"Case Report: Primary Sclerosing Cholangitis (PSC) Manifestation During Pregnancy Complicated by Liver Cirrhosis"

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ABSTRACT

Background: Liver disease imposes a considerable risk to both the mother and the fetus during pregnancy and may develop inadvertently during pregnancy. Primary sclerosing cholangitis (PSC) is a rare cause of liver disease in pregnancy. PSC is an uncommon chronic cholestatic liver disease characterized by inflammatory damage of the intrahepatic and/or extrahepatic bile ducts, which results in bile stasis, fibrosis, and ultimately cirrhosis.

Case Description: We present here a unique case of PSC that was diagnosed 2 months postpartum as the patient presented to the gastroenterology clinic with pruritis that did not subside after delivery. Clinical observations noted a jaundiced appearance and underweight status. Laboratory investigations also revealed elevated enzyme levels. Serology tests for hepatitis and the human immunodeficiency virus returned negative results. Magnetic resonance cholangiopancreatography imaging revealed an enlarged liver with intrahepatic biliary dilatation and strictures, accompanied by multiple varices and splenomegaly, indicative of primary sclerosing cholangitis with early cirrhotic changes. This confirmed the diagnosis of PSC complicated by liver cirrhosis. The patient was effectively managed with ursodeoxycholic acid at a dosage of 250mg orally three times a day and mesalazine at 1g three times a day; however, due to the cirrhotic stage, the patient was additionally referred to a transplantation facility.

Conclusion: In pregnancy, as a body undergoes various physiological and hormonal changes, pregnant patients may present with symptoms of liver diseases, which normally subside after delivery. However, diagnosis and occurrence of PSC during pregnancy is quite rare but cannot be ignored. Therefore, critical attention shall be paid to pregnant women who report any fluctuations in liver enzymatic levels or complain of pruritis, as late diagnosis can lead to severe complications and maternal and fetal mortality.

Keywords: liver, disease, PSC, pregnancy, diagnosis

INTRODUCTION

Liver disease imposes a considerable risk to both the mother and the fetus during pregnancy. Preeclampsia, hemolysis, high liver enzymes, low platelets (HELLP) syndrome, obstetric cholestasis, hyperemesis gravidarum, and acute fatty liver disease are among the liver diseases that typically manifest during pregnancy and are particular to it (1). Due to these diseases' shared symptoms, diagnosing liver disease during pregnancy can be challenging. Liver disease may develop inadvertently during pregnancy. Primary sclerosing cholangitis (PSC) is a rare cause of liver disease in pregnancy (2).

PSC is an uncommon chronic cholestatic liver disease that sometimes may necessitate liver transplantation as well. It is characterized by inflammatory damage of the intrahepatic and/or extrahepatic bile ducts, which results in bile stasis, fibrosis, and ultimately cirrhosis (3). PSC is seldom identified for the first time during pregnancy. While pregnancy-related factors should be considered, the timing of symptoms plays a significant role in identifying the underlying cause. PSC has no known cure that can slow down the spread of the disease. This may be due to its rare occurrence. A multidisciplinary team is needed to manage PSC during pregnancy to maximize results for both the mother and the fetus (4).

Before PSC is diagnosed, liver-related symptoms are commonly seen during pregnancy, and in certain patients, pregnancy may reveal the pre-clinical stage of PSC. In patients with known PSC, increasing symptoms during pregnancy may be associated with death and unfavorable long-term clinical outcomes from liver transplantation. The existence of more severe liver disease during pregnancy may be related to this. Pregnant patients with deteriorating symptoms have a worse transplant-free survival rate (5). We present here a unique case of PSC that was diagnosed 2 months postpartum as the patient presented to the clinic with pruritis, which did not subside after delivery.

CASE PRESENTATION

A forty one-year-old Saudi female, married and mother of four children, presented at the Gastroenterology Clinic two months after giving birth, reporting a persistent generalized pruritus that initiated a few months prior, initially localized to her hands and feet before spreading across her entire body. She did not have a history of any chronic illnesses except a prior admission to the Maternity and Children's Hospital due to elevated liver enzymes. An abdominal ultrasound conducted during the admission revealed the presence of minute gallstones; however, surgical intervention was not advised. The patient was discharged with prescribed medications. There is no documented history of

intensive care unit admissions or blood transfusions. The patient is not currently taking any medications and has no reported allergies. Additionally, there is no familial background concerning liver disease or malignancy.

Despite consulting multiple dermatologists and trying various topical creams providing temporary relief, her condition did not improve. The pruritus intensified during pregnancy, escalating throughout the day with heightened severity at night, disrupting her sleep. Concurrently, she observed yellowish discoloration in her eyes accompanied by dark urine. Post-delivery, she sought care at the Primary Health Center for the pruritus, which led to a referral to the gastroenterology clinic due to elevated liver enzyme levels. Furthermore, she reported a history of chronic watery diarrhea, occurring 4-5 times per day, occasionally presenting with blood. This was associated with an unintentional weight loss of approximately 13 kg over a span of 1 year.

Upon admission, the patient underwent a thorough examination. Clinical observations noted a jaundiced appearance and underweight status. The patient remained conscious, alert, and fully oriented. Vital signs were within normal ranges. Generally, no stigmata is suggestive of a liver disease observed during the examination. The abdominal exam revealed a soft, lax, and non-tender abdomen with visible striae and scratching marks. Splenomegaly was detected, noted to be firm, and positioned approximately three fingers below the costal margin. Dullness was observed during percussion. Additionally, the liver was enlarged, approximately two fingers' breadth below the costal margin, displaying a firm and smooth texture, and was non-tender. Auscultation revealed normal bowel sounds.

Laboratory analyses indicated elevated levels of aspartate transaminase (100 U/L), alanine transaminase (105 U/L), and alkaline phosphatase (782 U/L). Total serum protein was 37 g/L, while albumin measured 377 g/L. The coagulation profile remained within the normal range. Serology tests for hepatitis and human immunodeficiency virus yielded negative results. The immunological profile revealed an elevated erythrocyte sedimentation rate (65 mm/h), while antinuclear antibody and celiac disease markers were negative. Notably, specific antibody tests including anti-mitochondrial antibody, liver-kidney microsomal antibody, and anti-smooth muscle antibody were unavailable at the hospital. Magnetic resonance cholangiopancreatography (MRCP) imaging revealed an enlarged liver with intrahepatic biliary dilatation and strictures, accompanied by multiple varices and splenomegaly, indicative of primary sclerosing cholangitis with early cirrhotic changes. Subsequent to the radiological investigation, endoscopic evaluations were conducted. Upper GI endoscopy demonstrated a duodenal ulcer with grade I varices, and biopsy results were negative for H. pylori. Lower GI endoscopy revealed features consistent with pan-ulcerative moderate colitis **(Figures 1 and 2).**

The patient's management included the administration of ursodeoxycholic acid (UDCA) at a dosage of 250mg orally three times a day and mesalazine at 1g three times a day. Additionally, a referral was made to King Faisal Specialist Hospital-Riyadh for consideration of a liver transplant.

DISCUSSION

In 1867, Hoffman coined the term sclerosing cholangitis in medicine. Several case series were examined in the middle of the 1960s, documenting many other clinical traits of a PSC and demonstrating the association with inflammatory bowel disease. The era of the 1970s witnessed the widespread use of endoscopic retrograde cholangiography (ERCP), which significantly aided in diagnosis and specified the criteria for radiography, histopathology, and clinical evaluation. Subsequently, in suspected PSC cases, MRCP has been suggested as the primary diagnostic technique (6). The British Society of Gastereonology recommends that the primary imaging modality for the examination of suspected PSCs should be MRCP. Patients with biliary strictures who require tissue acquisition, such as cytological brushings, or who benefit from therapeutic intervention should only undergo ERCP (7). In our case, the diagnosis of PSC was also confirmed through MRCP. However, in our patient, no comorbidities, including autoimmune diseases, were detected at that time except the presence of gallstones.

Similarly, the findings of a meta-analysis concluded that for the diagnosis of PSC, MRCP has a very high specificity and high sensitivity. MRCP can often be used to diagnose suspected PSC cases, negating the need for ERCP and its attendant risks (8). Moreover, Selvaraj et al. commented that since MRI/MRCP allows for the simultaneous assessment of biliary anomalies and liver parenchyma, it is a more favorable option than ERCP as a marker of disease activity and prognosis in PSC. Interval MRI/MRCP changes in the morphological appearance of the liver and biliary tree are frequently utilized to infer whether the illness is stable or has advanced (9). The MRCP findings of our case exhibited an enlarged liver with intrahepatic biliary dilatation and strictures, along with splenomegaly. However, we assume that in our case, the late diagnosis of PSC may have led to the complicated stage of cirrhosis.

Our patient reported that pruritis significantly aggravated during the pregnancy and did not settle with any of the advised topical therapeutic modalities, hence leading to a referral to a gastroenterology clinic. Similar to our case, Slade et al. reported a case of a 28-year-old pregnant female who presented to the clinic with jaundice and pruritis. The MRCP findings showed dilatation of the intrahepatic duct, suggestive of PSC. Although she gave birth to a healthy baby and experienced spontaneous preterm labor, eleven months

after the birth, her health worsened, and she had to undergo a liver transplant (4). Ferrigno et al. described that compared to before the start of pregnancy and the postpartum period, women with PSC showed a higher risk of experiencing new or worsening pruritus throughout gestation. Pruritus can be quite debilitating and, if neglected, can lead to an early pregnancy induction. It's interesting to note that, despite the fact that pruritus was a common pregnancy symptom, it occurred in 25% of patients with primary biliary cholangitis and 14% of patients with PSC, although the rates of biochemical flare-ups in both diseases did not increase during gestation (10).

Unfortunately, in present times, there is no effective therapeutic strategy that can slow down the disease's progression or increase transplant-free survival. Novel pharmacological treatments have surfaced in recent times with the following objectives of altering the composition of bile; regulating immunity; focusing on the gut microbiome; and addressing fibrosis. However, the key to successful PSC therapy will probably be an individualized mix of various pharmacological modalities along with endoscopic care (11). The hydrophilic bile acid UDCA has been the subject of the most research studies among potential pharmaceutical therapies for PSC. However, its function in PSC management is highly debatable. At doses of 13 to 15 mg/kg per day, UDCA is anticipated to protect cholangiocytes against harmful hydrophobic bile acids by stimulating hepatobiliary secretion, preventing hepatocyte apoptosis caused by bile acid, and inducing antioxidants. Research has indicated that although high-dose UDCA may reduce hepatic inflammation and enhance liver biochemistry, it is unquestionably not beneficial for transplant-free survival (12).

Bjornsson et al. also stated that the non-steroidal FXR agonist Cilofexor, obethicolic acid, UDCA, and Aldafermin, a synthetic counterpart of FGF-19, are the most promising medical treatments that have shown success in phase II trials (13). Similarly, our patient was effectively managed with UDCA 250mg orally three times a day and Mesalazine at 1g three times a day. However, since the case was complicated by liver cirrhosis, an additional referral to the liver transplantation facility was also made. Since, for patients with life-limiting liver disease, which can manifest as primary hepatic malignancies, end-stage chronic liver disease, acute liver failure, or inborn metabolic abnormalities, liver transplantation is a vital therapeutic option (14).

It can be challenging to distinguish between intrahepatic cholestasis during pregnancy (ICP) and persistent cholestatic diseases. After delivery, ICP should completely subside, and liver tests should return to normal. If not, a suitable workup should be started to identify the underlying pathology. Both the mother and the child may experience severe morbidity or even death in the event of a missed diagnosis (15). In our patient, pruritis and elevated enzyme levels persisted 2 months postpartum, indicating that it was not the case with ICP and leading to further diagnostic imaging. Through this report, we highlight the importance of assessment of liver profile and diseases in pregnancy, additionally discussing the diagnostic and therapeutic strategies for effective management of PSC. Moreover, it is critically important to look out for these symptoms and conditions during pregnancy since they are associated with poor maternal and fetal outcomes. However, this report has certain limitations, and we were not able to define if the patient experienced liver problems or the status of liver enzymes in all past pregnancies. Secondly, we could not describe the follow-up to liver transplantation and its outcome.

CONCLUSION

In pregnancy, as a body undergoes various physiological and hormonal changes, liver-related disorders may be encountered or presented in clinical practice, and they normally subside after delivery. However, the diagnosis and occurrence of PSC during pregnancy is quite rare but cannot be ignored; therefore, critical attention shall be paid to pregnant women who report any fluctuations in liver enzymatic levels or complain of pruritis, as a late diagnosis can lead to severe complications and maternal and fetal mortality.

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AUTHORS' CONTRIBUTIONS

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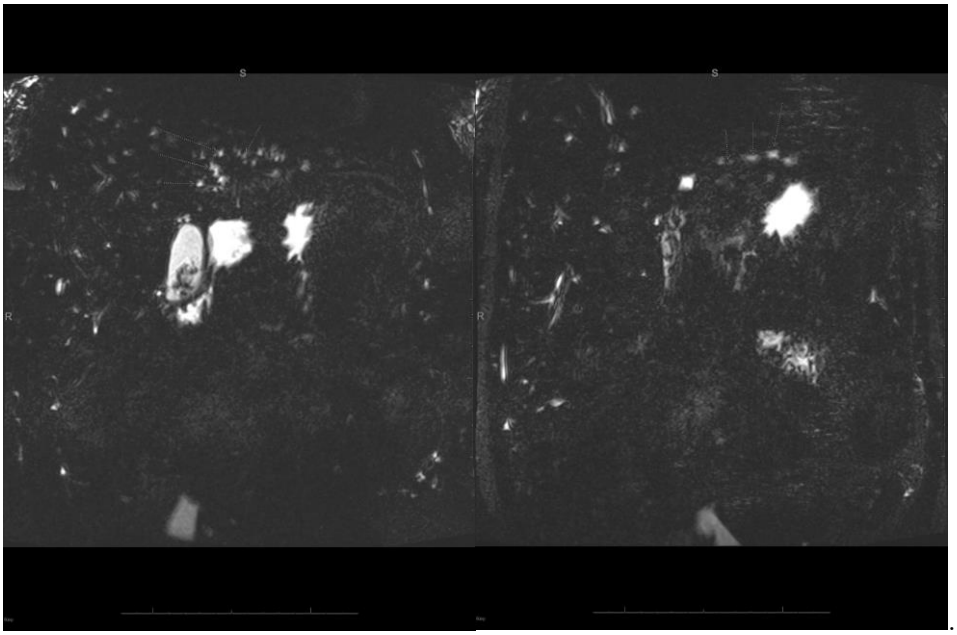

Figure 1 and 2: MRCP imaging revealed an enlarged liver with intrahepatic biliary dilatation and strictures, indicative of primary sclerosing cholangitis with early cirrhotic changes.