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CASE REPORTS

NEONATAL CHOLESTASIS WITH CONGENITAL PORTOSYSTEMIC SHUNT AND ABCB4 MUTATION

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ABSTRACT

A 15-day-old female presented with jaundice and clay-coloured stools for one week. She was detected to have multiple muscular ventricular septal defects (VSDs) on echocardiography (2D ECHO). Liver biopsy revealed ductopenia. Whole exome sequencing was suggestive of mutation in the ABCB4 (-) gene in exon 4 with variant c.193A>G Progressive familial intrahepatic cholestasis - 3 (PFIC 3) of uncertain significance. The child was given fat soluble vitamin supplements, ursedeoxycholic acid (UDCA). Her jaundice resolved at 5.5 months of age. However at 11, 15, and 22 months, ultrasound (USG) with doppler thin right portal vein and an intrahepatic shunt between the right portal vein and inferior vena cava (IVC). Repeat 2D ECHO at 15 months was normal. The patient is currently asymptomatic and on regular follow-up.

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KEYWORDS

Neonatal Cholestasis, Congenital portosystemic shunt, PFIC 3.

Introduction

Neonatal cholestasis, a condition marked by impaired bile flow in newborns, is often linked to factors like sepsis, metabolic disorders, biliary obstruction, and shock.[1] A less common but significant contributor is the presence of Congenital Portosystemic Venous Shunts (CPSS), which are rare vascular anomalies that create an unusual connection between the portal and systemic venous systems.[2] These shunts can also lead to cholestasis. Moreover, there is evidence suggesting a genetic component linking to CPSS, with reports of familial cases.[3]

The precise mechanisms behind how CPSS and neonatal cholestasis interact remain elusive. Differentiating whether the shunt is causing cholestasis or it's unrelated is somewhat complex. This query arises because the increased resistance within the liver due to cholestatic liver diseases might redirect blood flow through the shunt. As a result, even if a shunt is identified, it's crucial to continue exploring other potential causes of neonatal cholestasis.[4,5]

Case Report

A 15-day-old female neonate, weighing 2.58 kg, presented with yellowish discoloration of the eyes since 1 week of life, accompanied by clay-coloured stools and yellow urine. Physical examination revealed jaundice, hepatosplenomegaly and a systolic murmur at the parasternal region. She was on exclusive breast feeds and birth weight was 2.6 kg. Investigations are illustrated in Table 1. Echocardiography (2D Echo) detected multiple muscular ventricular septal defects (VSDs), while an abdominal ultrasound showed calcific liver foci and a collapsed gall bladder. Cytomegalovirus(CMV) IgG was positive. Other TORCH IgM and IgG were negative. Liver biopsy revealed ductopenia, and whole exome sequencing was suggestive of heterozygous mutation in the ABCB4 (-) gene in exon 4 with variant c.193A>G PFIC 3 of uncertain significance. She was treated with fat-soluble vitamin replacement, ursedeoxycholic acid (UDCA). Her jaundice resolved at 5.5 months of age. However at 11, 15, and 22 months, ultrasound (USG) with doppler thin right portal vein and an intrahepatic shunt between the right portal vein and inferior vena cava (IVC). Repeat 2D ECHO at 15 months was normal. The patient is currently asymptomatic and on regular follow up.

Discussion

Neonatal cholestasis presents a diagnostic challenge due to its various potential etiologies.[1] In our case, a 15-day-old patient exhibited classic cholestatic symptoms, with multiple possible causes under consideration. Elevated ferritin levels raised suspicion of hemochromatosis while liver biopsy was suggestive of ductopenia suggestive of non-syndromic bile duct paucity syndrome. Although hemochromatosis can lead to neonatal cholestasis, it usually results in symptoms of hepatocellular failure appearing shortly after birth.[6] This was not the case for our patient. Non-syndromic bile duct paucity syndrome presents with varying prognoses, with approximately half of the patients progressing to cirrhosis and portal hypertension, often resulting in liver failure within the first year of life.[7] It›s worth noting that our patient did not experience liver failure and child's neonatal cholestasis resolved on follow up. Also genetic testing was suggestive of PFIC type 3 with a variant of unknown significance. In early childhood, PFIC commonly emerges with intrahepatic cholestasis symptoms like itching, dark urine, pale stools, and fatigue. GGT levels differ in PFIC types and remains high in PFIC 3. Treatment involves dietary support, vitamins, and medium-chain triglyceride supplementation.[8] In our patient, since the variant was

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Table 1. Serial clinical and lab.

	15 DAYS	30 DAYS	45 DAYS	2 MONTHS	3.5 MONTHS	5.5 MONTHS
TOTAL BILIRUBIN (mg/dl)	11.2	12	10.5	9.05	3.62	0.8
DIRECT BILIRUBIN (mg/dl)	8.15	8.18	8.2	7.28	2.67	0.5
SGOT (IU/L)		336	184		191	28
SGPT (IU/L)		197	70		173	47
FERRITIN (ng/ml)	3622					
SGPT (IU/L)	NORMAL		11.8/1		15.7/1.2	-
TOTAL PROTEIN (g/L)		4.31	5.1			5.0
ALBUMIN (g/L)		2.86	3.4			3.8
ALBUMIN (g/L)		539			377	180
GGTP (U/L)		58.6	61		199	90

of unknown significance, it is unlikely that it was the cause of neonatal cholestasis.

Following treatment, the patient showed symptom improvement. However, during follow-up imaging, an unexpected finding was observed - a congenital portosystemic shunt of type 2a, an intrahepatic shunt connecting the right portal vein and the inferior vena cava.

Transient neonatal cholestasis can coincide with intrahepatic and extrahepatic CPSS.[4,5,10] It may present with complications like portal hypertension, encephalopathies, high output cardiac failure, pulmonary hypertension or may just be totally asymptomatic.[9] Managing CPSS whether through conservative or interventional means depends on shunt ratio, type, and complications. Conservative treatment suits mild metabolic issues and some asymptomatic intrahepatic shunts, which might regress by age 2 years. Complex cases need long-term monitoring, especially with persistent issues like pulmonary hypertension, to detect shunts that need closure.[10]

At present, our patient is asymptomatic and is on regular monitoring to track her condition's progress.

Compliance with Ethical Standards

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