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Case Report

A rare case of early onset intrahepatic cholestasis of pregnancy

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ABSTRACT

Intrahepatic cholestasis of pregnancy (ICP) is an important complication of pregnancy requiring increased surveillance by the obstetricians due to its increased foetal morbidity and mortality in the form of preterm birth, foetal distress, RDS including sudden IUD and stillbirth. The incidence of ICP is increasing due to IVF and routine administration of progesterone in early pregnancy. ICP usually presents in late second and third trimester. Here authors are presenting a case of early onset ICP (14 weeks) which developed in an IVF conception.

Keywords: Intra hepatic cholestasis of pregnancy, In vitro fertilisation, Progesterone

INTRODUCTION

Intrahepatic cholestasis of pregnancy (ICP) is a reversible form of cholestasis in late pregnancy, persisting until delivery.¹ Obstetric cholestasis is diagnosed when otherwise unexplained pruritus occurs in pregnancy and abnormal liver function tests (LFTs) and/or raised bile acids occur in the pregnant woman and both resolve after delivery. Pruritus that involves the palms and soles of the feet is particularly suggestive. Initially, bile acids were first thought to be the direct cause of pruritus, but it is now known that the itch does not typically correlate with bile acids levels and other pruritic agents have been identified, including lysophosphatidic acid and sulphated progesterone metabolites, liver enzymes are raised by about 2-3 fold, As pruritis is very common in pregnancies occurring in 50% of normal pregnancies, pruritis with liver function abnormalities clinches the diagnosis.² Pruritis may precede the onset of abnormal LFT's by 2-3 weeks.³ ICP should be differentiated from other causes of jaundice in pregnancy like viral hepatitis, acute fatty liver of pregnancy, HELLP syndrome and other dermatological condition.⁴

METHODS

Though ICP is commonly seen in late second and third trimester of pregnancy, here authors are presenting a case of early onset ICP occurring at 14 weeks of an IVF conception. A 37-year-old G2A1 married for 7 years presented at Chinmaya at mission hospital (CMH) Bangalore, with chief complaints of itching over soles and palms gradually increasing all over the body without any skin rashes. Her LFTs showed normal bilirubin, SGOT and SGPT increased 2 to 3-fold and bile acids 18.1 micromol/ltr. A diagnosis of ICP was made and she was put on ursodeoxycholic acid 300 mg twice daily and antihistamines SOS. Progesterone's were stopped. Her symptoms improved and she was followed up with fortnightly LFTs. She developed pruritis again in 3rd trimester when her LFTs, APTT were deranged again. Her UDCA was increased to 300 mg three times daily to which she responded well. She also developed GDM in the third trimester which was well controlled with diet. Around 37 weeks after explaining the risks to her and taking consent, she was given steroids and elective LSCS was done. In healthy male baby of 3.5 kgs delivered.

Post-operative period was uneventful and her LFTs after 1 week were within normal limits.

DISCUSSION

The etiopathology of ICP is multi factorial including genetic, hormonal and environmental factors. Genetic factors can explain familiar cases and the high incidence seen in some ethnic groups. Genetic defects occur in genes involved in bile canalicular transporting system leading to cholestasis. ABCB4 gene encoding the multi-drug resistance 3 protein (MDR3) which is a canalicular phospholipid trans locator is primarily involved in subtype of progressive, familial intrahepatic cholestasis.⁵

Oestrogen and progesterone hormones play an important role in the causation of ICP; oestrogen is known to cause cholestasis.⁶ ICP is common during 3rd trimester and in multiple pregnancies associated with higher levels of hormones. ICP is known to occur much earlier in cases conceived by IVF where high oestrogen levels can be present.⁷

High progesterone also plays a role in the aetiology of ICP and its much earlier occurrence. 34 out of 50 women in a French prospective series conducted by BACQ Y et al observed 68% of ICP cases who were treated with oral micronized natural progesterone for risk of premature delivery.⁸

The levels of progesterone metabolites especially the 3 β sulphated progesterone metabolite epiallopregnenalolone sulphate is raised more than normal in the serum of ICP pregnancies.² The interaction between this metabolite of progesterone and the Farnesoid X receptor (FXR) results in the aberrant expression of bile acid homeostasis.⁹

Progesterone's are administered routinely in cases conceived by IVF and in cases of recurrent unexplained miscarriages which may increase the incidence of ICP.¹⁰

There is not only a higher risk of ICP among HCV-infected pregnant women but also an increased risk of later HCV infection among ICP patients. Asymptomatic hepatitis C is associated with increased risk of ICP.¹¹

The risk of foetal death appears to increase not only with high bile acid levels but even within the physiological range after 37 weeks of gestation. Antepartum testing to identify foetuses at risk of IUD is unproven.¹² Several studies reported intrauterine foetal death occurring within a few days of a reactive NST. NST may be used on alternate days to detect the rare foetal heart tracing suggesting foetal compromise and the need for early delivery. The pathology of sudden foetal death is the entry of bile acids into the cardiac muscle and cause toxicity resulting in bradycardia, arrhythmias and sudden death.¹³ The risk of foetal complication is statistically increased at bile acids levels ≥ 40 micromol/ltr.¹⁴

ICP affected pregnant women are at increased risk of developing PE, GDM, chorioamnionitis, PPh, CS.¹⁵ These women may be associated with subsequent development of hepatobiliary cancer, DM, thyroid disease, Cohn's disease and other immune mediated disorders.¹⁶

UDCA has emerged as the most promising first line treatment for ICP. It increases bile flow and is used to relieve pruritis and improve liver biochemical tests, lowers bile acids and liver enzyme levels and reduces neonatal complications.

Induction of delivery is usually done after 36-37 completed weeks. Delivery before 36 weeks maybe indicated in cases with severe unremitting pruritis where pharmacotherapy has failed, where bile acids levels are more than 100 micromol/ltr.¹⁷

Postpartum LFTs should be checked 6-8 weeks after delivery there has been a high incidence of gallstones in females with history of IHCP. IHCP recurs during subsequent pregnancies in 40-60% cases with varying severity of recurrent episodes.¹⁸ Overall maternal prognosis is good and symptoms resolve rapidly within 48 hours of delivery. Long term follow up of the woman with history of ICP is recommended.

CONCLUSION

Progesterone's be avoided or given in lower doses in pregnant women with a previous history of ICP and immediately withdrawn when cholestasis occurs during pregnancy. Patients with a history of cholestasis, either in pregnancy or with oral contraceptives should be monitored carefully during IVF and should be mildly stimulated. Every woman with ICP should be screened for hepatitis C.

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