

## Observation Letters

# Infantile cholestasis presenting as recurrent pruritus

Sir,

Pruritus is a common cutaneous symptom and often challenging to diagnose. A good history, clinical examination and basic laboratory investigations help to detect the underlying cause. Cholestatic syndromes are due to inborn or acquired disorders of bile formation and transport.<sup>[1]</sup> The prognosis depends on the cause and can range from spontaneous recovery to chronic liver disease and hepatocellular failure.<sup>[2]</sup> Most cases of post-neonatal cholestasis are due to viral infections or drug-induced hepatotoxicity. Rare causes include syndromes of intrahepatic cholestasis. Benign recurrent intrahepatic cholestasis is a rare hereditary disorder characterized by recurrent jaundice and intense pruritus with a normal extrahepatic biliary tree. It usually resolves spontaneously with no significant liver damage.

An 18-month-old girl, born of a non-consanguineous marriage, was referred to us with symptoms of recurrent and intense pruritus that began at the age of nine months. Initially, pruritus used to last only for a few days with symptom free intervals in between but these episodes then began to persist for weeks leading to sleep disturbance and irritability. Episodes of pruritus coincided with frequent bouts of loose stools. Antihistamines, topical medications and alternative medicine were tried for months with no relief. The child had mild icterus, no pallor, high colored urine and pale stools. Multiple excoriations were visible over her hands and feet. A few ecchymotic patches and hyperpigmentation were also seen. Systemic examination revealed that her growth parameters were normal and she had no dysmorphism. There was mild hepatomegaly. Cardiac, auditory and ophthalmic evaluations were within normal limits. There was no family history of liver disease.

An initial provisional diagnosis of cholestatic pruritus was confirmed with laboratory investigations. The serum bilirubin levels were mildly elevated with a raised conjugated fraction and increased alkaline phosphatase levels. The serum transaminases, serum albumin, serum protein, serum cholesterol, serum ceruloplasmin and alpha-1 antitrypsin levels were

normal. The prothrombin time was initially prolonged but improved with Vitamin K administration. The gamma glutaryl transpeptidase (GGT) levels were very low. There was no evidence of TORCH infection. Ultrasound examination of the abdomen showed mild hepatomegaly with a normal echotexture and hepatobiliary tree with no biliary tract dilatation. A liver biopsy was not pursued due to parental concerns. The DNA analysis was not done due to financial constraints.

The incidence of infantile cholestasis is about 1 in 2700. A study by Bhavne and Bavdekar revealed that it accounts for 30% of all pediatric hepatobiliary disorders.<sup>[3]</sup> The usual presenting features are jaundice, high coloured urine and clay coloured stools. Cholestasis leads to elevated levels of bile acids in the blood due to its retention in the liver. Bile acid deposition and subsequent irritation of cutaneous receptors leads to pruritus. Jaundice is a characteristic symptom. However, this may not be apparent in all cases and a high index of suspicion is necessary for diagnosis.

We considered a diagnosis of benign recurrent intrahepatic cholestasis, also known as Summerskill-Walshe-Tygsup syndrome, a type of familial intrahepatic cholestasis syndrome in our patient for the following reasons:

- Recurrent episodes of intense pruritus, associated with jaundice, high colored urine and steatorrhea in an apparently healthy child with symptom-free intervals. Pruritus is the chief complaint, predominantly affecting the hands and feet. It is usually nocturnal and associated with hyperpigmentation
- Conjugated hyperbilirubinemia with raised alkaline phosphatase levels but with low gamma-glutamyl transferase levels (contrary to most other cholestatic conditions) and with a normal hepatobiliary tree on ultrasound examination
- The benign course of the illness. The serum transaminases remain normal even during symptomatic exacerbations indicating a good prognosis. Persistently elevated transaminase levels with raised cholesterol would have favoured a diagnosis of progressive familial intrahepatic cholestasis.

The child was treated with cholestyramine and ursodeoxycholic acid. Her steatorrhea, jaundice and

pruritus subsided. The serum bilirubin, alkaline phosphatase and prothrombin time returned to normal once the symptoms resolved. She was healthy and her liver function tests remain normal after a year of follow-up.

Progressive familial intrahepatic cholestasis, earlier known as Byler's disease, refers to a group of hereditary liver disorders of childhood. These are characterized by defects in biliary transport at the hepatocellular level causing cholestasis in early childhood with an average age of presentation of around five months. Both sexes are equally affected. The condition was originally described in Amish descendants of Jacob Byler. The exact prevalence is unknown and the estimated incidence is around 1 in 50,000–100,000 live births. India has a relatively low incidence of 8.5% cases of neonatal cholestasis syndromes.

Three types of progressive familial intrahepatic cholestasis (PFIC) have been described based on the genetic defect of hepatocellular transport of bile acids. PFIC1 and PFIC2 usually appear in the early months of life. PFIC3 is seen in adulthood. These conditions present with cholestatic symptoms of pruritus, jaundice and steatorrhea. PFIC1 and PFIC2 have low to normal gamma-glutamyl transferase levels whereas it is elevated in PFIC3. The disease can progress to cause chronic liver disease, cirrhosis and end-stage liver failure. Early recognition of these conditions is essential.

In the spectrum of hereditary cholestatic disease, benign recurrent intrahepatic cholestasis is a benign variant. It is characterized by intermittent episodes of cholestasis that result in pruritus, jaundice and steatorrhea. It presents in early infancy and there are years of relatively symptom free intervals. Pruritus is the typical presenting feature and sometimes occurs much before the appearance of jaundice. During exacerbations, conjugated bilirubin and alkaline phosphatase levels are elevated which return to normal during the asymptomatic periods. There is no progression to chronic liver disease and the prognosis is good. However, the pruritus can be intolerable and distressing to the patient and often goes undiagnosed. Symptomatic relief is obtained with rifampicin, ursodeoxycholic acid and cholestyramine.

The prevalence of the condition is unknown. The diagnosis is based on clinical history (at least 2–3 episodes of cholestasis in early infancy), typical serum biochemistry (elevated conjugated serum bilirubin, elevated alkaline phosphatase levels and normal gamma-glutamyl transpeptidase levels). These tests are normal during asymptomatic periods. A complete evaluation includes normal liver histology with plugs in the biliary canaliculi. Molecular genetic testing confirms the genetic mutation, located on 18q21-q22.<sup>[3]</sup>

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#### Conflicts of interest

There are no conflicts of interest.

**Aparna Anand Gulvadi, V. K. Sreenivasan**

Department of Pediatrics, Amala Institute of Medical Sciences, Thrissur, Kerala, India

**Address for correspondence:** Dr. Aparna Anand Gulvadi, Department of Pediatrics, Amala Institute of Medical Sciences, Thrissur - 680 555, Kerala, India.  
E-mail: appubabu1966@gmail.com

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