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Intrahepatic Cholestatsis of Pregnancy: A Rare Outcome

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Abstract

This case report concerns a primigravida woman (period of gestation-34weeks) diagnosed with intrahepatic cholestasis of pregnancy (IHCP). She had been married for 2 years and this is her first pregnancy. The patient was admitted to gastroenterology ward of KLE Prabhakar medical college Belgaum with chief complaints of itching all over the body since one and half months and icterus since 15-20 days. Patient had increased in severity of itching over the umbilical area, palms and sole since last 20 days. During the physical examination, the rashes were seen on legs and abdomen and arm. 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 deranged liver transaminases and raised bile acids.

After all the required investigations, she was diagnosed with IHCP with moderate anemia . 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, pruritis, raised serum bile acid, third trimester.

Introduction

Intrahepatic cholestasis of pregnancy (ICP) appears in the second and third trimester of pregnancy and is characterized by pruritus and an increase of serum bile acid concentration.

Cholestasis is associated with many hepatic-biliary disorders that produce extrahepatic biliary tract obstruction and/or intrahepatic biliary perturbation. A key symptom associated with cholestasis is pruritus, and could range in severity from mild to moderate (i.e. where sleep is disrupted) and to extreme (i.e. when the lifestyle of the patient is completely disrupted).The incidence of ICP varies greatly not only throughout the world, but throughout different regions in the United States as well. Evidence of family clustering and prevalence in certain ethnic groups may partially explain the geographic variation in incidence.

While ICP is more common in South Asia, South America, and the Scandinavian countries, the incidence in the United States varies greatly. The United States has a heterogeneous population, and thus the incidence has a wide range, 0.32-5.6%. [2, 3, 4] ICP also shows seasonal variation, occurring more frequently in the winter months. [5] Other risk factors for ICP include advanced maternal age, a personal or family history of cholestasis with oral contraceptive use, and multiparity. [6] In addition, women

with twin pregnancies are 5 times more likely to develop ICP than women with a singleton pregnancy. [17]

From a maternal viewpoint, the main consideration is intense pruritus, which may become so intolerable that delivery is considered as early as 35-37 weeks. [8] The fetal viewpoint is more concerning, as even with modern treatment the risk for fetal demise can range from 2-11 %. Thus, many would advocate induction at 37 weeks. [8,9] Other authors believe that a significant rise in bile acids or persistent increases in transaminases despite adequate UCDA treatment should prompt consideration for delivery. [10,11,12,13]

Case Report

A 27-year-old female primi gravida with 34 weeks gestation came with chief complaints of itching since one and half months and yellowish discoloration of sclera and body for 20 days. patient had itching initially in the palm and sole further progressed to the entire body and increased in intensity in the form of alteration of sleep due to pruritis. patient also noticed yellowish discoloration of skin and clear since 20 days .

No H/O Nausea ,vomiting,any bleeding manifestations ,fever, pain in abdomen, altered sensorium or any past history of similar complaints.no h/o any features suggestive of eclampsia or pre-eclampsia were present.no significant family history or personal history.

On general physical examination patient was conscious, oriented and co-operative

She was afebrile, pulse rate was 104 bpm regular and bp of 130/90 mmhg in right upper arm supine position and a respiratory rate of 23 cycles/min and she was icteric and had pruritic rashes all over her leg on the anterior aspect and soles and also her arm and abdomen.

Systemic Examination

CVS- S1S2 heard no murmurs, RS- air entry bilaterally equal with no adventitious sound, CNS – conscious oriented, no flaps. P/A- gravid uterus (34 weeks of gestation)

Blood parameters

15/2/2017	18/2/2017	23/2/2017	10/3/2017(FOLLOW UP)
Haemoglobin: 12.3gm/dl Red cell count:4.42 WBC: 10,600 PLATELET:2, 18,000 PERIPHERAL SMEAR: normocytic normochromic anemia with neutrophilia.	TOTAL BILIRUBIN:4.23 DIRECT: 3.93 TOTAL PROTEIN :5.6 ALBUMIN:2.8 A: G RATIO:1 SGOT:27: SGPT:19 ALP:284	HB:10.2 TOTAL BILIRUBIN:2.50 DIRECT BILIRUBIN:2 TOTAL PROTEIN :4.9 ALBUMIN:2.5 A: G RATIO:1 SGPT:16; SGOT:20 ALP:218	TOTAL BILIRUBIN :1.36 DIRECT BILIRUBIN :1.04 TOTAL PROTEIN:6.6 ALBUMIN: 3.4 A: G RATIO:1.1 SGPT:25; SGOT:22 ALP:220
Urine routine and microscopy: NAD	MINI RENAL: WNL	MINI RENAL: WNL	
Lipase : 121 Amylase:110			
RBS:80 MG/DL UREA:30 CREATININE :0.74 SODIUM:137			

POTASSIUM: 3.87 CHLORIDE:96,HCO3-21 TOTAL BILIRUBIN;6.39 DIRECT:6.30 ALP:265 SGOT;46 :SGPT;59 TOTAL PROTEIN:6 SR.ALBUMIN:3.2 GGT:8			
HBSAG; NA HIV:NA HCV:NA HAV:NA HEV:NA			
INR:0.92			

Based on clinical profile and blood parameters diagnosis of intrahepatic cholestasis of pregnancy was made. Patient was treated with ursodeoxycholic acid 300 mg in three doses each in day and cholestyramine 5 mg twice day. further in the course of hospital stay patient developed labour pain and delivered through normal vaginal delivery of a baby with appropriate weight and no complications. eventually after delivery and with continuation of treatment the symptoms relieved in a span of two weeks and liver parameters normalized in 3 weeks which was noted on subsequent follow up.

Discussion

We gave particular importance for quick identification of ICP associated with a 32 weeks pregnancy, in a symptomatic context dominated by pruritus and associated with deranged hepatic profile.

To reach the diagnostic of ICP, we first eliminated:

pregnancy pruritus, pruritus gravidarum, where the test show normal hepatic function and normal bile acids, gestational pemphigoid, rare autoimmune condition characterized by IgG complement fixation antibodies with rashes that develop into high tensioned blisters, associated with an increased risk of preterm delivery and small for gestational age, ectopic pregnancy eruption showing dry red rashes, with or without small blisters which typically affect the trunk and flexions of the limbs, prurigo of pregnancy with red-brown groups of papules on the abdomen and inner surfaces of the limbs, pruritic folliculitis of pregnancy with acneiform rash on the shoulders, upper back, thighs and arms, follicular papules and pustules that can be filled with pus, the culture being usually sterile, rashes improve with advancing pregnancy.

We have also eliminated the serious conditions that can be associated with hepatic cytolysis syndrome and pruritus, when the life of mother and fetus are at risk. We refer to specific causes of liver failure in pregnancy,

acute fatty liver of pregnancy (AFLP) with the emergence of nausea and vomiting in the III trimester which are not caused by hyperemesis gravidarum, patients with AFLP are often associated with renal failure, coagulopathy, hypoglycemia and pre-eclampsia. HELLP syndrome where hypertension and proteinuria in which are the main characteristics. Hyperemesis gravidarum that occurs in early pregnancy with nausea, vomiting, affected hepatic samples which normalize with drug treatment. We have also ruled out viral hepatitis.

Literature on Intrahepatic Cholestatsis Of Pregnancy

The cause of ICP is unknown, but genetic, hormonal and environmental factors are probably involved (14). Environmental factors may also influence the manifestation of the disease.

Genetic factors might explain familial cases and the higher incidence in some ethnic groups. The adenosine triphosphate binding cassette, subfamily B, member 4 gene, encoding drug resistance-associated (a canalicular phospholipid translocator) protein is mainly involved in a subtype of progressive familial intrahepatic cholestasis called PFIC3(15). Heterozygous mutations in this gene have been reported in a large consanguineous family.

Several women had pregnancy repeated episodes of cholestasis (16,17). Estrogens are known as cholestasis causal factors in both experimental and clinical conditions, probably having a role in cholestasis of pregnancy (18).

ICP occurs mainly in the third trimester, when serum concentrations of estrogen are at maximum level. Cholestasis is more common in twin pregnancies, which are associated with higher levels of circulating estrogen than in singleton pregnancies (19). Cholestasis of pregnancy may be associated with haltered metabolism of progesterone and progesterone administration may be a risk for cholestasis (20). The onset of cholestasis of pregnancy is usually marked by the development of pruritus. It is often generalized but predominates on the palms and soles and manifests more violently at night. Pruritus may precede laboratory abnormalities (22).

Total serum concentration of bile acid increase in cholestasis of pregnancy and may be the first or only laboratory abnormality (21,22,23). Serum cholic acid increases more than chenodeoxycholic acid, resulting in a marked increase in the ratio cholic acid/chenodeoxycholic acid compared to pregnant women without cholestasis of pregnancy (24.).Other laboratory results reflecting cholestasis may also be present. These include increases in alkaline phosphatase (ALKP) serum concentrations, 5 'nucleotidase, and concentrations of total and direct bilirubin. Total levels of bilirubin infrequently go beyond 6 mg/dl. However, uncommonly, serum levels of gamma-glutamyl transpeptidase (GGT) are normal or slightly elevated, which is unusual in many other forms of cholestatic liver disease in which GGT levels are similar to other cholestatic markers.

Most women are diagnosed in the second or third trimester. Cholestasis of pregnancy diagnosis is based on the presence of pruritus associated with elevated levels of total serum bile acids and/or aminotransferases, and the absence of other diseases that can cause similar symptoms and laboratory results, the diagnosis being one of exclusion. Liver biopsy is rarely necessary for diagnosis. When it is performed, histopathology is characterized by cholestasis without inflammation (25). Portal circulation is not affected.

Conclusion

In patients with pruritus and abnormal serum liver tests, especially in advanced stage of pregnancy, intrahepatic cholestasis of pregnancy should not be disregarded. The affected pregnancies have an increased risk of prematurity and *in utero* fetal death. In this case it is highly recommended to consider the treatment with ursodeoxycholic acid and to try to deliver after 34 weeks of pregnancy.

The main conditions incriminated in differential diagnosis and which should be considered in the context of an advanced pregnancy, especially in the third trimester, are: acute fatty liver of pregnancy, preeclampsia, sHELLP syndrome (hemolysis, elevated liver enzymes, low platelet count).

The risk of recurrence in subsequent pregnancies is variable. There is a possibility that the risk for intrahepatic cholestasis' occurrence in subsequent pregnancies cannot be accurately predicted.

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