Intrahepatic cholestasis of pregnancy

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Key words: intrahepatic cholestasis of pregnancy, atonic uterus, postpartum hemorrhage

Introduction

Intrahepatic cholestasis during pregnancy is not common but is a serious condition.

Case report

A 22 years old gravida 2 para 1 living 1 was admitted as an emergency patient at 11 pm on 18th February, 2005 at 35 weeks of gestation, with complaints of vomiting off and on for 3-4 days, and vaginal leaking for about an hour. She had no antenatal checkup during the last 4 weeks. At 26 weeks, on her first antenatal visit she had complained of itching all over the body. All routine antenatal investigations were normal. In view of the complaint of pruritus, liver function tests (LFT) were done which were normal. Antenatal check-ups at 28 weeks and 31 weeks of pregnancy had shown no abnormality. She had a normal delivery at 38 weeks 2 years back but she had intrahepatic cholestasis of pregnancy (IHCP) in the 3rd trimester of that pregnancy. There was no relevant family history. She was deeply icteric and afebrile, with tachycardia of 102/minute. Fundal height was 34 weeks, presentation cephalic and uterus irritable. Fetal heart beats were regular. On speculum examination frank leaking of yellow clear liquor was seen. On vaginal examination the cervix admitted one finger, was not effaced, and membranes were absent. Blood was sent for LFT, blood counts and coagulation profile. Injection ampicillin 1g intravenously and injection Vitamin K 10 mg intramuscularly daily were given. After 5 hours of admission (i.e. at 3.59 am on 19th February, 2005) spontaneous preterm vaginal delivery with episiotomy resulted. A female baby weighing 2.26 kg was delivered. Apgar at 1 minute was 5 and at 5 minutes 6.

She had atonic postpartum hemorrhage (PPH). Uterine massage was done. On catheterization 500 mL clear urine was drained. Twenty units oxytocin by intravenous drip, methylergometrine maleate 0.4 mg intravenously, six doses of 250 µg prostaglandin Fα intramuscularly, and three doses of 400 µg misoprostol rectally were given over the next 9 hours along with continuous uterine massage. Investigations done showed prothrombin time (PT) 1 minute 32 seconds, direct bilirubin - 16.3 mg%, total bilirubin - 17.6 mg%, SGPT - 126U/L, SGOT - 88U/L, and hemoglobin 10.6g/dL. She was also given two ampoules of revici (N-butanol 0.26mg with citric...
acid 2.5 mg per ampoule of 5 mL) intravenously and another two ampoules in a pint of ringer lactate with 10 units syntocinon, 8 units of fresh frozen plasma, and two units of whole blood transfusion. Patient was shifted to ICU for monitoring. Uterus remained atonic. Hemoglobin dropped to 6.45/dL, PT to 20 seconds and APTT to 39 seconds. Emergency hysterectomy was done for severe atomic PPH under general anesthesia 10 hours after delivery. At laparotomy the uterus was flabby and all the tissues were bile stained and yellow. Total hysterectomy was done and hemostasis achieved. Two drains were placed, one intraperitoneally and one subcutaneously. Skin was closed with mattress silk sutures. She was put on a ventilator. Ryle’s tube and CVP line were inserted. Tachycardia (140-160/minute) persisted. Urine was clear and output was adequate. Viral markers were negative. Injection vitamin K 10 mg was given intramuscularly. Injection amoxycilllin + clavulanic acid 1.2 g was given intravenously 12 hourly. Injection tinidazole 800 mg in 400 mL of 5% glucose was given by intravenous drip. She also received 12 units of fresh frozen plasma (FFP), 11 units of cryoprecipitate and 4 units of packed cells. Bleeding from the side of the subcutaneous drain continued. Intraperitoneal drain showed minimal discharge. After 4 hours, four stitches were cut, a 3 x 5 cm hematoma removed and hemostasis achieved. Skin stitches were reapplied. Bleeding from the drain still persisted. No bleeding from any other site occurred.

In view of the persistent oozing sonography (USG) was done the next day, which showed a 4 cm hematoma above the rectus sheath and minimal fluid in the peritoneal cavity. Patient’s vitals remained stable. Due to persistent bleeding from subcutaneous drain site hemoglobin dropped to 4 g/dL. Inspite of blood transfusion. Exploratory laparotomy was done under general anesthesia on 20th February, 2005 at 11.30 am. Subcutaneous hematoma of 2.5cm was removed. Few small clots present in the peritoneal cavity were removed. Right ovary looked congested and covered with blood clots. Right salpingo-oophorectomy was done. All tissues were friable. Few prophylactic stitches were taken on the vault. Hemostasis achieved. Intraperitoneal and subcutaneous drains were placed and the abdomen closed. Postoperatively cefotaxime 1g intravenously 8 hourly and amikacin 500 mg intravenously 12 hourly were given. Investigations showed hemoglobin 4.7g/dL, PT 20 seconds, APTT 35 seconds. Direct bilirubin 19.2 mg%, total bilirubin - 27.9 mg%, SGPT - 34U/L, SGOT-71U/L, and platelets 80,000/mm³. Four units of whole blood, 7 units of FFP, 4 units of platelet concentrate and 8 units of cryoprecipitate were transfused.

Dressing stayed dry. Her condition improved. On the 2nd day she was extubated and the Ryle’s tube removed. Oral sips were allowed. Subcutaneous drain was also removed. Patient was followed up with daily LFT, platelet count, electrolytes and renal function tests which all improved gradually.

On the 5th day intraperitoneal drain was removed, full diet was allowed and breast feeding initiated. Her hemoglobin was 10.9g/dL, PT-16 seconds, APTT-32 seconds, direct, bilirubin - 4.9 mg%, total bilirubin-6.4 mg%, SGPT-29U/L, SGOT-34U/L and platelet count 120,000/mm³. On the 11th day stitches were removed and all antibiotics discontinued. She was discharged on the 13th day in good condition. She had received a total of 6 units of whole blood, 4 units of packed cells, 27 units of FFP, 4 units of platelet concentrate and 18 units of cryoprecipitate.

**Discussion**

Intrahepatic cholestasis of pregnancy (IHCP) is also known as obstetric cholestasis, recurrent jaundice of pregnancy and hepatosis of pregnancy. It is the most common condition peculiar to pregnancy and is second only to viral hepatitis as a cause of jaundice in pregnancy. Its etiology is not known but it probably has a genetic predisposition for increased sensitivity and altered membrane composition of bile ducts and hepatocytes to normally produced estrogens and progestogens and their metabolites. Histology of liver shows only simple cholestasis. There is dilatation of centrilobular bile canaliculi and many of these contain bile plugs. Electron microscopy shows swelling, distortion and atrophy of canalicular microvilli.

Clinical features of this syndrome include generalized pruritus which is the chief manifestation. It starts usually in the 3rd trimester. Early onset of symptoms denotes the severity of cholestasis. Jaundice is usually mild and mainly obstructive (serum bilirubin not > 6mg% with predominantly conjugated bilirubin). Mild elevations of SGPT and SGOT (2-10
times normal) and alkaline phosphatase (4 times normal) are noted. Diagnosis of IHCP is based primarily on clinical features.

In IHCP there is prolonged PT because of malabsorption of fat soluble vitamin K. PPH is reported in 8-22% of cases following delivery. IHCP is associated with fetal distress (nonreassuring fetal heart rate patterns), preterm labor, meconium stained liquor and sudden unexplained intrauterine deaths. Early onset is reported to be associated with more severe symptoms and a higher incidence of fetal distress. The improvement in both pruritus and jaundice begins promptly after delivery, most often within 24-48 hours. In rare cases jaundice may continue for several days (maximum 8 weeks) postpartum. Recurrence of the syndrome of cholestasis is noted in subsequent pregnancies upto 45-70% but is not inevitable. IHCP may skip consecutive pregnancies.

Our patient had complained of pruritus as early as 26 weeks of gestation and had a history of IHCP in her last pregnancy also. When she came to the casualty she was deeply icteric which is unusual for cholestasis due to pregnancy. She had no signs of preeclampsia or evidence of hemolysis. Also there was no evidence of obstructive gallstone disease or viral hepatitis. Viral markers were negative. On LFT the direct bilirubin was markedly raised with mildly elevated SGPT and SGOT which promptly decreased after delivery. These findings support the diagnosis of IHCP. Deranged coagulation profile was corrected by replacement of blood and its products. However it is unusual for IHCP to present with such severe jaundice and to result in such severe atonic PPH necessitating hysterectomy.

References
