Cholestasis in Pregnancy

Background
1. Definition
   - Liver disorder of pregnancy
2. General info
   - Can occur at any gestational age, but usually third trimester
   - Presents with itching and skin lesions caused by excoriations
   - Jaundice develops in 10-50% of cases (intrahepatic jaundice of pregnancy)
   - Condition usually resolves within few days (up to 2 wks) after delivery

Pathophysiology
1. Pathology of dz
   - Etiology unknown however probably multifactorial
     - Hormonal
     - Genetic
     - Environmental
     - Possibly dietary factors
2. Incidence/prevalence
   - <0.2% of pregnancies in most areas of Central and Western Europe and North America
   - More common in Baltics, Scandinavia and Chile
3. Risk factors
   - Hx of condition in prior pregnancy
     - Recurrence in subsequent pregnancies occurs in 60-70%
   - Family hx in 50% cases
   - Association with multiple gestation
4. Morbidity/mortality
   - Maternal
     - Pruritis, discomfort, jaundice
     - Jaundice can be complicated by
       - Subclinical steatorrhea with subsequent Vit K deficiency
       - Prolongation of prothrombin time
         - Incr risk of hemorrhage (rare)
     - Association with incr risk of cholelithiasis remains debatable
   - Fetal
     - Fetal distress, stillbirth, and preterm delivery
       - Possibly as a result of placental anoxia
       - Preterm delivery: odds ratio, 2.73

Diagnostics
1. History
   - Severe generalized pruritus
     - Incl palms and soles d/t intradermal deposition of bile acids
   - 2 wks after onset of pruritis, jaundice occurs in 10-50% of women
   - Usually 2nd or 3rd trimester
2. Physical exam
   - Excoriations, jaundice
Stigmata of liver dz or encephalopathy rare
  • Should trigger further eval of other etiologies of liver dz

3. Diagnostic testing
  o Laboratory eval
    • 5-10 fold incr in alkaline phosphatase
    • Bilirubin elevated, but usually not above 5 mg/dl (mostly direct or conjugated bilirubin)
    • If lasts more than several wks, prolongation of prothrombin time
    • Serum transaminase levels are usually normal or moderately elevated (seldom exceed 250 U/L)
    • GGT: usually nl or mild elevation
    • Serum cholesterol and triglyceride levels may also be markedly elevated
    • Prolonged prothrombin time (if condition lasts for several wks)
    • Serum total bile acids
      • Fasting chenodeoxycholic acid, deoxycholic acid, and cholic acid are greater than 3 times normal
  o Diagnostic imaging
    • Ultrasound: no bile duct dilatation; nl hepatic parenchyma
  o Other studies
    • Liver biopsy rarely indicated

Differential Diagnosis
  1. Key DDx
    o Acute Hep B
      • Transaminases >1000 and bilirubin >5; no coagulopathy
    o Acute fatty liver
      • Transaminases <500 and bilirubin <5; coagulopathy present;
      • Other features: Coma, renal failure, hypoglycemia
    o HELLP
      • Transaminases >500 and bilirubin <5; coagulopathy present
      • Other features: Hypertension, edema, thrombocytopenia
  2. Extensive DDx
    o Chronic Hepatitis C
    o Cholelithiasis/cholecystitis

Therapeutics
  1. Acute tx
    o 3 main mechanisms of intervention
      • Decr bile production
        • Dexamethasone
        • Phenobarbitone
      • Binding bile acids in intestine facilitating their elimination and preventing enterohepatic recirculation
        • Activated charcoal, guar gum, cholestyramine
      • Detoxifying bile acids thereby reducing their adverse cellular effects
        • SAMe, Ursodeoxycholic acid [UDCA]
Recommendations for tx

- Manage symptomatically w/resolution following delivery
  - Emollients and topical antipruritics
- 2001 Cochrane concluded insufficient evidence (small trials w/inconsistent/inadequate reporting) to recommend guar gum, activated charcoal, SAMe and UDCA alone or in combination in tx women w/cholestasis of pregnancy
  - Cholestyramine PO
    - May relieve itching in mild cholestasis (up to 50-70% efficacy)
    - Does not alter hepatic process and possibly ineffective in severe ICP
    - Needs to be admin for several days to up to 2 wks before pruritus improves
    - May precipitate Vit K that leads to coagulopathy
    - 8-16 g/day in three to four divided doses
    - Prothrombin time should be checked at least wkly w/use
    - Supplemental Vit K may be needed before delivery
- Small and more recent studies suggest that UDCA may be useful in severe cases to reduce pruritis and serologic abnormalities
  - Daily doses between 450 and 1200 mg
  - Efficacy of UDCA may incr further when co-admin w/S-adenosylmethionine

2. Further mgmt (24 hrs)

- Antepartum fetal heart rate testing and intense surveillance w/delivery if indicated are standard of care
  - Although evidence shows that this surveillance w/NST, U/S or estradiol failed to predict fetal compromise
- Consider induction of labor at term or when amniotic fluid studies indicate fetal lung maturity

Follow-Up

1. Return to office
- Frequency of visits depends on maternal sx control and need for fetal surveillance

Prognosis

1. Maternal
- Usually resolves w/in 2 days of delivery (up to 2 wks after delivery)
- Recurrence in subsequent pregnancies occurs 60-70% of time

2. Fetal
- Prematurity: incr risk
- Meconium staining: incr risk
- IUFD: incr risk, recommend incr prenatal surveillance
- Cerebral hemorrhage: some incr risk

Prevention

1. No known preventive intervention
References

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