Cholestasis

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Intrahepatic Cholestasis of Pregnancy Definition and Clinical Signs

Description

Pregnancy-associated liver diseases are the most frequent cause of liver dysfunction in pregnancy, affecting up to 3% of parturients. Of those, intrahepatic cholestasis of pregnancy (IHCP) is the most common [1]. IHCP typically presents during the second or third trimesters with pruritus and elevated bile acid levels. The disease process is considered reversible with resolution of symptoms soon after delivery. Associated lab value abnormalities usually return to normal within 6 weeks of delivery [1].

Etiology

The etiology of IHCP is thought to be multifactorial, involving genetic and hormonal as well as environmental components.

Incidence

The incidence of IHCP varies around the world ranging from 0.2% to 25%, with the highest frequency being in South Asian (0.8–1.46%) and South American (9.2–15.6%) populations [2]. The incidence is much less in the United States with an occurrence rate of less than 0.3% [3].

Risk Factors

1. There is an increased incidence of cholestasis of pregnancy in the following situations: advanced maternal age (>35 years), multiparity, history of IHCP in previous pregnancies, history of oral contraceptive use, and family clustering (higher prevalence in certain cultures such as the Mapuche) [2]. IHCP occurs more commonly in pregnancies with multiples and in women who have undergone fertility treatments [1].
2. For those women who have experienced cholestasis in prior pregnancies, the recurrence rate is reported to be 40–60% with subsequent pregnancies [2].

Clinical Signs and Symptoms

1. IHCP is characterized by mild to severe pruritus that starts in the second or third trimesters and resolves within 48 h of delivery. This itching is usually confined to the palms and soles and may worsen at night.
2. Jaundice is relatively uncommon, but if present it will develop after the onset of pruritus. The incidence of jaundice in IHCP is 14–25% [2].
3. Less common signs and symptoms of IHCP include insomnia, fatigue, anorexia, malaise, weight loss, epigastric discomfort, steatorrhea, and dark urine.

Interaction with Pregnancy

1. Abnormal liver tests occur in about 3–5% of pregnant patients [4]. With the exception of alkaline phosphatase and alpha-fetoprotein (both produced by the placenta), the remaining liver tests remain normal even in pregnancy.
2. *Maternal* effects are usually benign, with symptoms resolving soon after delivery.

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3. The effects on the fetus, however, are more ominous and include higher risks of preterm delivery, meconium passage, fetal distress, and fetal death.
   (a) With bile acid levels above 40 μmol/L, the risk of adverse fetal outcomes increases.
   (b) Adverse outcomes include spontaneous preterm labor, stillbirth, and admission to the neonatal intensive care unit [1].
   (c) The risk of perinatal death is significantly increased for each 10 μmol/L increase in bile acids [5].
   (d) Although the exact pathophysiology of these fetal effects has yet to be elucidated, it is known that the fetus has a decreased ability to clear bile acids leading to accumulation. Bile acid accumulation can result in cardiotoxicity which leads to fetal dysrhythmias and even sudden intrauterine fetal death [2]. Bile acids are also known to cause vasoconstriction of the umbilical veins, which may be responsible for fetal hypoxia. Bile acids may stimulate myometrial contractions and can increase oxytocin bioactivity, leading to preterm labor [2].
   (e) Given these risks, delivery of the fetus usually occurs as soon as fetal lung maturity is confirmed.

Testing

According to the Royal College of Obstetrics and Gynaecology guidelines, the diagnosis of IHCP is made in patients with characteristic pruritus with associated elevated serum bile acids [1]. In general, after a diagnosis of IHCP, liver function tests should be followed weekly until delivery [6]. If jaundice is present before the onset of pruritus, other diagnoses should be excluded. A liver biopsy is indicated in the case of jaundice in the absence of pruritus, or if symptoms begin before 20 weeks, or lab findings remain elevated more than 8 weeks after delivery [2].

Management

Obstetric Management

1. Elective induction of labor at 37 weeks is undertaken in an effort to reduce the risk of stillbirth [6].
2. Pharmacologic interventions are not therapeutic bur rather utilized for symptom relief. Ursodeoxycholic acid has been shown to help with the intense pruritus associated with IHCP. The typical starting dose is 500 mg twice daily with a max of 500 mg three times daily or 10–15 mg/kg/day [6]. Diphenhydramine and lorazepam are also used.

Anesthetic Management

1. Anesthetic management is only affected in the rare circumstances when liver dysfunction is present. Patients with IHCP have impaired vitamin K absorption and theoretically impaired coagulation.
2. Some small studies investigated the incidence of coagulopathy in pregnant women with IHCP with conflicting results.
3. A retrospective cohort study by DeLeon et al. reviewed the results of coagulation tests (prothrombin time, partial thromboplastin time, and platelet count), estimated blood loss, and liver function tests in 319 parturients. The main finding was reassuring, noting the lack of abnormal coagulation profiles in parturients with cholestasis of pregnancy [7]. Further investigations are needed in this area, but in general it is wise to review the patient's recent liver function tests.

References

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