International Journal of Trend in Scientific Research and Development (IJTSRD)
Volume 6 Issue 1, November-December 2021 Available Online: www.ijtsrd.com e-ISSN: 2456 – 6470

A Case Report on Intrahepatic Cholestasis of Pregnancy

Ms. Rana Kamar[1], Dr. Rajwant Randhawa[2], Dr. Priyanaka Choudhary[3]

[1]PhD (Nursing) Scholar, [2]Professor (CHN), [3]Associate Professor (MSN),
[1,2,3]Desh Bhagat University Off to NHI, Mandi Gobindgarh, Punjab, India

ABSTRACT

This case study is about a primigravida mother (period of gestation 29 weeks and 5 days) diagnosed with intrahepatic cholestasis of pregnancy (IHCP). She had been married since 1 year and it is her first pregnancy. The patient is having gestational diabetes mellitus and hypothyroidism. The patients was admitted to antenatal ward of St. Stephen's Hospital , New Delhi, with chief complaints of itching in palms, soles and over umbilical area since 2 weeks. During the physical examination the rashes were seen on abdomen, legs and breast. Per abdomen examination and ultrasound revealed that vertex presentation of the fetus and FHR as 136/ min and fetal weight as 1923 gram and presence of low lying placenta. Routine blood examination revealed that patient was also a case of gestational diabetes mellitus and hypothyroidism. After all the required investigation she was diagnosed with IHCP with gestational diabetes mellitus and hypothyroidism. IHCP is a pregnancy related liver disorder characterized by pruritus, most often in the late second or early trimester of pregnancy and raised serum bile acids. The maternal outcome after treatment is fair but fetal outcomes becomes adverse in most of the conditions.

KEYWORDS: *Intrahepatic cholestasis of pregnancy (IHCP) Rh-negative pregnancy, Gestational diabetes mellitus, Hypothyroidism*

How to cite this paper: Ms. Rana Kamar | Dr. Rajwant Randhawa | Dr. Priyanaka Choudhary "A Case Report on Intrahepatic Cholestasis of Pregnancy" Published in International Journal of Trend in Scientific Research and Development (ijtsrd), ISSN: 2456-6470, Volume-6 | Issue-1, December 2021, pp.1644-1647, URL: www.ijtsrd.com/papers/ijtsrd49087.pdf

IJTSRD49087

INTRODUCTION

A 26 – year old primigravida mother came to antenatal ward of St. Stephen's Hospital, New Delhi with chief complaint of itching in palms, soles and over umbilical area since 2 weeks and presence of rashes on abdomen, legs and breast. The patient is having 29 weeks and 5 days of gestation and is also a case of gestational diabetes mellitus and hypothyroidism. The patient has 2 previous antenatal visits and no previous complaint of anything. There was no history of previous pregnancy, miscarriage of any medical or surgical treatment. The patient weighted 58 kg, height 155 c.m and had been married for 1 year. There were no history of consanguineous marriage of parents and there was family history of diabetes mellitus, her parents were on insulin therapy but there were no other history of obstetrics and gynecological disease in her family. Her age of menarche was 13 years and menstrual cycle was irregular and dysmenorrhea was present. She had no significant pas history of diabetes, hypertension, tuberculosis or any other medical illness. Physical examination shows the presence of rashes on abdomen, legs and breasts. During abdominal examination vertex presentation, longitudinal lie and uterus was relaxed and soft. Abdominal girth and fundal height were according to gestational age. The fetal heart rate was found to be 136/ min and fetal weight was 1923 gram and presence of low lying placenta. Routine blood examination showed that the patient was also a case of gestational diabetes mellitus (Fasting: 99 gram/dl, 1st hour: 184 gram/dl, 2nd hour: 153 gram/dl), hypothyroid (TSH level: 3.88) and serum bilirubin level was also raised (0.99 mg/dl). The SGOT (131 IU/L) and SGPT (227 IU/L) were also raised. The blood group of the patient was O positive (O+ve). After all the examination she was diagnosed with intrahepatic cholestasis of pregnancy with gestational diabetes mellitus and hypothyroid. Intrahepatic cholestasis of pregnancy (ICP) is a pregnancy-specific liver disorder characterized by maternal pruritus in the third trimester, raised serum bile acids and increased rates of adverse fetal outcomes.[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:

CP is observed in 0.4–1% of pregnancies in most areas of Central and Western Europe and North America, while in Chile and Bolivia as well as Scandinavia and the Baltic states roughly 5–15% and 1–2%, respectivelyand 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:

Genetic predisposition and hormonal factor play key roles in the pathogenesis of ICP. Evidence of primary role of hormonal factors of ICP was provided by the following observations:[4]

1. The disease starts in the last trimester which is the period of highest concentration.
2. Twin pregnancies display both a higher incidence of ICP and more pronounced rises in hormonal level.
3. ICP resolves promptly after delivery when placental hormone returns to normal.
4. In further pregnancies ICP re-occur in 45-70% cases.

Estrogen in a particular glucuronides like estradiol 17Beta D- glucuronide were found to be cholestatic in animal studies where they diminished the uptake of bile acids at the basolateral membrane of hepatocytes. An increased permeability of tight junction and a decreased fluidity of the sinusoidal membrane have been suggested as underlying mechanism.[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.[2]

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.[1]

Clinical Features

In the past icterus was believed to be the major clinical findings in ICP. However the most common symptom is severe pruritus, which most typically appear in the third trimester and starts in palm and soles.

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

Liver function test are to be performed in every pregnant woman who experiences pruritus. The increases serum bile acids in combination with severe pruritus is very much suggestive of ICP.

Among standard liver test alanine transaminase(ALT) is a very sensitive parameter for ICP.

Differential Diagnosis

The main differential diagnosis of pruritus of ICP without icterus are skin disease, allergic reaction and pruritus related to abdominal striae.

Management

Intrahepatic cholestasis of pregnancy is common condition with high impact of fetal morbidity and mortality. A regimen including weekly cardiotocographic monitoring from 34th week of gestation and induction of labor from 38th week of gestation in mild cases and in the 36th weeks of gestation in severe cases can reduce perinatal mortatlity to control levels. Since fetal prognosis correlate with disease severity, the aim of treatment should be reduction of bile acids in order to prolong the pregnancy and reduce both fetal risk and maternal symptoms.

Pharmacological management

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 17β-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, dehydro epiandrosterone 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.[7]

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.[1]

In this patient Tab- ursodeoxycholic acid 600mg B.D used to reduce the symptoms along with Tab - Thyroxin 25 $\mu g$and diebetic diet has been given to the patient to improve the condition. Pruritus has been resolved with the treatment and patient kept on continue follow up.

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.[8]

Conflict of Interest: None

References

[1] Victoria G, Williamson C. Intrahepatic Cholestasis of pregnancy. World Journal of Gastroenterology May 7, 2009; 7: 15(7); 2049-66.

[2] Fidelma B Rigby, Ronald M Ramus. Intrahepatic Cholestasis of Pregnancy. Obstetrics and Gynaecology Journal Feb 2016.

[3] P. Thomas, B. Ulrich, Intrahepatic Cholestasis of pregnancy, Orphanet Journal of Rare Diseases, May 29, 2007, 98(3).

[4] Kreek MJ. Female sex steroids and cholestasis Semin liver dis 1987, 7:8-23.

[5] Davis RA, Kern F, JR Shoulter R, Sutherland E et al, Alteration of hepatic Na^+/ K^+ ATPase and bile flow by estrogen and effect on liver surface

membrane lipid structure and function. Proc nadal acad sci USA 1978, 75:4130-4.

[6] Gonzaleze MC, Reyes H et al. Intrahepatic cholestasis of pregnancy in twin pregnancies. J Hepatol July 1989; 9(1): 84-90.

[7] Reyes H, Simon FR. Intrahepatic cholestasis of pregnancy: an estrogen related disease. Semin Liver Disease Aug 1993; 13(3): 289-301.

[8] https://en.wikipedia.org/wiki/Intrahepatic_cholesta sis_of_pregnancy