Primary Biliary Cholangitis - Full Clinical Guideline

Reference no.: CG-T/2012/214

PBC is a chronic cholestatic disease with a progressive course that may extend over decades. Patients are increasingly diagnosed with early asymptomatic disease.

Symptoms:
Fatigue - does not correlate with severity of disease. No specific treatment.
Pruritus - effects 1/3 patients (see management of pruritus in cholestasis)
Dry eyes/ mouth (Sicca syndrome)

Diagnosis:
ALP > 1.5 x ULN for ≥ 6/12 and positive anti-mitochondrial antibody (AMA) ≥ 1:40
(AMA positive in < 1% of normal controls and < 5% of PBC is AMA negative)
typically ↑ IgM ,↑ cholesterol (disproportionately HDL - no ↑ risk of atherosclerosis)
Liver biopsy usually not required: consider If PBC suspected and AMA negative or ALT > 5 x ULN and considering overlap syndrome (consider a 3/12 trial of UDCA first)

Management of PBC:
AMA + individuals with normal LFTs → annual LFTs in 1° care (median time to abnormal LFTs 6yrs)

UDCA (13-15mg/kg/d) - associated with biochemical improvement (90% seen within 6-9/12)
histological improvement
↓ need for transplantation for PBC
- More favourable response in early disease, but offer to all patients

Obeticholic acid (OCA) – see non-responders section below

PBC-AIH overlap: ≈ 5-10% of patients with PBC (overdiagnosed)- ≈30% of PBC patients have positive ANA - multiple nuclear dots and rim-like/membranous immunofluorescence patterns are characteristic of PBC. The addition of prednisolone to UDCA in patients with a mild/ moderate interface hepatitis does not improve the biochemical response.

Paris criteria for primary biliary cirrhosis (PBC)–autoimmune hepatitis (AIH) overlap

- **PBC features (2 or more parameters)**

ALP >2× ULN or GGT >5× ULN
Antimitochondrial antibody (AMA) ≥1:40
Liver biopsy showing florid duct lesions
and

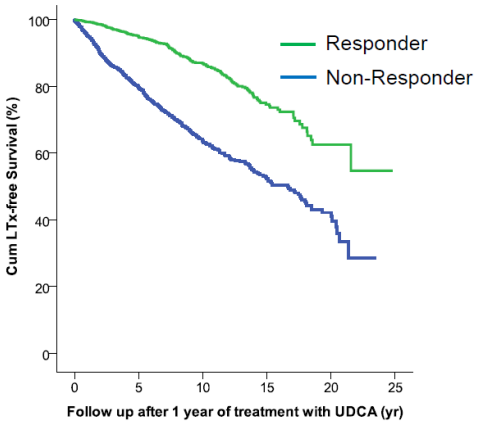
- **AIH features (2 or more parameters)**

ALT >5×ULN
IgG >2×ULN or positive smooth muscle antibody (SMA)
Liver biopsy showing moderate or severe periportal or periseptal lymphocytic piecemeal necrosis

Treatment: UDCA + immunosuppressive treatment as for AIH

Management of complications:
Screen for coeliac disease
Osteoporosis: Affects 1/3 of patients with PBC (RR 4.4 for age/sex matched population)
Lifestyle advice and Adcal-D3 2 tablets daily depending on adequacy of diet (if no history of renal stones)
DEXA scan at diagnosis with follow-up @ 2-5yrs depending on outcome.
Portal hypertension: May rarely be seen in PBC in the absence of cirrhosis (consider if platelets < 140). In cirrhotic patients follow variceal surveillance guidance

Monitoring:
The majority of patients (excepting those with significant co-morbidities) should undergo risk stratification following 1 year of UDCA therapy. UK PBC risk calculator used to calculate their risk of a liver related event (death/ transplantation) at 5, 10 and 15 years. Current life expectancy in UK is 80.4yrs. Consider 1° care follow-up if at low risk of progressive disease



ALP < 1.67 x ULN and normal bilirubin after 1 year of UDCA (responder) predicts a low risk group with better outcome. Low risk patients should have annual LFTs and repeat risk stratification every 3 years.

Annual LFTs, TFTs (20% lifetime risk of hypothyroidism)
Annual Vit A, D, E and clotting if Bilirubin > 34

Non-responders:
Patients with a ALP > 1.67 X ULN and/ or elevated bilirubin (< 2 x ULN) after 1 year UDCA or who are intolerant of UDCA should be discussed at the end of the Wednesday am viral MDT with regard to add on/ substitution with Obeticholic acid (OCA) (initial dose 5mg od, increasing to 10mg at 6 months if tolerated). Patients felt to be appropriate for OCA are referred to the Nottingham regional MDT. Drugs are dispensed by Nottingham through homecare and treatment should be reviewed in the Derby clinic in 3 months.

A PBC MDT referral template and patient letter for OCA approved patients can be located in the Hepatology shared drive.

Patients with Child A cirrhosis and portal hypertension should have monthly blood tests at the outset, to monitor for decompensation. Child B/ C patients should have the dose adjusted to 5mg/ week (with maximum dose of 10mg/wk)

OCA is associated with a dose dependent exacerbation of pruritus in up to 10% of patients.

Bezafibrate 400mg od has also been showed to result in a complete biochemical response (normal Bilirubin, ALP, AST, Albumin and PT) in 31% and normalisation of ALP in 67% of patients with an inadequate response to UDCA (Corpechot et al. NEJM 2018)

Patients should be considered for transplantation when Bil > 50 and listed when > 100 or MELD >12/ UKELD > 49

Familial risk/ testing: Screening of relatives not recommended. Siblings have RR of 10 and daughters of PBC mothers a RR of 35, but against a background of 350/million prevalence.

Further reading:
The British Society of Gastroenterology/UKPBC guidelines GUT Jan 2018
AASLD guidelines, Hepatology, July 2009 AASLD guideline
EASL guidelines, J Hepatol, August 2009 EASL guidelines

Documentation Controls

Development of Guideline:	Dr Adam Lawson
Consultation with:	Hepatology consultant and specialist nurse team
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Key Contact:	Dr Adam Lawson