

Secondary Sclerosing Cholangitis During Pregnancy

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ABSTRACT

We report a case of secondary sclerosing cholangitis that manifested itself during pregnancy. A tentative diagnosis of intrahepatic cholestasis of pregnancy was considered, but after her third delivery, a liver biopsy and imaging, as well as review of past records, confirmed the diagnosis of secondary sclerosing cholangitis. Maternal and fetal outcomes of primary sclerosing cholangitis have been reported, and this case highlights the importance of considering other diseases besides the benign intrahepatic cholestasis of pregnancy as a cause of cholestasis in pregnancy.

INTRODUCTION

Common liver problems encountered during pregnancy include preeclampsia, hemolysis, elevated liver enzymes and low platelets in pregnancy syndrome, intrahepatic cholestasis of pregnancy (ICP), hyperemesis gravidarum, and acute fatty liver of pregnancy.¹ Among cholestatic liver diseases, maternal and fetal outcomes of primary sclerosing cholangitis (PSC) and primary biliary cirrhosis have been described.^{2,3} One case of secondary biliary cirrhosis in pregnancy has also been reported in the literature.⁴

CASE REPORT

A 24-year-old Hispanic woman without history of alcohol or drug abuse presented with symptoms of intermittent jaundice and itching 2 weeks after delivering her third child. Her past medical records revealed that she had a complicated cholecystectomy at age 13 years, when her cystic duct was noted to come directly off the left hepatic duct and was completely transected. The right hepatic duct was also injured, leading to a hepaticojejunostomy.

At age 15 years, she had forceps assisted vaginal delivery of a 3,401 g baby girl at 40-4/7 weeks of gestation. Five years later, she presented for the first time with itching and abnormal liver tests in the second trimester of her second pregnancy: aspartate aminotransferase (AST), 86 IU; alanine aminotransferase (ALT), 62 IU; alkaline phosphatase, 385 IU; and bilirubin, 0.4 mg/dL. She delivered a 2,494 g baby at 36-6/7 weeks of gestation, after labor was induced with prostaglandin suppositories. Liver tests were monitored twice after delivery showing AST, ALT, alkaline phosphatase, and bilirubin to increase to 210 IU, 288 IU, 601 IU, and 0.7 mg/dL but trended down 2 weeks later to 27 IU, 30 IU, 207 IU, and 0.3 mg/dL, respectively.

At age 23 years, she presented in the first trimester of her third pregnancy with upper abdominal pain and jaundice: AST, 177 IU; ALT, 127 IU; alkaline phosphatase, 1426 IU; and bilirubin, 4.6 mg/dL. She reported no problems between her second and third pregnancy. Liver ultrasound was again reported normal. She was treated with ursodeoxycholic acid (URSO) at 900 mg/d; however, at 33 weeks of gestation, she had premature rupture of membranes, and fetal bradycardia occurred, leading to an emergency low transverse cesarean section and delivery of a 2,109 g baby girl.

Hepatitis serologies were negative. Antinuclear, antimitochondrial antibody, antismooth muscle, and antineutrophil cytoplasmic antibodies (ANCA) were also negative. A magnetic resonance imaging study showed hypertrophied

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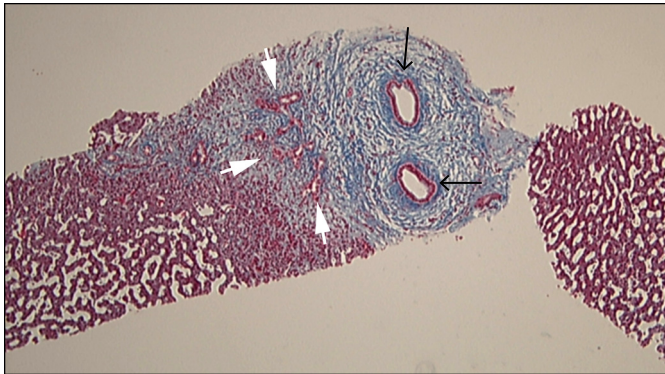


Figure 1. Portal tract with segmental bile ducts showing concentric fibrosis (black arrows). Proliferation of bile ducts is also seen (white arrow). Trichrome stain, 10x.

caudate lobe and splenomegaly. An ultrasound-guided liver biopsy showed bile duct damage and proliferation as well as classic onion skin appearance of the bile ducts (Figure 1). An endoscopic retrograde cholangiopancreatography through the native ampulla showed a 4-cm distal bile duct stump without any filling of the proximal biliary tree (Figure 2). The biliary anastomosis could not be reached despite inserting a

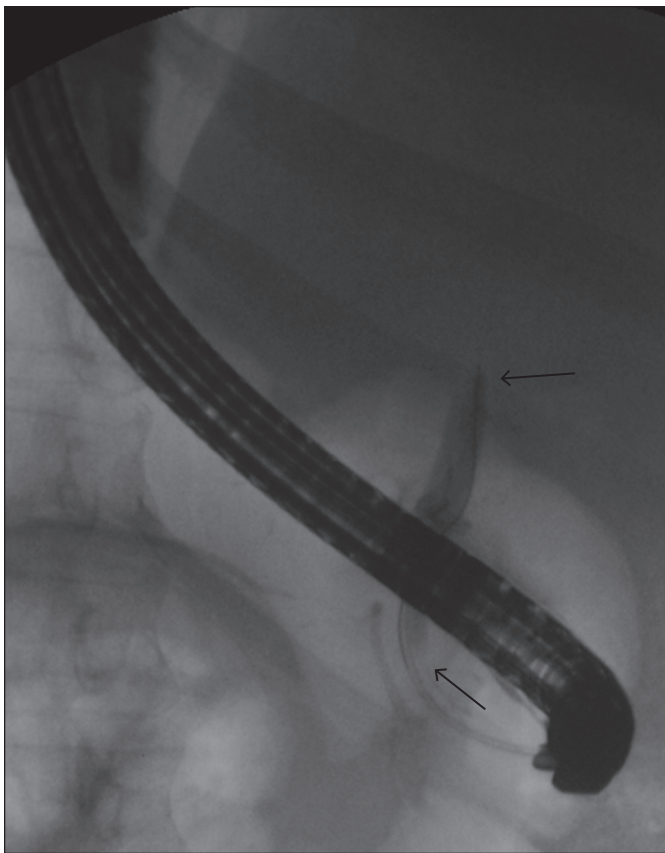


Figure 2. A fluoroscopy image of endoscopic retrograde cholangiopancreatography showing the distal bile duct duct stump (black arrows) without any filling of proximal bile ducts.

colonoscope 35-cm distal to the ligament of treitz. A percutaneous transhepatic cholangiogram showed narrowing of hepaticojunostomy, several stones in the remnant bile duct, and dilation of the intrahepatic biliary tree (Figure 3). Her colon biopsies did not reveal colitis.

At age 25 years, she presented with upper gastrointestinal bleeding related to esophageal varices and required band ligation; otherwise, her liver function remained relatively preserved while she was being treated with ursodeoxycholic acid at 1500 mg/d: AST, 163 IU; ALT, 79 IU; alkaline phosphatase, 725 IU; bilirubin, 1.5 mg/dL; and albumin, 3.9 g/dL.

DISCUSSION

This is the first report of secondary sclerosing cholangitis (SSC) manifesting itself during pregnancy. A case of secondary biliary cirrhosis has been reported, where a 33-year-old Asian patient with recurrent pyogenic cholangitis was diagnosed with secondary biliary cirrhosis and delivered a healthy 2800-g baby at 37 weeks of gestation, despite having hepatic decompensation.⁴

In the described case, sclerosing cholangitis developed as a consequence of chronic biliary obstruction. A presumptive diagnosis of ICP was made until the review of her medical records revealed a history of complicated cholecystectomy. Further workup documented anastomotic biliary stricture on percutaneous transhepatic cholangiogram and cholestasis as well as classic hepatic fibrosis on the liver biopsy. The

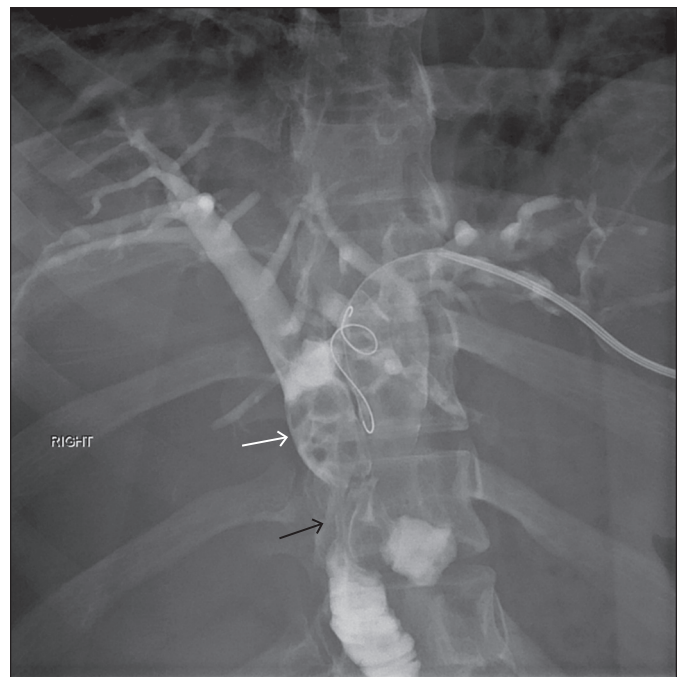


Figure 3. Bile duct stones (white arrow), anastomotic stricture (black arrow), and dilation of intrahepatic biliary tree.

absence of ANCA and normal colon histology further support a diagnosis of SSC instead of PSC. Nonetheless, both PSC and SSC are chronic diseases with similar phenotypical, clinical, and cholangiographic features, except in SSC, a cause of biliary obstruction such as biliary stones, iatrogenic bile duct injury (as in this case), chemotherapy, trauma, and chronic pancreatitis is identified. Only 31 cases of SSC were identified at Mayo Clinic Rochester after a diligent follow-up over a decade indicating the rarity of SSC.^{5,6} Cholestatic liver diseases like primary biliary cirrhosis and PSC have been reported to exacerbate or manifest during pregnancy, and no association of these disorders with hormonal changes in pregnancy has been described.^{2,7}

Other differential diagnoses of cholangitis include Asian cholangitis and AIDS-related cholangitis. However, our patient migrated to United States from Mexico and tested negative for HIV. Asian cholangitis or recurrent pyogenic cholangitis can result in biliary stricture formation, chronic biliary obstruction, hepatic fibrosis, and SSC.^{8,9} Nonetheless, the most common cause of recurrent jaundice during pregnancy is ICP, which is a unique disorder associated with pregnancy, most likely related to hormones, presents in the second or third trimester of pregnancy, runs an indolent course, and frequently resolves after delivery.¹

A review of medical literature reveals that fetal loss, preterm delivery, cesarean section, and vacuum-assisted delivery can occur among pregnant PSC patients.^{3,7,10} For such patients, high dose URSO, combination of URSO and prednisone, and endoscopic therapy have been utilized to reduce itching, fetal complications and relief of biliary obstruction.¹¹⁻¹³

As this case highlights, differentiating chronic cholestatic disorders from ICP of pregnancy can be a daunting task. Intrahepatic cholestasis of pregnancy should completely resolve with normalization of liver tests after delivery; however, if liver tests remain abnormal, appropriate workup should be initiated to diagnose the underlying pathology. In the case of a missed diagnosis, significant morbidity and even mortality are possible for both the mother and the baby.

DISCLOSURES

Author contributions: A. Nadir supervised manuscript writing and is the article guarantor. Y. Abdulqader collected the data, reviewed the chart, and wrote the manuscript. K-Y. Chuang and J. Ravi formatted the images and edited the manuscript.

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Informed consent was obtained for this case report.

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