PFIC

What is PFIC?

PFIC (Progressive Familial Intrahepatic Cholestasis) is a rare genetic disorder which mainly affects the liver. Essentially, patients with PFIC cannot properly transport bile out of their liver cells, leading to liver damage and its manifestations.

There are 3 subtypes of PFIC. They are classified according to the genetic defect and presence of low vs. high levels of serum GGT activity (a liver associated enzyme).

PFIC1, also known as Byler's disease or FIC1 disease, is caused by mutations in the *ATP8B1* gene.

PFIC2, also termed BSEP disease, is due to a mutation in the *ABCB11* gene.

PFIC3, more appropriately named MDR3 disease, is caused by mutations in the *ABCB4* gene.

FIC1, BSEP, and MDR3 are abbreviations for the names of the proteins- the gene products-absent or malfunctioning in forms of PFIC.

What are the symptoms?

The disease typically manifests itself in the first year of life, and may present with jaundice, irritability, growth failure, diarrhea, bleeding disorders, and/or enlarged liver. The hallmark feature of this disorder is severe debilitating pruritus (itching).

There are several clinical differences in the three subtypes.

PFIC1 (low GGT) FIC1 disease is a systemic disease and can include problems in addition to liver disease; pancreatitis, diarrhea, hearing problems, growth failure.

PFIC2 (low GGT) solely involves the liver but has a more severe progressive course if untreated, including the possible development of liver and bile duct malignancy.

PFIC3 (high GGT) has a broad clinical spectrum. In partial deficiency, the effects are milder and may include gallstones and intermittent itching– it may not present until adulthood. In complete deficiency, the effects are quite severe, and often progress to cirrhosis and liver failure within the first few years of life.

How is it diagnosed?

Until recently, no specific test confirmed the diagnosis of PFIC. Typically, it is characterized by elevated liver enzymes, elevated total and conjugated bilirubin, abnormal bleeding times, low or normal GGT in PFIC1 and PFIC2 and high GGT in PFIC3.

Two types of tests are now available. These tests are fee-for-service and may not be covered by insurance.

Immunostaining can test liver tissue to document absence of a gene product within liver cells. Such testing is available at **King's College Hospital in London** -for information contact : Alex Knisely, MD, Consultant Histopathologist (e-mail alex.knisely@kcl.ac.uk).

Genetic testing is also available on a clinical basis to confirm the diagnosis of PFIC. The CETT genetics lab at **Houston Baylor College of Medicine (TX)** is currently the only CLIA-certified lab in the U.S. which performs this test. Information can be found on the lab website at www.bcm.edu/geneticlabs/tests/alltests.

For a current listing of other testing facilities see http://genetests.org.
Click on Gene Reviews for a laboratory directory searchable by disease name.

How is it treated?

In most cases, medications are tried first. The medications most commonly used include ursodeoxycholic acid, rifampin, and supplemental fat-soluble ADEK vitamins. These medications are not FDA approved for these purposes.

If medications fail, surgery is inevitable. Currently three surgical approaches are available: partial external biliary diversion (PBED), ileal exclusion, and liver transplantation. Experience with PBED and ileal exclusion is greatest for PFIC1 and PFIC2.

The most commonly used approach is partial external biliary diversion (PEBD). It is frequently helpful in alleviating the itching and possibly preventing progression of disease.

An alternative surgical approach is ileal exclusion. Experience with this procedure in children with PFIC is limited.

Liver transplantation is reserved for children whose liver disease has progressed to cirrhosis or if biliary diversion fails to relieve the mutilating pruritus.

Will my other children be affected?

PFIC is an autosomal recessive (AR) disorder, which means that each parent carries an abnormal copy of the affected gene. With an AR disorder each sibling of an affected child has a 25% chance of being affected by the disorder and a 50% chance of being a carrier: that is, a 75% chance of being clinically well.

Related Links

PFIC.org
www.pfic.org

CLiC
http://rarediseasesnetwork.epi.usf.edu/clic

Information in this pamphlet was brought to you by PFIC.org, a resource for families with Progressive Familial Intrahepatic Cholestasis. This information is presented for educational purposes only and is not intended as a substitute for the diagnosis, treatment and advice of a licensed medical professional.

Related Links

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Information for Parents