RIVER CITY
GASTROENTEROLOGY

Primary Biliary Cholangitis (PBC)

Understanding chronic bile duct inflammation and its management

WHAT IS PRIMARY BILIARY CHOLANGITIS?

Primary biliary cholangitis (PBC), previously called primary biliary cirrhosis, is a chronic autoimmune liver disease in which the immune system gradually destroys the small bile ducts inside the liver. Bile is a fluid produced by the liver to aid digestion and is normally transported from the liver through bile ducts to the small intestine. When the small bile ducts are damaged, bile accumulates in the liver (a condition called cholestasis), causing progressive liver inflammation and scarring.[1,2]

Despite the old name, most people with PBC do not develop cirrhosis if the condition is detected and treated early. The name was changed in 2015 to better reflect the autoimmune nature of the disease and to reduce stigma associated with the word "cirrhosis".[1]

PBC predominantly affects middle-aged women (over 90% of cases). It is estimated to affect approximately 1 in 3,000 to 1 in 4,000 adults in Western countries. It often coexists with other autoimmune conditions, including Sjogren's syndrome, thyroid disease, and coeliac disease.[1]

WHAT CAUSES PBC?

The exact cause is unknown, but PBC results from a combination of genetic susceptibility and environmental triggers. The immune system produces antibodies (particularly anti-mitochondrial antibodies, or AMA) that mistakenly attack a specific protein on the surface of the bile duct cells, causing progressive damage. Environmental triggers under investigation include infections, chemical exposure, and hormonal factors.[1,2]

SYMPTOMS

PBC is frequently diagnosed in people who have no symptoms, either through routine blood tests or investigation of another autoimmune condition. When symptoms occur, they may include:[1,5]

Early symptoms:

- Fatigue: the most common and often most debilitating symptom; not always related to the degree of liver disease
- Pruritus (itching): caused by bile salts accumulating in the skin; can be severe and significantly affect quality of life; often worse at night or in warm temperatures

Later symptoms (with disease progression):

- Jaundice (yellowing of the skin and eyes)
- Right upper abdominal discomfort
- Dry eyes and dry mouth (associated with Sjogren's syndrome, which commonly coexists)
- Bone pain and fractures due to reduced bone density (osteoporosis)
- Xanthelasmas: yellow fatty deposits around the eyes from elevated cholesterol
- Symptoms of cirrhosis and portal hypertension in advanced disease

DIAGNOSIS

PBC is diagnosed when at least two of the following three criteria are met:[1,2]

- **Elevated alkaline phosphatase (ALP) and/or GGT**: the hallmark blood test abnormality in PBC, reflecting cholestasis (impaired bile flow).

- **Positive anti-mitochondrial antibodies (AMA)**: present in 95% of patients with PBC. A positive AMA titre of 1:40 or higher, in the context of elevated ALP, is highly specific for PBC and usually sufficient to make the diagnosis without a liver biopsy.
- **Liver biopsy**: not required when AMA is positive and ALP is elevated, but may be performed when the diagnosis is uncertain (AMA-negative PBC) or to accurately stage the degree of fibrosis. Shows characteristic non-suppurative destructive cholangitis.

Additional tests include FibroScan to assess fibrosis, abdominal ultrasound, and screening for associated autoimmune conditions (thyroid function, coeliac serology, and Sjogren's syndrome markers).

TREATMENT

Treatment cannot cure PBC, but it can significantly slow disease progression and improve symptoms. Treatment response is assessed by monitoring liver enzymes (ALP, bilirubin) after 12 months.[1,4,5]

Ursodeoxycholic acid (UDCA)

UDCA (ursodiol) is the first-line treatment for PBC and the only treatment approved worldwide for this purpose for decades. It is a naturally occurring bile acid that, when taken in high doses, reduces the accumulation of toxic bile acids in the liver, reduces liver inflammation, and slows fibrosis progression. It is taken daily as tablets or capsules (13-15 mg/kg/day). UDCA is well tolerated with minimal side effects. Approximately 40% of patients do not respond adequately to UDCA alone and require additional therapy.[1,2]

Obeticholic acid (OCA) - Ocaliva

Obeticholic acid is approved as a second-line treatment for PBC in patients who do not respond adequately to UDCA or who cannot tolerate it. OCA is a synthetic bile acid derivative that activates the farnesoid X receptor (FXR) in the liver, reducing bile acid synthesis and liver inflammation. It is taken once daily in combination with UDCA. The main side effect is worsening pruritus (itching), which can be significant.[4]

Emerging therapies

Several newer agents are in late-stage clinical trials for PBC, including elafibranor (a PPAR agonist) and seladelpar. These are expected to provide additional options for patients with inadequate response to existing treatments.

Managing symptoms

- **Pruritus (itching)**: managed with cholestyramine (a bile acid sequestrant, taken before meals), rifampicin, or naltrexone. Antihistamines are generally not effective for bile salt-related itch. Naltrexone can cause opioid withdrawal symptoms and is started at a very low dose.
- **Fatigue**: unfortunately, fatigue in PBC does not respond well to any specific treatment. Good sleep hygiene, regular gentle exercise, and psychological support can help manage fatigue and its impact on quality of life.
- **Osteoporosis**: calcium and vitamin D supplementation are recommended for all patients. Bisphosphonate therapy (e.g. alendronate) is indicated for patients with established osteoporosis, though bisphosphonates should be used cautiously in people with oesophageal disease.
- **Dry eyes and dry mouth (Sjogren's features)**: artificial tears, good oral hygiene, and dental care are important.

MONITORING

Regular monitoring is essential to assess treatment response, detect complications, and screen for associated conditions:[1,5]

- Liver function tests (ALP, bilirubin, albumin) and full blood count every 3-6 months
- FibroScan or liver imaging to assess fibrosis progression annually
- Bone density (DEXA) scan every 2-3 years
- Thyroid function and coeliac serology at diagnosis and periodically
- 6-monthly liver ultrasound and AFP blood test if cirrhosis is present (liver cancer surveillance)
- Upper GI endoscopy if cirrhosis develops (to assess for varices)

PROGNOSIS

With early diagnosis and treatment with UDCA, most people with PBC who respond adequately to therapy have a normal or near-normal life expectancy. People who do not respond to UDCA are at higher risk of disease progression and should be assessed for second-line therapy and, in advanced cases, liver transplantation. Liver transplantation is very effective for PBC, with excellent long-term outcomes.[1,2]

RESOURCES AND SUPPORT

- **Australian Liver Association:** www.australianliver.com.au - Find a hepatologist and access resources on autoimmune liver disease in Australia
- **Liver Foundation Australia:** www.liver.org.au - Patient support and information for people with primary biliary cholangitis
- **PBC Foundation (UK, with resources useful for Australian patients):** www.pbcfoundation.org.uk - International patient organisation with comprehensive PBC resources and community support

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