Primary Sclerosing Cholangitis and Cholangiocarcinoma - Full Clinical Guideline

Reference no.: CG-T/2012/217

PSC is a chronic, cholestatic disease characterised by inflammation and fibrosis of both intra and extrahepatic bile ducts, leading to the formation of multifocal bile duct strictures.
2:1 Male with mean age at Δ of 40 years
Associated with an ↑ risk of cholangiocarcinoma (lifetime incidence 10-15%, 50% Δ in 1st yr).

60-80% have concomitant IBD (majority UC). Colitis in PSC is typically mild with a pancolitis (87 vs 54%), backwash ileitis (51 vs 7%) and rectal sparing (52 vs 6%)

Symptoms:
RUQ pain, fatigue, pruritus (see management of pruritus in cholestasis), weight loss. 40% asymptomatic at diagnosis.

Diagnosis:
MRCP
Liver biopsy only indicated if MRCP normal and either small duct PSC suspected or in cases where an AIH overlap suspected
Serum IgG4 should be checked once at initial diagnosis. If raised then a liver biopsy to look for evidence of an autoimmune cholangiopathy is indicated
25% of cases have only intrahepatic disease on cholangiogram, < 5% only extrahepatic
Small duct PSC has better prognosis (transplant free survival 29 vs 17 yrs)
No role for the routine use of autoantbodies in diagnosis (including p-ANCA)

Management:
Other than liver transplantation there is no proven treatment for PSC
UDCA (13-15mg/kg/d) - no conclusive prove it either ↓ risk of colorectal/ cholangiocarcinoma, or alters progression of liver disease. High dose (up to 25mg/kg/d) may be harmful.
(EASL give no specific recommendation, AASLD recommend UDCA not given)

Dominant stricture (defined as < 1.5mm diam in CBD or < 1mm in right or left hepatic ducts)

- Investigate for dominant stricture with MRCP if ↑ bilirubin or pruritus
- If advanced PSC (evidence of portal hypertension and/or severe intrahepatic beading) avoid ERCP and consider for transplant assessment
- If early PSC and jaundice → CT/EUS to exclude cholangiocarcinoma (CCA) before ERCP and brushing (note sensitivity for CCA < 40%) + dilatation (stenting reserved for refractory cases)
- If CCA suspected a Ca 19-9 > 130u/ml has a sensitivity 79% and specificity 98%
- Consider post ERCP antibiotics for 3-4 days in addition to pre-procedure antibiotics in patients with PSC who undergo ERCP

PSC-AIH overlap: predominantly children/ young adults; typically sequential with AIH first. Characterised by biochemical and histological appearance of AIH, with cholangiographic appearance of PSC. Low threshold for MRCP in young patient with AIH Treat AIH element with immunosuppressive therapy.

Monitoring:
The median time from diagnosis to death or transplantation is 10-12 years
All patients should have an initial colonoscopy as the colitis in PSC patients is often mild.
Those with colitis should have an annual colonoscopy– 30% risk of CRC over 20yrs – 76% right sided
Annual USS – lifetime risk of GB cancer 2% and HCC 2%. Any GB mass (even < 1cm) should lead to consideration of cholecystectomy. Note lymphadenopathy common in PSC.
No role for routine measurement of Ca 19-9
Annual Vit A, D, E and clotting if Bilirubin > 34
Portal hypertension: Variceal surveillance if platelets < 140 or known cirrhosis. In cirrhotic patients follow variceal surveillance guidance

Osteoporosis: Less common than in PBC
DEXA scan at diagnosis with follow-up @ 2-5yrs depending on outcome

IgG4 associated cholangitis/ Autoimmune pancreatitis:
Biochemical and cholangiographic features may mimic PSC or carcinoma of the pancreas. Associated with ↑ IgG4 in serum (present in ≈ ¾ patients) and staining on histological specimens.
85% of patients are men. Patients are older than the typical PSC patient and no association with IBD.

Cholangiocarcinoma (CC)

20% intrahepatic, 50-60% perihilar, 20% distal; extrahepatic and 5% multifocal

Diagnosis:
MRCP/ MRI liver
CT to assess for distant metastases
Carbohydrate antigen (Ca19-9) is raised in 85% of patients with cc, but also increased in PSC and other cases of non-malignant obstructive jaundice (PPV for cc 16-40%)
Ca125 raised in 65%
IgG4 to exclude an autoimmune cholangiopathy
ERCP – standard cytology positive < 50% of cases of cc. Combined with biopsy increases yield to 40-70%

At presentation 50% have lymph node and 10-20% peritoneal involvement. < 1/3 patients are suitable for surgery at diagnosis
Staging Laparascopy – only 50% of perihilar cc undergoing laparotomy are ultimately suitable for curative resection

Treatment
Surgery
Palliative stent insertion
Chemotherapy if ECOG performance status 0 or 1 – medial survival with Cisplatin and Gemcitabine was 11.7 mths

Further reading:

AASLD guidelines, Hepatology, July 2009 AASLD guideline
EASL guidelines, J Hepatol, August 2009 EASL guidelines
BSG guidelines (cholangiocarcinoma), GUT 2012
ACG clinical guideline: PSC. Am J Gastro May 2015

Documentation Controls

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