**INTRODUCTION**

Intrahepatic cholestasis of pregnancy (ICP) is a liver disease that occurs during the second half of pregnancy and persists until delivery. It is characterized by pruritus and elevations in serum total bile acids (STBA), abnormalities of liver function tests, or both. While ICP poses little maternal risk, there is an increased risk of preterm delivery, high rates of abnormal intrapartum fetal heart rate patterns, meconium staining of amniotic fluid and intrauterine fetal death. The mechanism by which fetal death is associated to ICP is unknown and several lines of evidence suggest that it must be a sudden event. Fetal intracranial hemorrhage was described as a possible cause of fetal death in ICP but, to our knowledge, it has been seldom documented and only by postmortem examination of the fetus.

**CASE REPORT**

A 28-year-old woman, (gravida 2 para 1), was referred to our Unit at 32 weeks with complains of generalized pruritus for two days. No other complains, namely jaundice, fever, vomiting or abdominal pain were noticed and there was no history of hepato-biliary disease, hepatotoxic drugs intake or intrahepatic cholestasis on the previous pregnancy. Her pregnancy was uneventful until that moment and routine fetal ultrasound showed no fetal abnormalities. Physical examination was normal including blood pressure values. Laboratorial tests showed increased transaminases (AST 1294 U/L [normal <40 U/L]; ALT 738 U/L [normal <40 U/L]) and slightly elevated serum total bile acids (STBA) (13.4 mol/L [normal ≤10 mol/L]); no other abnormalities were noticed, including coagulation tests. Viral serologies (CMV, Hepatitis A, B and C and Coxsackie) were negative. Maternal abdominal ultrasound showed no hepatic or biliary system abnormalities. Fetal ultrasound examination revealed intraventricular hemorrhage with severe enlargement of left lateral and IIIrd ventricles, also confirmed by MRI. Daily cardiotocography showed a reactive fetus. No medication was prescribed and at 33 weeks the patient was discharged with clinical and laboratorial stabilization.
Weekly fetal ultrasound showed no increase of the intraventricular hemorrhage and biweekly cardiotocography showed a reactive fetus. At 36 weeks, she was admitted in spontaneous labor and a cesarean was performed due to known fetal condition. The newborn weighed 3140g and Apgar score was 9/10 at 1st and 5th minutes. All laboratorial tests done in neonatal period were normal including platelet number and clotting parameters. One month after delivery, the mother was asymptomatic and all the laboratory analyses became normal (STBA: 7.0 mol/L; AST 15 U/L; ALT 39 U/L). The newborn post-partum follow-up did not reveal any major disabilities.

**DISCUSSION**

This was an uncommon case of intrahepatic cholestasis of pregnancy. Although, transaminases levels are usually 4-10 times elevated in ICP, higher levels cannot exclude this diagnosis. In patients with high transaminases, acute viral, toxic or autoimmune hepatitis and choleodocholithiasis need to be excluded as we did in this case.

The mechanism by which ICP causes fetal death is unknown. During ICP there is an increased flux of bile acids from the mother to the fetus, as indicated by increased bile acid levels in amniotic fluid. Bile acids have been shown to induce vasoconstriction of human placental chorionic veins and increased myometrial sensitivity to oxytocin, which could possibly lead to an abrupt reduction in oxygenated blood flow to the fetus. Bile acids also have a direct effect on cardiac contractility, which led to sudden fetal blood pressure variation followed by changes in cerebral blood pressure. As a result, rupture of the fragile premature capillary bed or capillary–venous junction of the germinal matrix may have occurred, causing severe intracranial hemorrhage. This mechanism has been proposed to explain intracranial hemorrhage in fetus of preeclamptic mothers.

Management of patients with ICP is controversial. The current methods of antepartum evaluation are not able to anticipate all fetal deaths, because it may still occur within 24 hours of a normal CTG or a few hours after a normal biophysical profile.

As long as we know, this is the first case of a newborn with intracranial hemorrhage that can be secondary to ICP. This reveals that sudden fetal complications can occur with a low TBA levels.

The authors declare no conflict of interest.

**REFERENCES**

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Fetal intracranial hemorrhage in a patient with intrahepatic cholestasis of pregnancy


