CASE REPORT

Successful pregnancy with autoimmune cirrhosis

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SUMMARY

Pregnancy with liver cirrhosis is a rare and dangerous event that exposes mother and fetus to potentially lethal risks. During pregnancy, hepatic decompensation could suffice and the development of hepatic failure and encephalopathy could occur. The incidence of obstetric complications is also increased with a high rate of pre-eclampsia, postpartum bleeding, preterm delivery and stillbirth. We report a case of a 27-year-old woman with autoimmune hepatitis and liver cirrhosis complicated by splenomegaly, oesophageal varices and severe thrombocytopaenia. During pregnancy, close clinical and analytical surveillance was performed. She was medicated with corticosteroids, azathioprine and propranolol. At the 25th week of gestation, an upper gastrointestinal endoscopy was performed to control oesophageal varices. This patient had an uneventful pregnancy until 37 weeks. At 37th week of gestation, after spontaneous rupture of membranes, signs of acute fetal distress were observed, and an urgent caesarean was performed. Good neonatal and maternal outcomes were achieved.

BACKGROUND

Autoimmune hepatitis (AIH) is a rare liver disease, diagnosed in women of childbearing age,^{1 2} that could lead to liver cirrhosis.³ However, a good therapeutic response is usually achieved resulting in a more benign clinical course.¹ Reports regarding pregnancy exist from as early as the 1970s.⁴ Early published series reported unfavourable outcomes with a high incidence of obstetric complications⁴: fetal loss, severe pre-eclampsia, prematurity, fetal growth restriction, high rate of caesarean delivery and AIH flares, which could lead to hepatic failure and death.^{5 6} The maternal and fetal outcomes recently reported are much more favourable, secondary to better clinical management of this disorder.^{4 7–10} The risks associated with pregnancy with chronic liver diseases are increased when cirrhosis and portal hypertension are present.¹¹ Rupture of oesophageal varices is the most fearful event in pregnant women with cirrhosis, representing the leading cause of death in these patients.^{12 13} These patients usually also need medical treatment with immune modulating drugs, such as azathioprine, the safety profile of which, during pregnancy, is not yet fully defined.¹⁴

We report a case of an AIH patient with severe liver disease, complicated by cirrhosis and portal hypertension. This case highlights the importance of expert obstetrical care, including regular medical assessments, during and after pregnancy.

Figure 1 Hepatic parenchyma evolving to cirrhosis, with fibrous septal bridges, accompanied by ductular reaction and abundant lymphoplasmacytic inflammatory infiltrate (H&E, ×100).

CASE PRESENTATION

We report a case of a 27-year-old woman with AIH diagnosed during her infancy. Diagnosis had been performed based on clinical presentation, elevated serum transaminases, hypergammaglobulinaemia, circulating autoantibodies (positive antinuclear antibodies), presence of chronic active hepatitis on an liver biopsy (it was described interface hepatitis with lymphoplasmacytic infiltrates, piecemeal necrosis and lobular necroinflammatory activity) and response to immunosuppressive therapy; and absence of viral markers for hepatitis B and C, history of exposure to hepatic toxics or markers of genetic liver disorders. The patient fulfilled the criteria for a definitive AIH diagnosis according to the European Association for the Study of the Liver.¹⁵ Her medical history was noteworthy for histologically confirmed cirrhosis of 5-year duration (figures 1–3), complicated by portal

Figure 2 Extensive interface hepatitis lesions and lobular necroinflammatory activity, with ballooning hepatocytes (H&E, ×200).

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Figure 3 Fibrous septa (coloured in blue) involving regenerative hepatic parenchymal nodules, observed in cirrhotic stage of hepatic disease (Masson's trichrome, $\times 100$).

hypertension with evidence of oesophageal and rectal varices, splenomegaly and severe thrombocytopaenia. An episode of acute upper gastrointestinal bleeding occurred 4 years before pregnancy—it was controlled using local endoscopic treatment. The patient was a primipara, with menarche at the age of 14 years. She also had a history of oligomenorrhoea.

Her pregnancy had not been planned, so the first obstetric appointment occurred at the 7th week of pregnancy. She had no signs of liver decompensation at the initial physical examination. She was medicated with propranolol (40 mg three times a day), azathioprine (100 mg/day), ranitidine (300 mg/day) and prednisolone (5 mg/day). The risks related to a pregnancy with AIH complicated with cirrhosis, portal hypertension and severe

thrombocytopaenia were explained to her. She decided to keep the pregnancy, continuing all chronic medication, including azathioprine. Folic acid supplementation was added.

Initial laboratory tests were: aspartate aminotransferase (AST) 26 IU/L (reference value (RV): 10–30 IU/L), alanine aminotransferase (ALT) 13 IU/L (RV: 10–36 IU/L), c-glutamyl-transferase 31 IU/L (RV: 6–39 IU/L), total bilirubin 1.65 mg/dL (RV: 0.20–1.00 mg/dL), direct bilirubin 0.41 mg/dL (RV: 0–0.20 mg/dL), haemoglobin 12.3 g/dL (RV: 12–15 g/dL), thrombocytopaenia 35 000/ μ L (RV: 150 000–400 000/ μ L), prolonged prothrombin time (PT) 13.2 s (RV: 11.3 s) and positive antinuclear antibodies.

Obstetric surveillance with regular liver function evaluation was performed (figure 4). During the third trimester, periodic fetal evaluation showed that the fetus was growing accordingly to what was expected, and the amniotic fluid and umbilical artery Doppler indexes were always in the normal range for gestational age.

Throughout the pregnancy, transaminases remained within normal range, and total bilirubin and direct bilirubin remained slightly elevated, within the usual patient values. Severe thrombocytopaenia does not exacerbate during pregnancy. An oesophagogastrroduodenoscopy (OGD) was performed at 25 weeks of gestation to evaluate the oesophageal varices. It revealed hypertensive gastropathy with a marbled pattern in the gastric body, and fundus and a small varicose vein in the lower 1/3 of the oesophagus, but without indication for local treatment. These findings were similar to the previous OGD performed before the patient's pregnancy (figures 5 and 6).

At 37 weeks of gestation, she was electively admitted to prepare for delivery. After a spontaneous rupture of membranes, fetal monitoring showed signs of distress (spontaneous severe

Figure 4 Analytical evolution during pregnancy.

Figure 5 Oesophageal varices during pregnancy.

repetitive decelerations). An urgent caesarean section was performed under general anaesthesia. Before the delivery, the patient's platelet count was 33 000/L, so a platelet transfusion (2 units) was performed preoperatively, to minimise the risk of haemorrhage. A healthy newborn was born, weighing 2550 g, with an Apgar score of 7 at the first and 8 at the fifth minute. The cause of the abnormal non-stress test was a tight cervical cord. Tube ligation was performed as per the patient's wishes. The placental histological evaluation was accordant with the gestational age, without pathological signs.

The postpartum developed without complications, with AST, ALT and other hepatic function tests within normal range even 6 weeks after birth. To reduce the probability of a postpartum flare, prednisolone dosage was increased to 10 mg/day during the first month of puerperium.

DISCUSSION

The clinical course of AIH during pregnancy is unpredictable,¹⁶ and the ideal management and treatment of pregnant women with cirrhosis and portal hypertension is still unclear.^{13 17} Clinical improvement has been reported, however, pregnancy in these patients could be associated with adverse maternal and fetal outcomes.^{4 7–10} Disease flares are usually associated with poor control in the year preceding pregnancy and the absence

of therapy during gestation.^{4 14} A reduction in the live birth rate has been reported in patients with cirrhosis,⁸ with obstetric complications present in nearly half of these cases.¹³

Gastrointestinal bleeding is the most serious complication in these patients, it occurs in up to 50% of pregnancies with cirrhosis and portal hypertension.¹⁸ It is more frequent in the second half of gestation and during delivery, because maximum blood volume is achieved and the larger uterus causes elevation of venous pressure due to compression of the inferior vena cava.^{12 18}

All patients with cirrhosis, even without varices before pregnancy, should undergo OGD for assessment of varices in the second trimester.¹³ To decrease portal hypertension and to reduce the probability of bleeding, propranolol can be used (FDA category C), taking into account the risk of fetal growth restriction.¹³

AIH activity is often improved during pregnancy, however, most patients require pharmacological treatment to keep clinical stability or to treat flares.¹⁹ Corticosteroid therapy and azathioprine remain the mainstay of medical treatment of AIH. Corticosteroids are considered safe during pregnancy but are associated with an increased incidence of cleft palate when used during the first trimester.¹⁹ Azathioprine safety is classically less certain because it has been linked to congenital malformations in animals, and anaemia and myelosuppression.¹⁴ However, the expanding experience of its use in women with other autoimmune disorders and after heterologous transplantation shows that azathioprine is also a safe drug to use during gestation, and probably during breastfeeding as well.¹⁹

The mode of delivery is controversial, however, some authors consider that the rise in abdominal pressure in vaginal delivery using Valsalva manoeuvres increases portal hypertension and the risk of bleeding, that is the reason caesarean delivery is recommended.²⁰

AIH is not a contraindication for pregnancy, and satisfactory maternal and neonatal outcomes can be achieved. For this, pregnancy must occur when the AIH is silent and medically under control at conception. Additionally, the outcome strongly depends on the severity of organ dysfunction at the beginning of pregnancy. To recap, disease control before pregnancy, correct evaluation of organ dysfunction and expert obstetrical care with regular assessment are essential to achieve the best obstetric outcome possible.

Pregnancy in patients with underlying cirrhosis represents a major challenge, in which safety and ideal management remain largely unknown.⁴

Figure 6 Oesophageal varices 3 years before pregnancy.

Learning points

- ▶ Autoimmune hepatitis (AIH) is not a contraindication for pregnancy.
- ▶ Pregnancy should occur when the AIH is silent and medically under control at conception.
- ▶ Outcome strongly depends on the severity of organ dysfunction at the beginning of pregnancy.
- ▶ Oesophageal varices should be confirmed and treated during the second trimester to reduce the risk of upper gastrointestinal bleeding.
- ▶ Expert obstetrical care with regular assessment is essential to achieve good obstetric outcomes.

Competing interests None declared.

Patient consent Obtained.

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