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*CASE REPORT*

# Pregnancy in primary biliary cirrhosis complicated by portal hypertension: report of a case and review of the literature

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## Case report

A 39 year old woman came to the antenatal clinic for booking at the 12th week of her fifth pregnancy. She complained of pruritis, particularly over her hands and feet. The pruritis preceded her pregnancy by five months. There was no change in urine or stool colour and her appetite was good. Physical examination showed no abnormality. She had no rash, took no medication, and there was no family history of liver disease. She drank less than 15 units of alcohol per week before her pregnancy and had then become abstinent.

She had four previous pregnancies, the first pregnancy being complicated by pre-eclampsia at term, the second and third ending in miscarriages in the first trimester, and the fourth being an uneventful full term pregnancy. Five years previously she had attended her general practitioner with tiredness, nausea, headache, reduced appetite and her stool looking 'different'. Liver function tests revealed an elevated gamma-glutamyl transferase level at 112 iu/L. Ultrasound examination of her liver was normal. Liver function tests repeated one week later showed no change. As her symptoms had improved by the second consultation, no follow up was thought necessary. Her past medical history included infection with hepatitis A virus, and depression after her second miscarriage.

In this pregnancy liver function tests were abnormal (alkaline phosphatase 888 iu/L, alamine aminotransferase 101 iu/L, bilirubin 27 μmol/L). The differential diagnosis included cholestasis of pregnancy, primary biliary cirrhosis, cholelithiasis, primary sclerosing cholangitis and infiltrating diseases of the liver. She had IgG antibodies to the mitochondrial pyruvate dehydrogenase complex. A diagnosis of primary biliary cirrhosis was made.

We prescribed ursodeoxycholic acid 250 mg three times daily and cholestyramine 4 g twice daily from twenty weeks of gestation. Her liver function tests during her pregnancy are shown in Fig. 1. Her pruritus persisted, despite the improvement in her liver function tests. Chlorpheniramine 4 mg at night was added, without much benefit.

An ultrasound scan of the upper abdomen carried out at 30 weeks of gestation showed splenic varices, suggestive of portal hypertension. In view of the risk of rupture of oesophageal varices during delivery, we advised an elective caesarean section. Her coagulation screen was normal throughout her pregnancy. Vitamin K 10 mg per day was prescribed from the 26th week of gestation.

One week before to her delivery, she received two intramuscular injections of bethamethasone 12 mg, twelve hours apart[1], and an elective caesarean section was carried out in the 37th week of pregnancy. A female infant weighing 2.97 kg was born in good condition. She was able to breastfeed normally. There was no change in the woman's symptoms following her delivery. At the sixth week postpartum her liver function test had deteriorated, and she is receiving continuing care in the department of hepatology.

## Discussion

Primary biliary cirrhosis is a chronic disease of the liver characterised by slow progressive destruction of intrahepatic bile ducts, portal inflammation and scarring. It is a rare condition, with a prevalence of about 7.5 per 100,000. Ninety percent of patients with primary biliary cirrhosis are women aged between 35 and 60[2]. The usual symptoms are jaundice, fatigue and pruritis. Asymptomatic patients are usually identified by unexplained cholestatic liver function tests, with elevated serum alkaline phosphatase and gamma-glutamyl transferase. More than 90% of patients have the antibody to the pyruvate dehydrogenase complex, a tricarboxylic acid cycle enzyme found in the mitochondrial membrane; this is therefore a specific diagnostic test.

In women, primary biliary cirrhosis is associated with infertility. In a series of twelve patients studied by Ahrens and *et al.*[3], 11 had scanty, irregular or profuse periods and seven progressed to amenorrhoea[3]. Stellon and Williams[4]

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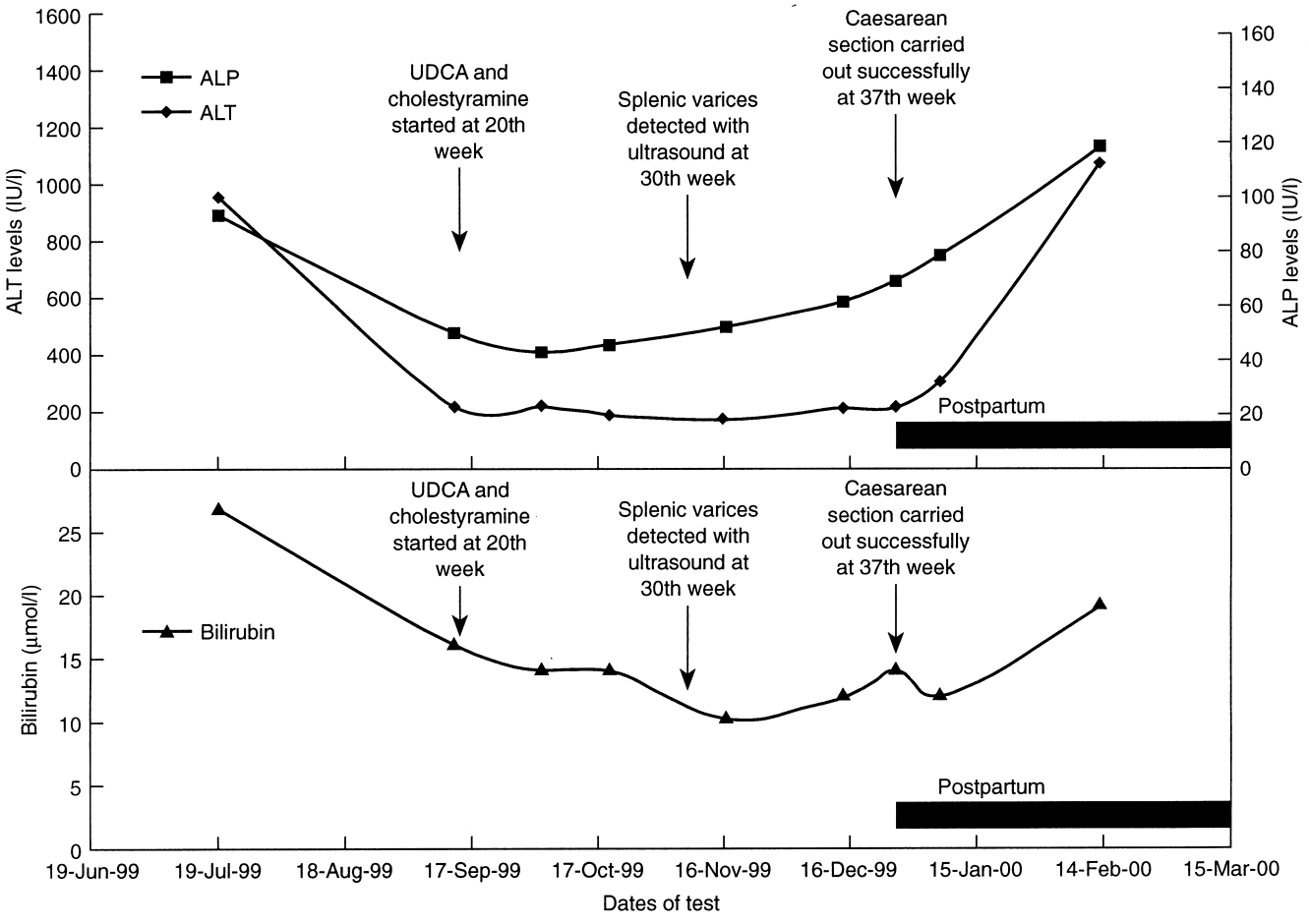


**Fig. 1**. Liver function tests in pregnancy and the postpartum period.

have also observed that women with primary biliary cirrhosis are more likely to undergo hysterectomy or dilatation and curettage for menstrual disorders when compared with age-matched healthy controls or women with other liver conditions.

The negative effect on fertility and the fact that primary biliary cirrhosis tends to affect women towards the end of their reproductive lives means that it is very rare for primary biliary cirrhosis to occur at the same time as pregnancy. Our knowledge of the interactions between primary biliary cirrhosis and pregnancy is thus scanty and effective treatment of this disorder in pregnancy has not yet been established.

Only 14 cases of pregnancy occurring in women with primary biliary cirrhosis have been reported in the English literature[3,5–10]. Six women had marked deterioration of liver function[5,9]. This was especially evident in the earlier series of Whelton and Sherlock[5], where all four pregnancies that progressed to the third trimester were complicated by worsening jaundice. Two other studies did not find deterioration of liver function during pregnancy[7,8]. Only two studies reported treatment of primary biliary cirrhosis in pregnancy[9,11]. It is not known whether pregnancy causes chronic deterioration of primary biliary cirrhosis.

Elevated levels of endogenous oestrogen can result in cholestasis[12]. Pruritis and jaundice with exogenous oestrogen (e.g. in oral contraception pills) occurs in women who are prone to cholestasis of pregnancy[13,14]. In Scandinavia cholestasis of pregnancy can affect 1.5% of all pregnant women[15]. Because of this effect of oestrogen on liver function it is probably wiser for women with primary biliary cirrhosis not to take the combined oral contraceptive pill.

Of the 14 pregnancies, 10 resulted in healthy children and there were four stillbirths or early miscarriages. The main risks to the infant in obstetric cholestasis are unexplained stillbirth and preterm labour. Fisk and Storey[16] studied 83 pregnancies complicated by idiopathic obstetric cholestasis between 1975 and 1984; 44% were premature and the perinatal mortality rate was 35/1000, considerably greater than the 11% preterm labour rate and the 12.7/1000 perinatal mortality rate reported in 1992 for all pregnancies in the United States[17].

Primary biliary cirrhosis almost certainly causes premature labour and stillbirth as with idiopathic obste-

tric cholestasis, but in addition there is a risk of portal hypertension. Ursodeoxycholic acid[18–20] and methotrexate[21] have been used with some success in the treatment of primary biliary cirrhosis in women who are not pregnant. Methotrexate, affects cell division and has been shown to have teratogenic effects in human pregnancies[22]. Orthotopic liver transplantation is at present the definitive treatment with the best outcome, but can only be offered for advanced disease[23].

In two cases the symptoms of primary biliary cirrhosis were successfully controlled during pregnancy by dexamethasone and ursodeoxycholic acid[9,24]. Ji *et al.*[9] gave a seven-day course of 12 mg/day of dexamethasone which was effective in controlling jaundice and pruritis in a woman whose pregnancy was complicated by primary biliary cirrhosis. Hirvioja *et al.*[24] confirmed that a short course of corticosteroids was effective and safe in the treatment of cholestasis of pregnancy. Perhaps greater use of corticosteroids could have been considered in our case.

Rudi *et al.*[11] reported that ursodeoxycholic given during pregnancy to women with primary biliary cirrhosis was safe and effective in the relief of pruritus, and this was confirmed in idiopathic cholestasis in a double blind randomised trial[25]. Perhaps we should have increased the dose of ursodeoxycholic acid in our case. Other possible treatments are antihistamines and cholestyramine[26].

If portal hypertension is present, vaginal delivery may carry a risk of rupture of oesophageal varices. On the other hand abnormal liver function may lead to deficiency of coagulation factors and an increased risk of haemorrhage during a caesarean section. Primary biliary cirrhosis will lead to malaborption of Vitamins A, D and K and calcium, and supplements should be given.

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