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Case Report
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Recurrent Intrahepatic Cholestasis Pregnancy: A Case Report

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Abstract

Intrahepatic Cholestasis of Pregnancy (ICP) is the most common pregnancy-related liver disease and it is characterized by onset of pruritus and elevated serum transaminases and bile acids (BA) in the third trimester of pregnancy. Symptoms and abnormal liver tests resolve following delivery but frequently recur in subsequent pregnancies. We represent a case of 37-year-old female who had intrahepatic cholestasis of pregnancy (ICP) in three pregnancies at intervals of 2 to 10 years.

Keywords: Intrahepatic cholestasis of pregnancy; Pruritus; Premature delivery

Introduction

Intrahepatic Cholestasis of Pregnancy (ICP) is getting more and more common in the obstetrics department in China. Especially for those women who have liver disease, family history of ICP, multiple gestations or have done the IVF-ET have a higher risk than others. Maternal symptoms include pruritus, elevation of transaminases, biliary enzymes, bilirubin levels, and abnormal liver function tests [1]. Fetal symptoms include spontaneous preterm labor, fetal distress, and intrauterine death [2]. While postpartum bleeding is the main adverse outcome of the maternal body. Early diagnose and treatment of Ursodeoxycholic acid (UDCA) and maturation of the fetus's lungs are very necessary for both of the maternal and the fetal outcome.

Case Presentation

A 25-year-old patient came to the outpatient clinic in 2005 with complain of generalized pruritus along with jaundice at 12 weeks of gestation (WG). Blood serum test showed elevated serum transaminases and bile acids and bilirubin. Hepatic virus and Cytomegalovirus were both normal, EB virus was negative. Ultrasound of the abdomen was done and it was normal, her blood pressure was also normal, she deny any disease in her past history and no hereditary disease was found in her family. So ICP (severe type) was diagnosed based on the patient symptom and laboratory tests (TBA>40 mmol/l). She was admitted in the obstetrics department and given supportive treatment, but the condition worsens. Gradually she felt decrease of fetus's movement; ultrasound showed still birth the patient gave birth to a dead fetus with natural delivery after few days. The pruritus disappears in 48 h after birth, jaundice progressively disappeared and the serum transaminases changed to normal after one month. One year later cholecystectomy was performed to this patient in the surgery department because of the gallstone with epigastrium uncomfort after meal. Three month later she had her second pregnancy and she choose drug abortion at the first trimester of pregnancy considering the short interval with last labor.

In 2007, she was admitted to our hospital representing at 28 weeks of gestation in the third pregnancy with generalized pruritus disturbing her daily life. After examination, she had scratch marks on lower limbs, abdomen, palm and sole. Her blood pressure was normal, no edema and proteinuria were found. Her serum total bile acid (TBA) level was 165 μmol/l, glycocholic acid (CG) >86, her aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum total bilirubin (TBIL) were 70 U/L, 115 U/L, 55 μmol/l. ICP (severe type) was again diagnosed. Oral administration of S-adenosyl-L-methionine (SAMe) and Vitamin C were given. After four weeks, jaundice and poor appetite appeared, and the serum bile acid kept increasing, then ursodeoxycholic acid (UDCA) was added to her treatment. At her 34 weeks of gestation, she complaint of irregular uterine contraction with premature rupture of membrane. The treatment for preventing preterm birth has been initiated and two 12 mg dose of dexamethasone at 12 h apart was given for accelerating fetal lung maturation. The irregular uterine contraction turned to be regular in the second day and also the fetal distress was diagnosed at the same time. Under the consideration for fetus safety, a cesarean

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section was performed at this time, the amniotic fluid was found to be contaminated. The weight of new born girl baby was 2,100 g. Apgar score was 10 and had a good postnatal evolution. After birth, pruritus and cholestasis syndromes disappeared and TBA, ALT, AST, TBIL decreased to 84 μmol/l, 33 U/L, 28 U/L and 31 μmol/l. In 2010 she did choledocholithotomy and no abnormality was found again during her later following up.

In 2016, after 9 years of last successful delivery, the same patient at her age of 37 came to clinic to consult the doctor about the preparation for her next pregnancy and any kind of abnormality was not found in all of her prenatal examination. However she was informed high risk of recurrent ICP because of her special history and she was hospitalized again with poor appetite, generalized pruritus and jaundice at her 26th weeks of gestation. This time her TBA was 140 μmol/l, ALT was 206 U/L, AST was 148 U/L, TBIL was 100.6 μmol/l, GC>40 μmol/l. ICP (severe type) was diagnosed again just like the last time. She was preferred for the same medication again but near to double dose with intravenous drip was administered (UDCA, SAMe) continuously until she had irregular contraction at 33 weeks. Then dexamethasone and ritodrine were also added for the fetus lungs maturation and the premature uterine contraction. Few days later, uterine contraction became uncontrollable. With the additional diagnose of scarred uterus and threatened labor, a second cesarean section seemed like inevitable. She gave birth to a live baby under a successful cesarean section with contaminated amniotic fluid. This time, the weight of new born baby boy was 2,470 g and apgar score was 10. The evolution of the patient during the puerperium was good with the normalization of the biochemical and pruritus disappeared. TBA, ALT, AST, TBIL decreased to 26.1 μmol/l, 32 U/L, 38 U/L and 26.5 μmol/l when she was discharged from hospital after one week from delivery time. The evolution of the newborn was also good with a normal intellectual and psychical development.

Discussion

The etiology of ICP is still unclear. While some factors are found to be related to the high prevalence of ICP which include: coexisting liver and biliary tract condition or abnormal metabolism of bile acid due to the high secretion of estrogen during pregnancy, older patients' age (>35-year-old), like our patient: hyperemesis gravidarum, multiple pregnancy, over stimulation of ovarian or oral contraception. Inheritance also plays an important role compare to those factors mentioned above. The most frequent ICP complication to the fetus is preterm delivery. The average number of cases it occurs in 30% to 40%. The risk of preterm is significantly higher for TBA>40 μmol/l. It was found that cholalic acid activity result in increased sensitivity of uterine muscle to oxytocin and in the increased oxytocin receptor expression. In the third trimester the level typically considered indicative of ICP is TBA>11 mol/l. The measurement of bile acid concentration is the basic test aiming at diagnose and therapy monitoring of the ICP. The differential diagnose of ICP should also include fatty liver disease, hepatobiliary disorder, HELLP, skin disease, renal pruritus, hyperemesis gravidarum. In pharmacological treatment of the ICP the key role is played by ursodeoxycholic acid (UDCA) [3-5]. Study on ICP therapeutical use of dexamethasone and S-adenosyl-L-methionine (SAMe) has been described in literature. In comparison to UDCA these therapy did not give results in better outcomes with regard to the reduction of laboratory and clinical signs of Cholestasis [3,6,7].

Conclusion

In our patient, age and history of biliary disease was on high risks of the recurrence of ICP. Recurrence of the same disease appeared to her symptoms indicates its close relation with inheritance. It is clearly showing that after the cholecystectomy, the onset of ICP delayed to 26 weeks gestation compared to earlier onset and worse results of 12 weeks at her first pregnancy. The cholecystectomy seems to be very necessary. After 10 years, ICP again appeared more serious and treated with double dose of medicine with intravenous drip for longer time than occurred in older pregnancy. This case represents many characteristics of ICP in the same patient: early onset, rapid progress, severe and recurrent phase. The treatment was addressed to the patient during the pregnancy both times as well as the fetus. The main object for the patient was attenuation of the pruritus. An intense monitoring of the fetus status is mandatory. About treatment, treatment of the primary disease is as same importance as other symptomatic approach. UDCA was a safe and effective therapy in causing rapid clinical improvement and resolution of deranged biochemistry. This was confirmed in a randomized double blind placebo-controlled trial in 16 patients with ICP [8,9]. UDCA normalizes the increased bile acid ratio, reduces plasma concentration and urinary excretion rates of sulfate steroid metabolites [8,10]. Although some medicines are proved to be effective, it still allows an improvement of the fatal prognosis, such as: fetal distress, fetal growth restriction, premature infant, fetal's cerebral dysplasia, contaminated amniotic fluid, acute respiratory distress, etc.

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