.,* 2014), (Ludvigsson *et al.,* 2014) . But those with cirrhosis are more likely to have maternal complications if they have underlying oesophageal varices (Hagstrom *et al.,* 2018). Incidences of preterm delivery is high in the women with PBC, is around 27% (Cauldwell *et al.,* 2020), specifically in those with maternal serum bile acid concentrations ≥40μmol/L (Ovadia *et al.,* 2019). *The UK* PITCHES trial showed that although there is no amelioration in bile acid concentration with Ursodeoxycholic acid use in women with ICP in pregnancy, it may provide hepatoprotection for mothers with PBC (Chapell *et al.,* 2019)

The current case we reported is unique by its nature of presentation-primary biliary cholangitis in a young woman of 25 years, even before childbearing which is rare. She also had moderate anaemia which had to be thoroughly evaluated before a surgical intervention for the ovarian cyst and liver biopsy could be done. Operative intervention for the ovarian cyst paved the way for a good liver biopsy tissue and thus diagnosis in this case. It is prudent to consider intraoperative liver biopsy in a patient undergoing surgery in favourable circumstances.

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