https://doi.org/10.33472/AFJBS.6.6.2024.7398-7403

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Progressive Familial Intrahepatic Cholestasis –A Case Report

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Article Info

Volume 6, Issue 6, July 2024

Received: 31 May 2024

Accepted: 28 June 2024

Published: 22 July 2024

doi: 10.33472/AFJBS.6.6.2024.7398-7403

ABSTRACT:

Progressive familial intrahepatic cholestasis (PFIC) is a rare group of inherited liver disorders affecting newborns and young children, leading to progressive liver disease and cirrhosis. With an estimated frequency of 1 per 50,000 to 1 per 100,000 births, PFIC is classified into six types, with PFIC-1 and PFIC-2 being the most common. This case report presents a 42-day-old male infant with jaundice and abnormal liver parameters, diagnosed with PFIC type 2 through clinical and investigative evaluation. The infant exhibited persistent jaundice, high-colored urine, and elevated liver function tests, including total serum bilirubin, SGOT, SGPT, ALP, and serum bile acids. A liver biopsy revealed giant cell hepatitis with mild portal fibrosis and bile duct proliferation, while a HIDA scan ruled out biliary atresia. Treatment included ursodeoxycholic acid, phenobarbitone, and fat-soluble vitamin supplementation, with a plan for liver transplantation.

PFIC is a distressing cholestatic liver disorder leading to end-stage liver disease. Diagnosis involves clinical, laboratory, and genetic evaluations. PFIC types 1 and 2 present early in infancy, while PFIC type 3 manifests later. Extrahepatic symptoms and elevated GGT levels aid in differentiating PFIC types. PFIC management is challenging, with medical therapies offering limited benefits and surgical options such as liver transplantation providing effective relief. Early diagnosis and intervention, including biliary diversion and transplantation, are crucial to prevent significant morbidity and mortality from end-stage liver disease.

Keywords: PFIC 1, PFIC 2, PFIC 3, PFIC 4, Neonatal jaundice, Liver transplantation, Giant cell hepatitis, Ursodeoxycholic acid.

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1. Introduction:

PFIC, or progressive familial intrahepatic cholestasis, is a rare group of disorders that primarily affect newborns and early childhood. They can be broadly classified into six types based on clinical presentations, laboratory results, liver histology, and genetic defects.[1] With an

overall estimated frequency of 1 per 50,000 to 1 per 100,000 births, PFIC-1 and PFIC-2 are comparatively more common, whereas PFIC-3 is extremely rare, with an estimated incidence of 1 per 500,000 births.[2] Here we are presenting a case of 42 days old baby brought with jaundice and deranged liver parameters found to have PFIC type 2 upon appropriate clinical and investigative evaluation.

Case report:

A 42 days old male , was brought with complaints of Yellowish discolouration of eyes, persisting since discharge from birth of the baby, aggravated for the past 7 days. High coloured urine for the past 7 days ; there was history of deep staining of diapers. H/o bad child rearing practices (giving gripe water). No h/o passing clay coloured stools (baby passing yellow coloured stools), No h/o fever, persistent vomiting, abdominal distension, No h/o inadequate weight gain, No h/o incessant cry, excessive bleeding from injection sites, hematemesis, No h/o seizures, crying during micturition, passing of oily bulky stools. Baby is exclusively breastfed.

Figure:1 shows yellow colour stools, Figure 2 shows yellow colour urine and figure 3 shows interdiction baby.

Antenatal History:

No h/o fever with rash, lymphadenopathy during pregnancy. No h/o pruritis, fatty liver of pregnancy.

Natal History:

Term / Birth weight- 2.640 kg/ Appropriate for Gestational age/ born via Emergency LSCS (Ind: non- progression of labour) / Baby cried immediately after birth (no birth asphyxia) , breastfed within 1 hour of birth,no h/o NICU admission. Urine and meconium passed within 24 hours of birth. No h/o phototherapy or exchange transfusion.

Investigations:

LFT- Total serum bilirubin- **12.9** mg/dl (elevated), Direct bilirubin- **1.7** mg/dl
SGOT- **970** IU/ L (elevated), SGPT- **440** IU/L (elevated), ALP - **865** IU/L (elevated),
GGT- **65** IU/L PT-INR - normal
CBC- Hb- 10.8 g%, Retic count - 2.4 %, Peripheral smear - Dimorphic anemia, no hemolysis
Direct Coombs test- negative
Thyroid Function test- normal
Urine routine - normal
USG abdomen - normal
Serum bile acid - 221.3 umol/ L
Pediatrics gastroenterology opinion was sought and liver biopsy was performed which showed Giant cell Hepatitis with mild portal fibrosis and bile ductal proliferation.
HIDA scan was done which was not suggestive of Biliary atresia.

Treatment:

The baby was started on Syp.Ursodeoxycholic acid, Syp. Phenobarbitone and fat soluble Vitamin supplementation. And the child was planned for liver transplantation.
Bidirectional ABCB11 gene sequencing of coding exons and their flanking intronic junction was sent results are pending.

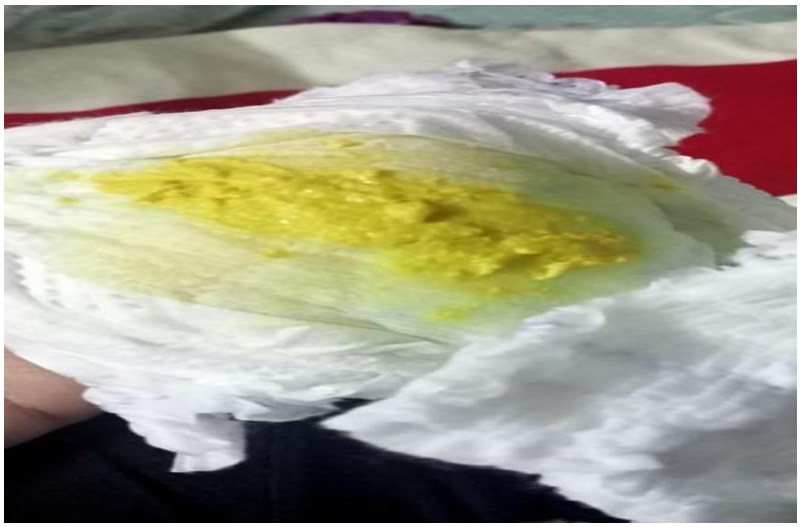

Figure:1

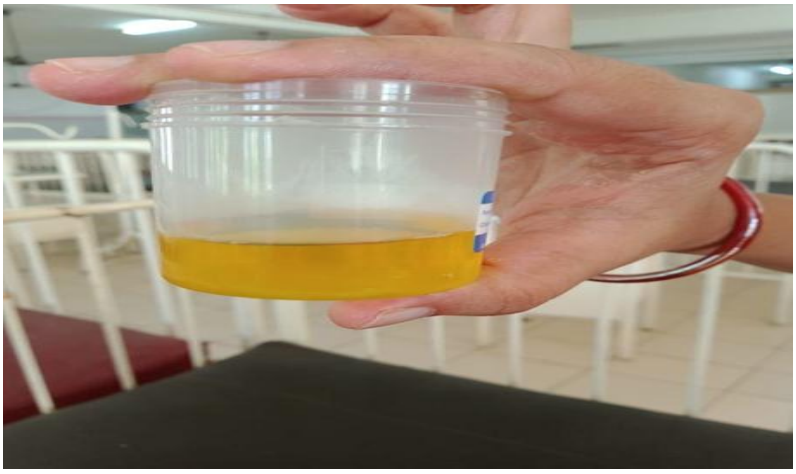

Figure: 2

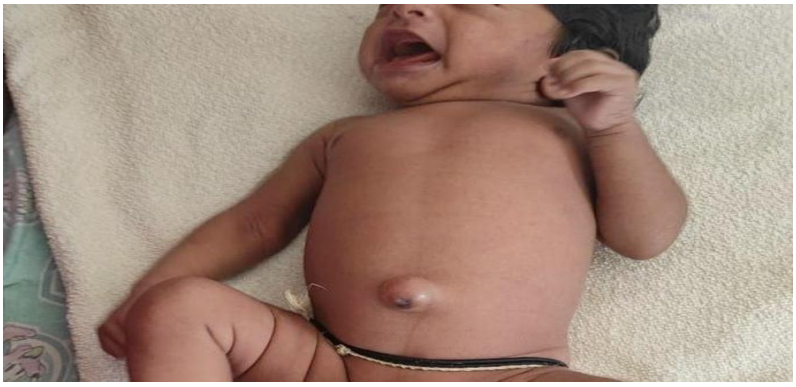

Figure:3

2. Discussion:

Progressive familial intrahepatic cholestasis is a group of rare inherited liver diseases which progress to end-stage liver disease and cirrhosis[3]. There are multiple forms of genetically proven PFIC; types 1 and 2 account for two-thirds of instances, and type 3 accounts for one-third of patients. These types of PFIC are among the most common sorts. Recently PFIC variation called PFIC 4 was discovered.[4] To identify the variant type, the diagnosis of PFIC,

the disease's onset, extrahepatic symptoms, GGT level, and molecular and genetic tests are all essential.[5] Babies with PFIC 1 &2 present with cholestasis in neonatal period or early in infancy whereas PFIC 3 later in infancy or later in life.[6] Persistent short stature, sensorineural hearing loss, chronic watery diarrhea, cholecystitis, pancreatitis, and high sweat electrolyte concentration are examples of extrahepatic symptoms of PFIC1. But extrahepatic symptoms are not seen in PFIC 2.[7] Learning impairments, osteopenia, and limited growth are seen in early onset of PFIC3. [6] On the other hand, gastrointestinal bleeding due to portal hypertension and liver cirrhosis is a common presentation of late-onset PFIC 3 in late childhood and adolescence.[6] Patients with PFIC 3 have elevated GGT levels, whereas those with PFIC 1 and 2 have low GGT levels. PFIC 1 & 2 are strongly associated with hepatocellular carcinoma and have rapid progression compared to type 3.[8][9] Some reports show PFIC4 may be linked to a higher risk of HCC, making early liver transplantation and continuous monitoring necessary for a better prognosis.

PFIC is a significantly distressing cholestatic liver disorder of childhood resulting in cirrhosis and end stage liver disease. There are a variety of medical therapeutics having limited benefits and there are some surgical options, defined having positive effects on symptoms and liver histology. Since relief from symptoms is not sustained in an acute manner, the disposable percutaneous transhepatic biliary drainage catheters are not suitable for this disease group. Living donor transplantation is reported to be safe and effective.[10] The knowledge on the biological role of bile acids in metabolic pathways is still evolving. Thus novel pharmaceuticals affecting bile acid circulation/ metabolism are also promising for PFIC patients.

3. Conclusion:

The diagnosis and treatment of patients with PFIC are difficult. They may result in end stage liver disease if not diagnosed before development of cirrhosis and hepatic fibrosis. The treatment strategy must be planned before hepatic fibrosis and cirrhosis develop. External or internal biliary diversion and liver transplantation approaches should be performed in selected cases. Early diagnosis and biliary diversions may prevent significant morbidity and mortality from end stage liver disease.

4. References:

1. Overeem AW, Li Q, Qiu YL, Cartón-García F, Leng C, Klappe K, et al. A molecular mechanism underlying genotype-specific intrahepatic cholestasis resulting from MYO5B mutations. *Hepatology*. (2020) 72(1):213–29.
2. Degiorgio D, Colombo C, Seia M, Porcaro L, Costantino L, Zazzeron L, et al.Molecular characterization and structural implications of 25 new ABCB4 mutations in progressive familial intrahepatic cholestasis type 3 (PFIC3). *Eur J Hum Genet*. (2007) 15(12):1230–8.
3. Davit-Spraul A, Gonzales E, Baussan C, Jacquemin E. *Orphanet J Rare Dis.* 2009;4:1.
4. Vinayagamoorthy V, Srivastava A, Sarma MS. *World J Hepatol.* 2021;13:2024–2038.
5. Baker A, Kerkar N, Todorova L, Kamath BM, Houwen RH. *Clin Res Hepatol Gastroenterol.* 2019;43:20–36.
6. Henkel SA, Squires JH, Ayers M, Ganoza A, Mckiernan P, Squires JE. *World J Hepatol.* 2019;11:450–463.
7. Amirneni S, Haep N, Gad MA, Soto-Gutierrez A, Squires JE, Florentino RM. *World J Gastroenterol.* 2020;26:7470–7484
8. Gunaydin M, Bozkurter Cil AT. *Hepat Med.* 2018;10:95–104.
9. Torfenejad P, Geramizadeh B, Haghighat M, et al. *Iran J Pediatr.* 2016;26:6497.

10. Cutillo L, Najimi M, Smets F, Janssen M, Reding R, De Goyet JD, Sokal EM. Safety of living- related liver transplantation for progressive familial intrahepatic cholestasis. Pediatric transplantation. 2006 Aug;10(5):570-4.