

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 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 [1]. We represent one 37 years old female who had Intrahepatic Cholestasis of Pregnancy (ICP) in three pregnancies at intervals of 2 and 10 years.

## Introduction

Intrahepatic Cholestasis of Pregnancy (ICP) is getting more and more common in the obstetrics department in China. Especially 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. 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 treatments of Ursodeoxycholic acid (UDCA) and maturation of the fetus's lungs are very necessary for both of the maternal and the fetal outcome.

## Case Report

A 25 years old patient, at 12 Weeks of Gestation (WG), came to the outpatient clinic in 2005 complaining generalized pruritus along with jaundice. Blood serum test showed elevated serum transaminases and bile acids and bilirubin, Hepatic virus and Cytomegalovirus were both normal, EB virus was also negative. Ultrasound of the abdomen 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>40mmol/l). She was admitted in the obstetrics department and given supportive treatment, but the condition worsen. Gradually she felt decrease of fetus's movement, ultrasound showed stillbirth. The patient gave birth to a dead fetus with natural delivery after few days. The pruritus disappear in 48 hours 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 uncomfot after meal. Three month later she had her second pregnancy. 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 28weeks of gestation in the third pregnancy with generalized pruritus disturbing her daily life. On 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 165umol/l, glycocholic acid (CG)>86, her Aspartateamino Transferase (AST), Alanimeamino Transferase (ALT), serum Total Bilirubin (TBIL)were 70U/L, 115U/L, 55umol/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 34weeks gestation, she complaint of irregular uterine contraction with premature rupture of membrane. The treatment for preventing preterm birth has been initiated and two 12mg dose of dexamethasone at 12 hours 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. Taken the fetus safety into consideration. A cesarean section was performed at this time, the amniotic fluid was found to be contaminated. The new born baby was a 2100g girl. Apgar score was 10 and had a good postnatal evolution. After birth, pruritus and cholestasis syndromes disappeared. TBA, ALT, AST, TBIL decreased to 84umol/l, 33U/L, 28U/L and 31umol/l. In 2010 she did choledocholithotomy and no abnormality was found again during her later following up.

In 2016, 9 years after 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. No abnormality was found in all of her prenatal examination. However she was informed high risk of recurrent ICP because of her special history. Few months later, she was hospitalized again with poor appetite, generalized pruritus and jaundice at her 26th weeks of gestation. This time her TBA was 140 $\mu$ mol/l, ALT was 206U/L, AST was 148U/L, TBIL was 100.6 $\mu$ mol/l, GC>40 $\mu$ mol/l. ICP (severe type) was diagnosed again just like the last time. Again the same medication 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 diagnosis 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. The newborn baby was a 2470g boy. Apgar score was 10. The evolution of the patient during the puerperium was good with the normalization of the biochemical and pruritus disappear. TBA, ALT, AST, TBIL decreased to 26.1 $\mu$ mol/l, 32U/L, 38U/L and 26.5 $\mu$ mol/l when she was discharged from hospital one week after birth. 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 patient's age (>35 years old), like our patient, hyperemesis gravidarum, multiple pregnancy, over stimulation of ovarian or oral contraception. Inheritance also plays an important role compared to those factors mentioned above. The most frequent ICP complication to the fetus is preterm delivery. The average number of cases it occurs in is 30-40%. The risk of preterm is significantly higher for TBA>40 $\mu$ mol/l. It was found that cholalic acid activity results 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 $\mu$ mol/l. The measurement of bile acid concentration is the basic test aiming at diagnosis and therapy monitoring of the ICP. The differential diagnosis 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 therapeutic use of dexamethasone and S-adenosyl-L-methionine (SAME) have been described in literature. In comparison to UDCA these therapies have not resulted 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 are the high risks of the recurrence of ICP. Recurrence of the same disease

appeared to her indicates its close relation with inheritance. It is clear showing that after the cholecystectomy. The onset of ICP delayed to 26 weeks gestation compared to earlier onset and worse outcome of 12 weeks at her first pregnancy. The cholecystectomy seems to be very necessary. 10 years later ICP again appeared more serious and treated with double dose of medicine with intravenous drip for longer time than before because of older pregnancy. This case represents many characteristics of ICP in the same patient: early onset, rapid progress, severe and recurrent. The treatment is addressed to both the pregnant patient as well as the fetus. The main object for the patient is 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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