Recurrent Jaundice in a Child: Case based Reviews

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CASE 1

A 7-year-old boy initially presented to his local hospital with mild fever, vomiting and anorexia for 1 week followed by jaundice with high colored urine. At this point fever had subsided but jaundice progressively increased. They had received symptomatic treatment. Parents noticed clearance of jaundice, improvement in appetite and some improvement in liver function tests were also observed (though still not normal). However, after 3 weeks jaundice increased along with worsening of liver function tests but no clinical deterioration. There was no history of recent travel/blood transfusion/ jaundice in family members recently. No history of recent drug intake e.g. antitubercular (ATT) or any other hepatotoxic drugs. Physical examination showed weight 20 kg, height 120 cm, icterus, no palmar erythema/spider nevi. Liver was palpable 3 cm below costal margin, soft in consistency, no splenomegaly or ascites. Other systems were normal on examination.

What is the differential diagnosis?

The child had presented with jaundice of acute onset with prodromal symptoms of fever, anorexia, and vomiting. High colored urine indicated it to be conjugated hyperbilirubinemia and not unconjugated one. Soft hepatomegaly, with no stigmata of underlying chronic liver disease and normal anthropometry are pointers towards acute onset hepatitic illness. Enlarged liver with no change in clinical condition makes the possibility of liver failure unlikely. Subsidence of fever in a few days makes malaria or typhoid unlikely as etiology. No pruritus, fever or pale stools makes obstructive jaundice unlikely. Absence of anemia, lymphadenopathy, bone pain, weight loss, and conjugated jaundice makes hemolysis an unlikely cause. Hence the differential diagnosis would be acute hepatitis (viral/bacterial/protozoal). Drug induced hepatitis should be suspected if history of hepatotoxic drugs especially ATT intake is present. Leptospirosis should be suspected in a patient with high grade fever, jaundice and decreased urine output. However in this case worsening of liver function tests after initial improvement suggests relapse of the initial, which is seen with hepatitis A.

Which investigation would you considers?

Complete Blood Count (CBC), Erythrocyte Sedimentation Rate (ESR), peripheral smear, Malarial Parasite (MP), Blood culture – To rule out hemolysis, malaria and typhoid.

Liver Function Test, Prothrombin Time – To look for rise in transaminases (which may be in thousands), however rise in Prothrombin Time (PT) International Normalized Ratio(INR) is more bothersome as it may indicate acute liver failure.

Ultrasonography abdomen – To look for ascites, pericholecystic edema (associated findings seen in acute hepatitis)

Viral serology for Hepatitis A (IgMHAV), Hepatitis E (IgMHEV), Hepatitis B (HbsAg)

Leptospiral serology – To rule out leptospirosis

Lab results

Liver Function Test showed Aspartate Aminotransferase/Alanine Transaminsae 1600/2440, Normal PT INR, IgM HAV positive. IgMHEV, HbsAg, Leptospiral serology was negative.

Why did the child have a relapse of jaundice? Management? Studies from the Indian subcontinent on acute viral hepatitis A (1), observe a double peak of jaundice or relapsing hepatitis in 11% of patients. The mean time to relapse was 3.4 weeks with a range of 2–6.7 weeks (2). Management of relapse of acute hepatitis remains symptomatic treatment.

Take home message

Relapse in HAV is seen in a subset of patients and management remains the same.

CASE 2

A 3-year-old girl presented with high-grade fever with jaundice, irritability and pale stools for 1 week. She had a similar episode of jaundice 6 months back lasting 2 weeks requiring hospitalization and intravenous antibiotics. There was no history of total parenteral nutrition or intake of antibiotics for a prolong period in infancy. Physical examination revealed weight of 15 kg, height of 90 cm, deep icterus and itch marks

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on skin. There was no hepato-splenomegaly or ascites and rest of the systemic examination was normal.

What is the differential Diagnosis?

This young child presented with two distinct episodes of cholangitis (jaundice, fever, pain abdomen). Jaundice, pale stools and itch marks suggests an obstructive pattern of jaundice rather than hepatocellular. Such a young age of presentation hints at congenital defect in the biliary system like choledochal cyst (CDC) or choledocholithiasis. Similar presentation of obstructive jaundice can be seen in biliary ascariasis in endemic areas (Jammu & Kashmir). In cases with biliary atresia there is persistent jaundice since neonatal period with pale stool and patients decompensate very early within a year short of Kasai portoenterostomy.

What investigation would you considers?

Complete Blood Count, Erythrocyte Sedimentation Rate (ESR) – neutrophilia and raised ESR suggest cholangitis/sepsis.

Liver Function Test, Gamma Glutamyl Transpeptidase (GGT), Prothrombin Time – Liver function tests will show direct hyperbilirubinemia with disproportionate increase in GGT and Alkaline Phosphatase (AP) compared to transaminases is suggestive of obstruction in biliary system.

Serum amylase and lipase – To rule out pancreatitis, which may be one of the complications of choledochal cyst.

Ultrasound abdomen – Dilated common bile duct with or without stones can be seen. Worms in bile duct can be seen in cases of biliary ascariasis.

Laboratory results/ investigations

Liver Function Test – showed total bilirubin 15 mg/dl with direct bilirubin 13 mg/dl. Aspartate Aminotransferase/Alanine Transaminsae 134/145, GGT 1120, Alkaline Phosphatase 990. Prothrombin Time and International Normalized ratio were normal.

Complete Blood Count – Hemoglobin 11 gm/dl, Total Leucocyte Count 15000/cumm, Differential Leucocyte Count neutrophils 90%, ESR 48 mm.

Ultrasonography abdomen – showed dilated common bile duct of 12 mm.

Further investigation – Magnetic Resonance Cholangiopancreatography was done which confirmed the findings of ultrasound & showed type 1 choledochal cyst with upstream intrahepatic biliary duct dilatation.

Management/ Treatment

Surgery is the definitive treatment. It involves radical cyst excision and reconstruction by hepaticoenterostomy. It aims for restoration of normal bile flow by bilioenteric anastomosis and reduction of the risk of malignancy by removing the most common sites of malignant transformation (i.e., the cyst wall and the gall bladder) (3–5). Timing of surgery in a case presenting with acute cholangitis is 4–6 weeks after cholangitis resolves.

Treat cholangitis with IV antibiotics with or without endoscopic retrograde cholangiopancreatography (ERCP) for biliary drainage. Antibiotics of choice are piperacillin/tazobactam, third generation cephalosporins and quinolones. Meropenem and Imipenem are resorted to in case of non-response to above antibiotics.

Take home message

In case of recurrent attacks of jaundice in young child with fever and pale stools, one needs to rule out obstructive causes esp. congenital defects in the biliary system.

CASE 3

A 15-year-old boy presented with a history of yellowness of eyes noticed once every year since 3 years of age. This yellowness subsided with or without treatment in 15–20 days and mostly observed during summers. Urine color during these episodes was always normal. There was no history of anemia, blood transfusion, bone pains , itching or any family member with anemia or hemoglobinopathy. On examination, weight was 50 kg with a height of 168cm. Mild icterus was present. There was no hepatosplenomegaly and rest of the systemic examinations were normal.

What is the differential diagnosis?

Important thing to note here is urine color being normal in presence of yellow sclera which is suggestive of unconjugated hyperbilirubinemia.

This distinction is important for making a correct list of differentials. In summary this boy had self limiting episodes of jaundice without any blood transfusion requirement/bone pains since young age. Thus the possibility of hemolytic episodes causing jaundice as in sickle cell disease is unlikely here. Infectious etiology with recurrent episodes without any complications with early onset is unlikely. Another differential could be Gilbert syndrome, where such episodes are commonly seen in the general population (prevalence 3–7%) (6). It is a heterogeneous condition in which bilirubin UDP glucuronosyltransferase gene (UGT1A1) is defective and hence a problem in bilirubin conjugation (7, 8).

Which investigation would you considers?

- Complete Blood Count , blood film, Reticulocyte count – To look for anemia or hemolysis.
- Liver Function Test – To look for unconjugated or conjugated hyperbilirubinemia and transaminases.
- Lactate Dehydrogenase – High LDH may indicate ongoing hemolysis.
- Hemoglobin electrophoresis – In presence of anemia and unconjugated hyperbilirubinemia, it should be done to rule out hemoglobinopathies.
- Ultrasound abdomen – to rule out cholelithiasis seen in hemolytic disorders.

Lab results

Laboratory investigations showed: Hemoglobin 13 gm/dl;total bilirubin 6 mg/dl; direct bilirubin 0.8 mg/dl; indirect bilirubin 5.2 mg/dl; Aspartate Aminotransferase/Alanine Transaminsae 22/23 and reticulocyte count 0.4%.

Further testing

Genetic testing for Gilbert's polymorphism for UGT1AI gene to confirm the diagnosis of Gilbert's syndrome.

Take home message

In case of jaundice, urine color is an important factor to distinguish conjugated and unconjugated hyperbilirubinemia. In a child with recurrent unconjugated jaundice and normal liver enzymes think about disorder of in bilirubin conjugation like Gilbert syndrome.

CASE 4

A 9-year-old girl presented with three episodes of jaundice in 2 years with dark urine. She also developed gross abdominal distension and pedal edema in the last episode. Previous 2 episodes lasted 2–3 weeks and were managed symptomatically at the local hospital. She had poor appetite and had lost weight in last 2 years. There was no history of encephalopathy, pruritus, bleed or melena. She had a family history of hypothyroidism. Physical examination revealed weight 22kg, height 120cm, icterus, palmar erythema and vitiligo patch on forehead. On abdominal examination the liver was palpable 2 cm below costal margin which was firm in consistency, and spleen 1 cm below costal margin with shifting dullness on percussion.

The given case represents a case of recurrent jaundice, hepatocellular in nature with recent decompensation as ascites. Differentials in such a case should consider causes of chronic liver disease in a young girl. Though the first differential for Chronic Liver Disease (CLD) in a 9-year-old child would be Wilson's disease but here is a young girl with family history of autoimmune disease, vitiligo and recurrent jaundice,so autoimmune hepatitis (AIH) is more likely etiology. Wilson disease must be ruled out, which may present in a similar fashion (11). Budd Chiari syndrome is another differential which may present as ascites alone. Hepatitis B, C are causes of chronic liver disease but they do not present as decompensated liver disease in <10 year of age.

What investigation would you consider?

Liver Function Test, Prothrombin Time – Increase in liver enzymes (Aspartate Aminotransferase/Alanine Transaminsae) suggest hepatocellular jaundice. Aspartate aminotransferase elevation may be more than Alanine transaminsae suggestive of chronicity. Reversal of Albumin Globulin ratio may indicate autoimmune hepatitis.

Ultrasonography abdomen and Doppler for liver (size, nodularity) and portal vein diameter and collaterals: Shrunken liver, nodularity of liver with splenomegaly indicate cirrhotic liver with portal hypertension.

UGI endoscopy to look for varices which signify portal hypertension.

Laboratory Investigations

Laboratory investigations showed: Liver Function Test - total bilirubin 5 mg/dl, direct bilirubin 3 mg/dl, Aspartate Aminotransferase/Alanine Transaminsae 840/536, serum albumin 2.8, total protein 7.1, serum globulin 4.3 and International normalized ratio 1.7.

Ultrasonography abdomen – showed coarse liver echotexture with liver size of 7 cm, mild splenomegaly and moderate ascites. Hepatic veins and inferior vena cava were patent and portal vein diameter was 12mm.

UGI endoscopy showed small esophageal varices.

Further investigation

Autoimmune markers – Antinuclear Antibody, SMA (1:20 dilution) & Anti LKM (1:10 dilution) to establish diagnosis of AIH.

S Ceruloplasmin, KF ring by slit lamp examination, 24-hour urine copper estimation to rule out Wilson disease.

Immunoglobulin G (IgG), C3, C4 levels: High IgG levels >1.5X normal and low C3, C4 indicate AIH.

Liver biopsy – interface hepatitis with dense plasma cell infiltrate are characteristic findings of AIH.

Lab results and management

Anti Smooth Muscle Antibody, Antinuclear Antibody were strongly positive suggestive of type 1 autoimmune hepatitis.

Liver biopsy done later after correction of coagulopathy and resolution of ascites confirmed the diagnosis of AIH. She was initially managed with steroids for induction and then switched to azathioprine and low dose steroids for maintenance. Her liver function tests normalized and ascites resolved.

Take home message

CLD in a female child who presents with recurrent jaundice and reversal of A:G ratio suggest AIH.

Wilson's disease should always be ruled out by doing S Ceruloplasmin; KF ring and 24-hour Urinary Copper estimation (2/3 criteria should be present).

FURTHER READING:

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