



Case Report on Intrahepatic Cholestasis of Pregnancy

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Abstract

This case report concerns a primigravida woman (period of gestation-37 weeks) diagnosed with intrahepatic cholestasis of pregnancy (IHCP). She had been married since 2 years and this is her first pregnancy. The patient is an Rh-negative mother. She did not receive anti-D at 28 weeks of gestation. The patient was admitted to antenatal ward of Hakeem Abdul Hakeem Centenary (HAHC) Hospital, New Delhi, with chief complaints of itching all over the body since 15–20 days with severe itching over the umbilical area and presence of rashes on legs and breasts since last 10 days. During the physical examination the rashes were seen on legs and breast. Per abdomen examination revealed cephalic presentation of the fetus with FHR as 140 bpm. Routine blood investigations revealed that the patient was also a case of moderate anemia and the blood group of the patient was AB-negative. After all the required investigations, she was diagnosed with IHCP with moderate anemia with Rh-negative pregnancy. IHCP is a pregnancy-specific liver disorder characterized by pruritus, most often, in the late-second or early third trimester of pregnancy and raised serum bile acids. The maternal outcome after treatment is good but fetal outcomes become adverse in most of the conditions.¹

Keywords: Intrahepatic cholestasis of pregnancy (IHCP), Rh-negative pregnancy, Anti-D, Anemia

Introduction

A 31-year-old primigravida woman came to antenatal ward of HAHC hospital, New Delhi, with chief complaints of itching all over the body with severe itching over the umbilical area since 15–20 days and presence of rashes on the legs and breasts. The patient is having 37 weeks of gestation and is also a case of Rh-negative pregnancy with no anti-D administered at 28 weeks of gestation. The patient never visited a hospital during her antenatal period until now and this was her first visit. There was no history of any previous pregnancy and miscarriage. The patient weighed 65 kg and had been married for 2 years. There was no history of consanguineous marriage of parents and there was no family history of any obstetrics and gynecological disease in her family. Her age at menarche was 14 years and her menstrual cycles were regular. She had no significant past history of diabetes, hypertension or any other medical illness. Physical examination revealed the presence of rashes on the legs and breasts of the patient and per abdomen examination revealed cephalic presentation of the fetus with relaxed uterus. Abdominal girth and fundal height were proportionate to the gestational age. The FHR was found to be 140 bpm. Routine blood investigations revealed that the patient was also a case of moderate anemia (Hb 7.02 g/dL) and the serum bilirubin level was also raised (0.44 mg/dL). The SGOT (99 IU/L) and SGPT (76 IU/L) were also raised. The blood group of the patient was AB-negative.

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After all the required investigations, she was diagnosed with intrahepatic cholestasis of pregnancy (IHCP) with moderate anemia and Rh-negative pregnancy. Intrahepatic cholestasis of pregnancy is an obstetric cholestasis or jaundice of pregnancy. It is a medical condition in which cholestasis occurs during pregnancy. It typically presents as troublesome itching and can lead to complications for both mother and fetus.¹ Cholestasis is a condition where bile cannot flow from the liver to the duodenum. It frequently develops in late trimester of pregnancy in individuals who are predisposed and it is the most common pregnancy-related liver disorder.²

Incidence

The incidence of ICP varies widely with geographical location and ethnicity. It is most common in South America, particularly in Chile, where early reports described an incidence of 10%, with higher rates seen in Auracanian Indian women. In India the prevalence rate is 0.08 according to the studies conducted from 2002–2004.³

Pathophysiology

Affected individuals have a defect involving the excretion of bile salts, which leads to increased serum bile acids. These are deposited within the skin, causing intense pruritus.⁴ The cause of ICP is unknown but is thought to be multifactorial with genetic, hormonal, and environmental involvement. Family clustering and varying incidence in different geographic regions speaks strongly for a genetic etiology of ICP.⁵

Up to 15% of IHCP cases are associated with the adenosine triphosphate binding cassette, subfamily B, member 4 (ABCB4/abcb4) gene. This gene, also known as multidrug resistant protein-3 (MDR3), encodes the transporter for phospholipids across the canalicular membrane of hepatocytes. Up to 10 different MDR3 mutations have been identified and any one of these mutations may result in loss of function and, therefore, raise bile acid levels.² MDR3 is also associated with progressive familial intrahepatic cholestasis.

Therefore, a careful and focused family history of a patient diagnosed with IHCP, looking for a personal or family history of IHCP or gallstones and cholestasis with oral contraceptive pill (OCP) use is important.

Changes induced by these genetic mutations lead to an increased sensitivity to estrogen. Estrogen has a known role in causing cholestasis, and, thus, cholestasis can arise from estrogen-containing OCPs. All steroids, estrogens, progesterones, and corticosteroids are

increased during pregnancy 1000-fold at term compared with the non-pregnant state. Sex hormones exert cholestatic effects via inhibition of the hepato-cellular bile salt export pump. Another mechanism for sex hormone interaction involves the association of higher sex hormone levels with impaired sulfation. The hepatic transport mechanisms for biliary excretion can be saturated by sulfated progesterone metabolites.²

Individuals with possible estrogen sensitivity should be monitored carefully and closely for the symptoms of IHCP during late trimester of pregnancy as estrogen is at its highest during the last trimester of pregnancy. Similarly, those with multiple gestations are at an increased risk for developing IHCP, owing to increased levels of estrogen above those seen with singleton gestations.⁶

Environmental factors are also responsible for the occurrence of IHCP. Low level of selenium is an important contributing factor of IHCP. Serum levels of selenium reduce with advancing gestation but normal serum levels can be maintained by adequate intake of balanced diet. Seasonal variation is also noted, with more severe cases in winter months.³

Clinical Presentation

The most common symptom of IHCP is itching or pruritus which is present in the patient as discussed.²

Apart from pruritus, other important symptoms are:

- Itching that increases in the evening
- Elevated LFT results as well as serum bile acid counts
- Itching that does not respond to anti-histamines or anti-itch remedies
- Stalk colored urine
- Light colored stools
- Fatigue
- Increased Nausea
- Decreased appetite
- Jaundice
- Right upper quadrant pain

Diagnosis

Most common diagnostic feature of IHCP is persistent or severe itch, especially on the palms and soles of the feet.

For the confirmation of diagnosis, LFT is advised by the obstetrician and serum bilirubin should be noted. If ALT levels are found to be elevated along with elevated

bilirubin level and presence of pruritus, then it could be considered as a potential IHCP case.

Management

The aim of the management is to reduce the maternal symptoms and fetal complications and

Drugs

Ursodeoxycholic acid (UDCA)

UDCA is a naturally occurring hydrophilic bile acid that constitutes <3% of the physiological bile acid pool in humans. It has been used with positive effects in the management of primary biliary cirrhosis and other cholestatic disorders for several years, and is gaining popularity as a treatment for ICP. There is evidence that UDCA stimulates biliary secretion by post-transcriptional regulation of BSEP and the alternative exporters MRP4 and MRP3. In addition, it has antiapoptotic effects and has been shown to reduce the mitochondrial membrane permeability to ions and cytochrome c expression.² Finally, UDCA lowers serum levels of ethinyl-estradiol 17 β -glucuronide, a major cholestatic metabolite of estrogen.

There are very few side effects reported with UDCA treatment. At higher doses, women may complain of gastrointestinal upset and diarrhea, but this is rare.

Dexamethasone

Dexamethasone inhibits placental estrogen synthesis by reducing secretion of the precursor, dehydroepiandrosterone sulfate, from the fetal adrenal glands.

Vitamin K

ICP is associated with a risk of malabsorption of fat soluble vitamins due to reduced enterohepatic circulation of bile acids and subsequent reduction of uptake in the terminal ileum. Therefore, many clinicians opt to treat women with oral vitamin K to guard against the theoretical risk of fetal antepartum and maternal intra- or postpartum hemorrhage. However, there have been no studies to support or refute this practice.⁵

Cholestyramine is an anion-exchange resin which acts by binding bile acids in the gut, thereby inhibiting the enterohepatic circulation and increasing fecal excretion of bile acids. There have been several studies suggesting that cholestyramine is effective at reducing pruritus in ICP.⁶ However, it has no effect on serum bile acid levels or other biochemical markers of cholestasis.

Furthermore, it may reduce the intestinal absorption of fat-soluble vitamins, thus depleting the levels of vitamin K and increasing the risk of hemorrhage for the mother and fetus. Cholestyramine is therefore no longer considered a first-line therapy for ICP.³

Risks of IHCP, if Untreated

Maternal Risks

- Intense and debilitating itching
- Premature labor
- Deranged clotting

Fetal Risks

- Fetal distress
- Meconium aspiration syndrome
- Sudden fetal death syndrome

Prognosis

Most women have no lasting hepatic damage, but ICP reoccurs in majority of the cases, with variations in intensity in the subsequent cases.

Recurrence is less likely following multiple pregnancies. Women with a history of ICP may also develop symptoms, if taking the combined oral contraceptive pill, or in the second half of the menstrual cycle.¹

Conflict of Interest: None

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