

## Case Report

# Byler Disease Progressive Familial Intrahepatic Cholestasis (PFIC)

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### Abstract:

A 20-month old boy delivered to consanguineous parents presented early in the infantile period with deep jaundice, his investigations showed progressive cholestatic jaundice, high liver enzymes and high GGT. Hepatitis and metabolic errors were excluded. The liver biopsy showed a prominent parenchymal bile stasis without features of bile obstruction or an evidence of paucity of bile ducts. These findings are going with the diagnosis of Byler Disease or progressive familial intrahepatic cholestasis (PFIC3) which is a chronic cholestasis syndrome that begins in infancy and usually progresses to cirrhosis and hepatic failure in the first few years of life. Few patients have survived into the third decade of life without treatment. Liver transplantation is the only effective treatment for this type of the disease.

### Introduction:

Progressive familial intrahepatic cholestasis (PFIC) is an inherited condition in which children are unable to drain bile from the liver even though the large bile ducts are open. It is extremely rare and affects only infants and children, with males and females affected equally. The disease is caused by defects in several genes that produce proteins needed for bile formation and the "transportation" or flow of bile throughout the body, it is of autosomal recessive inheritance with three different genes dividing the disease into three types; types PFIC1 and PFIC2 are of low to normal gamma-glutamyl-transferase (GGT) while type PFIC3 is called High-GGT PFIC which is the most severe type and leads to early cirrhosis. The disease usually begins in infants less than six months of age and may get worse very quickly. However, some children develop this condition later, and the condition progresses more slowly. In most cases, progressive familial intrahepatic Cholestasis leads to cirrhosis and liver failure. A liver transplant will most likely be necessary for survival. The most common symptoms of progressive familial intrahepatic Cholestasis include jaundice and severe itching caused by the buildup of bile salt in the body, poor weight gain and poor growth. Other symptoms may include abnormal enlargement of the liver and spleen, Poor feeding, nausea and vomiting. The complications of the disease include difficulty absorbing fats and fat-soluble vitamins (D, E, A, K) which depend on bile acids for absorption, failure to thrive, cirrhosis with liver failure, liver cancer and gallstones. The diagnosis of the disease is by high TSB and direct hyperbilirubinemia and high liver enzymes. GGT and genetic studies will help to determine the type of the disease. Liver biopsy will show the evidence of intrahepatic Cholestasis. Treatment of the disease includes medical and surgical treatment, some patients may respond to medical therapy, although surgical treatment is usually necessary for survival. The medical treatment of the disease includes the fat soluble vitamins, barbiturates and ursodiol which promote bile flow. Surgical treatment used in children with

Progressive familial intrahepatic Cholestasis includes partial external biliary diversion (PEBD) before cirrhosis and liver transplantation for patients with cirrhosis.

### Case Report:

20-month-old boy is a product of a full term normal delivery with birth weight of 2800 grams, pregnancy was uneventful, and his post-natal period passed without problems. His symptoms started at age of 2 months when the parent noticed that he has yellow discoloration of skin and sclera which was becoming deeper by time then he started to have severe itching to his skin. His parents are first degree cousins but no family history of similar condition. He is vaccinated up to date, he was on mixed feeding and started cereals at the age of 5 months and his developmental history was slightly delayed. On physical examination the child was deeply jaundiced with multiple scratch marks all over his body. His weight was 11.8kg, his height was 79cm and his head circumference was 47cm (all are below 25th centile). His spleen was enlarged to 1.5cm BCM. and his liver was enlarged 3 cm BCM. There was no ascites, and no other signs of chronic liver disease or rickets. The results of his investigations showed a normal CBC, urea, creatinine and electrolytes. Total bilirubin was 20.2 gm with a direct of 8.7 gm. His liver enzymes, alkaline phosphatase 552, AST: 509, ALT: 231, gamma-glutamyl transpeptidase (GGT): 72 IU/l (normal: 7-32). Prothrombin time was 14 seconds (control = 14 seconds) and partial thromboplastin time was 30 seconds (control 32 seconds), albumin, cholesterol and triglycerides levels were normal. Blood pyruvate, lactate,  $\alpha$ 1-antitrypsin and serum amino acids chromatography were normal. No organic acids or reducing substances were detected in the urine. Infectious screen for hepatitis A, B, C, and TORCH infections were all negative. TSH and T4 are normal. Serum zinc is normal. Abdominal ultrasound showed slightly increased echogenicity of the enlarged liver. Liver biopsy showed

prominent parenchymal bile stasis and partially distorted architecture but no features of bile obstruction or paucity of bile ducts. The patient is on medical treatment including fat soluble vitamins

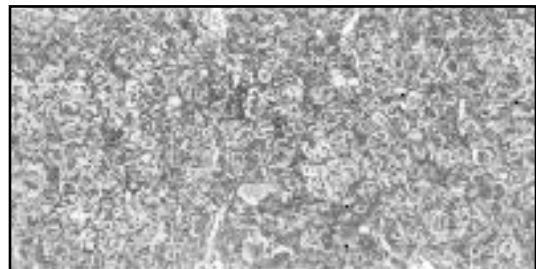


Jaundice and Pruritis in Byler Disease

#### Discussion:

This patient presented to my clinic in European Gaza Hospital at the age of two months with deep jaundice otherwise he was thriving well, his initial investigations showed direct hyperbilirubinemia with high liver enzymes and high GGT, then more investigations were done including TORCH screening, hepatitis panel, TSH, T4 and abdominal ultrasound, all of the results were normal. The child was given phenobarbitone and cholestyramine but with little improvement. As parents were first degree relative there was thinking in familial diseases and as the patient was deteriorating and we have no facilities to do the further investigations so the patient was referred to Egypt where the other investigations showed normal aminoacids in blood and negative aminoacids in urine, normal serum zinc and alpha-1 antitrypsin. Finally liver biopsy was done with informative results as it showed a prominent parenchymal bile stasis and partially distorted architecture but there were no features of bile obstruction or paucity of bile ducts. These results are in favor of the diagnosis of Byler Disease or Progressive Familial Intrahepatic Cholestasis (PFIC) and as the serum gamma-glutamyl-transferase (GGT) is high so it is Type3 (PFIC3) which is having poor prognosis and ends into liver cirrhosis early. Since that time the patient was given the fat soluble vitamins and I planned to give him ursodiol but it is not available now. His condition is deteriorating now with continuously increasing TSB and GGT with deteriorating liver function that is why I will refer him very soon for surgery either partial external biliary diversion (PEBD) or liver transplant which is the only curable treatment for the disease.

(A,D,E,K) and phenobarbitone without proper response and he is still having severe pruritis and deterioration of liver function so he will be referred for surgical treatment.



Typical liver biopsy findings in PFIC

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