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Primary biliary cholangitis: a rare diagnosis during pregnancy

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Abstract

Primary biliary cholangitis is an autoimmune disease that mostly affects women. It is uncommon in women of childbearing age and the diagnosis during pregnancy is rare and can be challenging. Described here is a case of primary biliary cholangitis first manifesting during pregnancy, with the onset of pruritus, jaundice, biochemical liver abnormalities and positive antimitochondrial antibodies. Although treatment with ursodeoxycholic acid was started at the time of diagnosis, there was a progressive worsening of cholestatic biochemical markers throughout pregnancy. In addition, fasting hyperglycemia with polyhydramnios was diagnosed, consistent with gestational diabetes. She had a spontaneous preterm delivery at 31 weeks of gestation, of a newborn who was admitted to the neonatal intensive care unit but who subsequently had no long-term sequelae of preterm delivery. A maternal postpartum flare occurred. Treatment with ursodeoxycholic acid was well tolerated during pregnancy and lactation.

Keywords

primary biliary cholangitis, liver disease, cholestasis, pregnancy

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Introduction

Primary biliary cholangitis (PBC), previously known as primary biliary cirrhosis, is a rare autoimmune cholestatic liver disease that is often progressive and can lead to cirrhosis and liver failure.[1] The hallmark of the disease is the presence of antimitochondrial antibodies.[1,2] It mostly affects middle age or elderly women; thus, its occurrence in women of childbearing age is rare and a first presentation during pregnancy is uncommon and challenging for the physician.[3] As in other autoimmune conditions, more data are needed to understand the course of the disease during and after pregnancy and its impact on maternal and fetal outcomes.

Case description

A 36-year-old Nepali woman was referred because of the development of pruritus and jaundice at 17 weeks of gestation. She had no previous relevant medical or surgical history and had never been pregnant before. Serial blood tests were performed showing direct hyperbilirubinemia and increased serum levels of liver enzymes, with a cholestatic predominance (see Figure 1). Bile acids were measured at 21 weeks and were high (91.1 µmol/L). Fasting hyperglycaemia was also identified, consistent with gestational diabetes. An abdominal ultrasound was performed revealing no signs of extrahepatic cholestasis or liver abnormalities. Acute viral hepatitis was excluded through serological tests and no medication or other potentially hepatotoxic agents were reported. Weakly positive fine speckled antinuclear antibody, increased immunoglobulin M and strongly positive antimitochondrial antibodies were identified, consistent with PBC.

Treatment with ursodeoxycholic acid (UDCA) was started at 750 mg/day (13 mg/kg/day). Initially, there was a slight improvement on the cholestatic parameters, which plateaued in the following weeks. Bile acids also improved to 40.2 µmol/L at 27 weeks. However, during the third trimester, there was a progressive worsening of the cholestatic biochemical abnormalities (bile acids 56.3 µmol/L at 29 weeks), raising the possibility of superimposed intrahepatic cholestasis of pregnancy (ICP). Her glucose control was satisfactory with dietary modification alone; however, the ultrasound assessment of fetal growth at 26 weeks revealed polyhydramnios (amniotic fluid index of 33.3 cm).

The patient was hospitalized at 27 weeks of gestation for maternal and fetal monitoring. During hospitalization, good glycaemic control was maintained with diet alone. Weekly ultrasound assessment revealed a decrease in amniotic fluid index (25 cm at 31 weeks). Fetal and maternal Doppler were always normal for gestational age.

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		Total Bilirubin (mg/dL)	Direct Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	GGT (U/L)	AP (U/L)	Bile Acids (μcmol/l)	Comments
Gestational age (weeks)	18-21	4.62	3.45	175	218	500	374	91.1	Start of UDCA
	24	2.16	1.6	90	81	345	419		
	27	1.91		167	192	465	613	40.2	
	29	2.06	1.48	152	230	472	646	56.3	
Delivery									
Time postpartum (months)	1	1.59	0.92	156	208	1431	1125		
	2	1.93	1.16	246	341	815	765		
	14	1.16		127	154	1106	577		
	21	0.6		85	91	788	413		

UDCA: ursodeoxycholic acid; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: γ-glutamyl transpeptidase; AP: alkaline phosphatase.

Figure 1. Biochemistry results.

At 31 weeks of gestation, the patient had a spontaneous onset of labour. Steroids for fetal lung maturation were given and she had a vaginal delivery of a male infant weighing 1515 g (15th centile on customised growth chart), with Apgar scores of 6, 8 and 8 at 1, 5 and 10 min, respectively. The infant was admitted to the neonatal intensive care unit and required continuous positive airway pressure ventilation for the first 8 days of life and high flow oxygen until day 11. He was discharged from the hospital 31 days after delivery.

The patient was evaluated postpartum, while breastfeeding. Her liver enzymes deteriorated after birth (Figure 1), compatible with her intermittent omission of medication. UDCA was restarted and she was referred to a Hepatologist. Seven months postpartum, a decrease in both alanine aminotransferase (ALT), and aspartate aminotransferase was observed while both levels of γ-glutamyl transpeptidase and alkaline phosphatase remained elevated. The patient again described intermittent use of her medication for economic reasons. A liver biopsy was performed 15 months after delivery and confirmed the diagnosis of PBC stage 2 of Ludwig/Scheuer classification.

Discussion

PBC is thought to be triggered by environmental factors in a genetically susceptible individual[1] which can occur during pregnancy when hormonal and immunologic conditions change.[3]

Pruritus is one of the most frequent symptoms in PBC, often worsening in pregnancies of affected individuals.[4] Jaundice and hyperbilirubinemia are usually present in more advanced disease.[5] However, the differential diagnosis of new-onset pruritus during pregnancy can be wide. In addition to viral infections and dermatological conditions, ICP must be considered, particularly in the third trimester.[3]

Pregnancy can make the diagnosis of underlying liver disease more challenging for the physician. Most diagnoses of PBC are made before or after pregnancy, with diagnosis during pregnancy being made rarely.[6] With improvements in immunologic diagnostic tools and biochemical screening methods, the identification of PBC appears to be increasing.[1]

Limited information is available regarding PBC in pregnancy and its outcomes, as well as the impact of pregnancy on the natural course of the disease.[2–4,6] Pregnancy in most women with PBC is uneventful, with clinical and biochemical remission or stability and no major adverse maternal outcomes.[2,4,7] However, postpartum flares are frequently reported (in more than 60% of pregnancies) (2,4). As was recently described, women with PBC also appear to have an increased risk of preterm birth (up to 33%) which might correlate with raised ALT at booking, peak bile acid concentration and bile acids near delivery.[7]

Indeed, in the present case initial ALT was raised and bile acids remained high throughout pregnancy (≥40 μmol/L), and a preterm birth occurred. However, other factors may have influenced the pregnancy outcome, importantly gestational diabetes complicated by polyhydramnios.

It is not clear whether women who manifest the first symptoms during pregnancy follow a different course compared to women with a previous diagnosis of PBC.

Rabinovitz et al.[6] in 1995 also reported a case of a woman who first presented with jaundice in the last trimester of pregnancy and was diagnosed with PBC stage 3 postpartum. This was followed by a clinical deterioration requiring referral for liver transplantation. The authors suggested a possible impact of pregnancy on the natural course of PBC and highlighted that PBC with symptom onset during pregnancy could have different outcomes than PBC diagnosed before gestation.[6] However, so far there is insufficient evidence and the impact of biochemical activation on disease progression is unknown.[2]

Lastly, this case supports previous data that UDCA is well tolerated during pregnancy and in the postpartum period (including lactation) with no reported adverse effects.[2,4,5,7]

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Ethical approval

Centro Hospitalar Universitário Lisboa Central does not require ethical approval for reporting individual cases or case series.

Informed consent

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Guarantor

Inês Felizardo Lopes is the guarantor for the present work.

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