A Child with Jaundice

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Jaundice: Definition

- Yellow staining of the skin and sclera by abnormally high blood levels of the bile pigment bilirubin.
- Normal?
Causes of physiologic jaundice

1. Increased bilirubin load due to physiologic increased RBC mass, decreased RBC life span.

2. Decreased immediate postnatal bilirubin uptake due to reduced ligandin activity.

3. Hepatic enzyme immaturity for bilirubin conjugation.

4. Increased enterohepatic circulation due to lack of intestinal flora, greater proportion of β-glucuronidase.
When is it physiologic?

- Indirect hyperbilirubinemia
- Starts after 48 hours
- Ends before 14 days
- Does not exceed 15 mg/dL
- Healthy newborn
Direct hyperbilirubinemia

• When the conjugated fraction rise to as high as 20% of the total bilirubin
• Always check a total and direct, so that you can be sure you are excluding conjugated hyperbilirubinemia, which has totally different etiologies and treatments.
• Conjugated hyperbilirubinemia is always pathologic
HISTORY

1. Gestational age: Prematurity is a risk factor for neonatal hepatitis
2. SGA: Congenital infections
3. Lethargy, decreased oral acceptance: Sepsis and Metabolic.
4. Worsening of general condition after initiation of feeds: Galactosemia
5. Bleeding manifestation: Liver dysfunction
6. Acholic stools: Biliary obstruction
7. Peculiar odour of urine: Tyrosinemia type 1 (cabbage colored urine)
8. Consanguinity: Metabolic disorders (AR disorders)
9. Maternal history: TORCH infections
PHYSICAL FINDINGS

• Assessment of general health:
  Sick looking- Sepsis, Metabolic, congenital infections
• Dysmorphic features: Alagille syndrome
• Head circumference: Microcephaly- TORCH
• Eye: Chorioretinitis- TORCH, Posterior embryotoxon and drusen: Alagille syndrome
• Hearing loss: Congenital CMV infection
• Stool inspection: Acholic stools- Biliary obstruction
Cardinal Feature

Appears within first 3 months of life
- Jaundice
- Dark urine
- Pale stools
- Hepatomegaly
Summary of the differential diagnoses..1

• Biliary system structural issues
  – Extrahepatic
    • Obstruction (EHBA)
    • Dilatation (Choledochal cyst)
  – Intrahepatic
    • Obstruction (Alagielle syndrome)
    • Dilatation (Caroli disease)
Summary of the differential diagnoses...

- Liver issues
  - Infections
    - Hepatitis B, C
    - TORCH
    - Idiopathic hepatitis
  
  - Genetic
    - Primary familial intrahepatic cholestasis (PFIC)
Neonatal cholestasis: metabolic etiology?

Metabolic etiology
Presenting as liver failure
Galactosemia
Tyrosinemia
N Haemachromatosis
Mitochondrial/FAOD
Nieman Pick C
HFI
Others
PFIC/ BASD
Cystic Fibrosis
AATD X
Citrin deficiency
Peroxisomal disorders (Zellweger)
Nieman Pick A, Wolmans disease
Cong Disorders Glycosylation
Gaucher’s etc

Classification

Neonatal Cholestasis

Intrahepatic disease

Hepatocyte injury
- Metabolic disease
- Viral disease

“Idiopathic” neonatal hepatitis

Bile duct injury
- Intrahepatic bile duct or paucity

Extrahepatic disease (bile duct injury or obstruction)

Biliary atresia
Neonatal Cholestasis?

Wilson’s Disease
Glycogen Storage Disease
Systemic

- Cystic Fibrosis
- Sepsis
- UTI
- Drugs
Endocrine

- Hypothyroid
- Hypopituitarism
INVESTIGATIONS

- The principal diagnostic concern to differentiate hepatocellular diseases from anatomical disorders & systemic illness
- Diseases which are managed medically from those requiring surgical intervention.
INVESTIGATIONS

1. LFT-
   • Serum Bilirubin-Total & Direct
     To establish cholestasis
   • Prothrombin time/ International normalized ratio (INR)-
     Measure severity of liver dysfunction
   • Serum Transaminases -sensitive indicators of
     hepatocellular injury. lack specificity.
   • Alkaline phosphatase high in biliary obstruction, low
     specificity
   • Gamma-glutamyl transpeptidase (GGTP) marker of biliary
     obstruction
     ✓ Elevated - cholestatic disorders
     ✓ Low or normal levels - progressive familial intrahepatic
       cholestasis (PFIC), disorders of bile acid synthesis
B. To detect conditions that require immediate treatment:

1. CBC
2. Urine R/E
3. Cultures of blood & urine
4. Serum $T_4$, TSH
5. To detect metabolic conditions—Urinalysis, urine for non glucose reducing substance
6. TORCHS IgM screening
C. To differentiate extrahepatic from intrahepatic causes of cholestasis

1. Imaging studies
   • Ultrasonography
   • Hepatobiliary scintigraphy
2. Percutaneous liver biopsy
3. Percutaneous trans-hepatic cholangiography
Early Diagnosis?

- Biliary atresia
- Sepsis
- Hypothyroid
- Metabolic disease
  - Galactosemia
Diagnostic algorithm for neonatal cholestasis

1. Basal lab chemistry (fasting)
   - Examine urine and stool
   - Exclude or assess:
     - Biliary atresia
     - Alagille syndrome
     - Neonatal sclerosing cholangitis
     - α1AT deficiency
     - Cystic fibrosis
     - Choledochal cyst
     - Biliary sludge

2. Ultrasonography (fasting)

3. Intraoperative cholangiography

Explaination:
- **Prolonged jaundice with direct hyperbilirubinemia?**
  - Yes
    - Feces depigmented?
      - Yes
        - Basal lab chemistry (fasting)
      - No
        - Basal lab chemistry (fasting)
  - No
    - Ultrasonography

**Exclude or assess:**
- Infection, sepsis (e.g. TORCHL)
- TSH, thyroxine, cortisol, ferritin, triglyceride levels, LDL, HDL.
- α1AT deficiency, cystic fibrosis
- PFICs (transaminases ↑↑, GGT ↓)
- Metabolic disorders and storage diseases
- Further differential diagnosis (table 1) and liver biopsy

**Basal lab chemistry for neonatal cholestasis:**
- Blood cell count with reticulocytes, total and fractionated bilirubin, coagulation parameters (incl. INR, ATIII), hemolysis parameters,
- Liver transaminases incl. GGT, plasma bile acids, lipase, glucose, lactate, ammonium, CrP.
GENERAL MANAGEMENT

- **Nutritional support:** NC children are underweight and will need nutritional support. Calorie requirement is 125% of the RDA.

- Breast feeding should be encouraged and 1-2ml/kg/day MCT oil should be administered in 2-4 divided dosed in EBM.
Thank You