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KEY WORDS:

A RARE CASE OF RECURRENT OBSTETRIC CHOLESTASIS OF PREGNANCY

Dr. Suprada Kothapalli MS OBG, Assistant professor, Department Of Obstetrics & Gynaecology Nri Medical College& Hospital Chinnakakani, Mangalgiri, Guntur District, Andhrapradesh.

Dr. Prabhadevi Kodey* MD DGO, Professor & Head Department Of Obstetrics & Gynaecology Nri Medical College& Hospital Chinnakakani, Mangalgiri, Guntur District, Andhrapradesh. *Corresponding Author

Dr. Rajesh .b MD DM Medical Gastroenterology, Assistant Professor, Department Of Gastroenterology ,nri Medical College.

Dr. Naga Pratyusha Indrakanti MSOBG , Assistant professor, Department Of Obstetrics & Gynaecology Nri Medical College& Hospital Chinnakakani, Mangalgiri, Guntur District, Andhrapradesh.

Dr. Pavani Pothula Postgraduate Department Of Obstetrics & Gynaecology Nri Medical College& Hospital Chinnakakani, Mangalgiri, Guntur District, Andhrapradesh.

Dr. Sowjanya. P Postgraduate. Department Of Obstetrics & Gynaecology Nri Medical College& Hospital Chinnakakani, Mangalgiri, Guntur District, Andhrapradesh.

INTRODUCTION

Obstetric Cholestasis Of Pregnancy also known as Intrahepatic Cholestasis of Pregnancy, usually presents in second half of pregnancy. It may rarely occur as early as 6 to 8 weeks of pregnancy. Affects 0.7% of pregnancies in multiethnic populations[1] and 1.2–1.5% of women of Indian–Asian or Pakistani–Asian origin.5% prevalence in women of Araucanian–Indian origin.[3]It typically recurr in subsequent pregnancies. Recurrence rate is 45-75 % in subsequent pregnancies. *Etiology* is complex and heterogenous possibly due to hormonal, environmental , dietary influences. *Risk factors* for intrahepatic cholestasis of pregnancy are Indian ethnicity, history of previous liver disease or gall stones or ICP or carrier of hepatitis, family history of mother or sister had ICP , assisted reproductive techniques multifetal pregnancy ,higher maternal age. *Symptoms* particularly on hands and feet (often only symptom),jaundice is less common. ICP is benign for mother but is associated with adverse fetal outcome. ICP increases the risk of preterm delivery (up to 19–60%), meconium staining of amniotic fluid (up to 27%), fetal bradycardia (up to 14%), fetal distress (22–41%) and fetal loss (0.4-4.1%), particularly when associated with fasting serum bile acid levels > 40 µmol/L .[15]

CASE REPORT:

A 35 year old $G_3P_2L_2$ with 36 weeks of gestation complaining of itching of palms and soles since 5th month of pregnancy. She conceived 7 years after previous pregnancy. Marital life of 10 years and non-consanguinous marriage. On examination uterus is 36 week size , relaxed, cephalic presentation , fetal heart rate 135 – 145 bpm. Investigations revealed Hb – 11 g% , urine microscopy is normal , PT- 12.40, INR- 1.00 , BT- 2 min , CT- 4 min, raised levels of Total Bile Acids – 38.6 micromol /L, ALP- 294 IU/L, SGOT-47.20 IU/L, SGPT- 82.86 IU/L, immunological tests- liver IgG tests M_2-PDH, LC1, LKM1, SLA were negative, ANCA (Anti neutrophil cytoplasmic antibody), AMA (Anti mitochondrial antibody), ASMA (anti smooth muscle antibody) were negative.

Diagnosis of ICP was made at 14 weeks of pregnancy and was on treatment with UCDA 300mg twice daily since then. Antenatal period was uneventful. She was given Vitamin K 10 mg per day orally from 34 week of pregnancy.At 36 weeks in v/o deranged liver function tests ,induced with 2 doses of PGE2 gel inracervically .she was delivered by Primary emergency LSCS due to failure of descent and dilatation along with bilateral tubectomy, delivered a male baby of 3kg weight with good APGAR.Intrapartum and postnatal period was uneventful.Liver function tests repeated 2 weeks after delivery showed serum total bile acids- 17 micromol/L, ALP- 139 IU/L, SGOT- 22 IU/L, SGPT_ 27 IU/L.

Previous history: During first pregnancy she was diagnosed as ICP at 14 weeks of gestation with lab investigations SGOT- 285 IU/L, SGPT- 250, ALP- 271IU/L, treated with UDCA since then. Antenatal period was uneventful she delivered by normal vaginal delivery, a female baby 2.5 kg with good APGAR. Intrapartum and postnatal period was uneventful. She had recurrence of ICP in second pregnancy also,diagnosed at 14 weeks of gestation with lab investigations showing total serum bile acids- 24.2 micromol/L, ALP- 441IU/L, SGOT- 155 IU/L, SGPT- 222 IU/L.Treated with UDCA 300 mg twice daily since diagnosis. Antenatal period was uneventful. At 35 weeks of gestation in v/o deranged liver function induced with 4 doses of PGE2 gel intracervically, delivered a female baby of 2.8 kg weight with good APGAR. Intrapartumand postnatal period was uneventful.

DISCUSSION

Obstetric cholestasis is a multifactorial condition of pregnancy characterized by pruritus in the absence of a skin rash with abnormal liver function tests (LFTs), neither of which has an alternative cause and both of which resolve after birth .**Pruritus that involves the palms and soles of the feet is particularly suggestive.**

Different synonymous used are: Intrahepatic cholestasis of pregnancy /Obstetric cholestasis/ Recurrent jaundice of pregnancy / Pruritus gravidarum/ Icterus gravidarum / Idiopathic jaundice of pregnancy[2]

the etiology of ICP is not completely understood and is still under discussion. Genetic, hormonal and also environmental factors may contribute to the pathogenesis of ICP[2]. Mutations in the hepatocellular phospholipid transporter, ABCB4 (MDR3), that mediates secretion of the major human phospholipid, phosphatidylcholine (le cithine) into bi le, have been estimated to account for up to 15% of all ICP cases[3,4,5].

Clinical signs that a pregnant mother shows during the second or third trimester of pregnancy includes pruritis (range from mild to severe), insomnia; psychological sufferings with or without suicidal ideations, elevated liver enzymes with evidence of Jaundice, prolonged prothrombin time due to vitamin K deficiency,

steatorrohoea due to malabsorption, gall stones, abdominal pain, malaise and other constitutional symptoms[4].

Pregnancy hormones affect gallbladder function, resulting in slowing or stopping the flow of bile. The gallbladder holds bile that is produced in the liver, which is necessary for the breakdown of fats in digestion. When the bile flow is stopped or slowed down, this causes a buildup of bile acids in the liver which can spill into the bloodstream[3]. High bile acid levels have been linked with fetal death,passage of meconium, abnormal cardiotocograph, prematurityand non-fatal asphyxial events.

Laboratory markers such as Liver function test values remain elevated specially serum bile acids, ALT, AST and serumbilirubin. Prolonged prothrombin time can be seen in mothers who are having vitamin k deficiency[7].

The newer diagnostic modalities include: Liver histology, Liver immunostaining, Electron microscopy,biliary lipid analysis, Molecular analysis, PMRS spectroscopy[8].

Some women will have pruritus for days or weeks before the development of abnormal liver function: in those with persistent unexplained pruritus and normal biochemistry, LFTs should be measured every 1–2 weeks.[9]Isolated elevation of bile salts may occur but this is uncommon; normal levels of bile salts do not exclude the diagnosis.[9,10-12]Postnatal resolution of symptoms and of biochemical abnormalities is required to secure the diagnosis[12].Routine measurement of LFTs should be deferred beyond first 10 days of puerperium as there may be physiological a rise, and can usually be performed before to the postnatal follow-up visit.

Obstetric cholestasis has been linked with an increased incidence of passage of meconium, premature delivery, fetal distress, delivery by caesarean section and postpartum haemorrhage Much of the prematurity (range 7–25%) is iatrogenic (the result of a medical decision to deliver the baby rather than spontaneous onset of labour), the risk of spontaneous preterm delivery being at most only slightly increased compared with the general population (range 4– 12%). As gestation advances, the risk of delivery (prematurity,respiratorydistress,failed induction) versus the uncertain fetal risk of continuing the pregnancy (stillbirth) may justify offering women induction of labour after 37-38weeks of pregnancyor earlier if there is suspicion of compromised fetal and maternal status.[16]

ICP can be treated with the help of antihistamines, anion exchange resins (Colestyramine), phenobarbital, S-adenosylmethionine (SAM), Dexamethasone and ursodeoxycholic acid (UDCA).

UDCA is considered to be the first line of treatment option for patients with primary biliary cirrhosis (PBC), where it improves the survival rate without liver transplantation. The recommended dose for UDCA is 15mg/kg/day.[13]

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

Cholestyramineis 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 suggestingthat cholestyramine is effective at reducing pruritus in ICP.[17]However, it has no effect on serum bile acid levels or other biochemical markers of cholestasis.

Vitamin K(Menadiol) 10 mg twicw daily from 34 weeks of gestation prevent the risk of fetal antepartum and maternal intra- or postpartum hemorrhage, since 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.

Antihistamines, such as Chlorpheniramine, may provide some sedation at night, but do not significantly impact on pruritus.

Topical emollients, includes Diprobase, calamine lotion and aqueous cream with menthol, are all safe to use in pregnancy. There is slight temporary relief from pruritus, although there is no trial data to support or refute this.

Follow-up:Maternal prognosis is good and symptoms resolve rapidly after delivery, accompanied by normalization of serum liver tests.. LFTs at 6 weeks after delivery and an appointment at 8 weeks is a suggested.Reassurance about the lack of long-term sequelae for mother and baby and discussion of the high recurrence rate (45–90%),[17]contraceptive choices (usually avoiding estrogen-containing methods) and the increased incidence of obstetric cholestasis in family members

Recurrence: There is a significant risk of recurrence with subsequent pregnancies and with the use of oral contraceptives or other estrogens.

ICP recurs during subsequent pregnancies in 45-90% [17] cases with varying severity of recurrent episodes.

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