

PRIMARY SCLEROSING CHOLANGITIS and GALLBLADDER POLYPS

Chronic progressive disorder characterized by inflammation, fibrosis, and stricturing of medium size and large ducts in the intrahepatic and extrahepatic biliary tree.

- 1-6/100,000
- Unknown etiology – genetic and immune factors likely involved
 - HLA-B8, HLA-DRw52a

Associated diseases

- Ulcerative colitis 60-75%
- Cholangiocarcinoma 15-35%
- Pancreatitis 10-20%
- Crohn's disease 5-10%
- Diabetes mellitus 5-10%
- Colon cancer 2%
- Pancreatic cancer 1%

Sequelae:

- ESLD/portal hypertension
- Cholestasis – Vit A, D, E, K deficiency, malabsorption
- Biliary stricture – 20%, rule out cholangiocarcinoma with cytology/brushings; treat with balloon dilatation/stenting
- Cholecystitis/cholangitis
- Cholangiocarcinoma – 10-15% lifetime risk
- Colon cancer – risk is higher in patients with UC and PSC as compared to UC alone
- Average survival without liver transplant is 12-18 years

Presentation

- Many are asymptomatic at time of diagnosis
- More common in white men in 40s
- LFT abnormalities, especially alkaline phosphatase elevation
- fatigue, pruritis, RUQ pain, fevers/chills

Diagnosis

- characteristic multifocal stricturing and dilation of intrahepatic and/or extrahepatic bile ducts on cholangiography(ERCP or PTC)
- MRC has comparable diagnostic accuracy to ERC
- Liver biopsy
 - Useful for staging, treatment planning
 - Shows fibrous obliteration of small bile ducts, with concentric replacement by connective tissue in an "onion skin" pattern – most specific finding

Staging

- Stage I – Enlargement, edema, and scarring of the portal triads, and mononuclear cell infiltration with some piecemeal necrosis and damage to isolated bile ducts. Proliferation of interlobular bile ducts with mononuclear and polymorphonuclear cells may also be present, although the inflammation is usually less dense than in primary biliary cirrhosis.
- Stage II – Expansion of portal triads with fibrosis extending into the surrounding parenchyma
- Stage III – Bridging fibrosis
- Stage IV – cirrhosis

Treatment

- Treatment begins with symptoms
- Medical therapy: high-dose ursodeoxycholic acid, cyclosporine, cholestyramine for pruritus
- Nonoperative therapy: endoscopic balloon dilatation of strictures – no advantage/possible harm from stenting
- Operative therapy:
 - Resection of extrahepatic biliary tree with Roux-en-Y hepaticojejunostomy may delay need for liver transplant and lowers risk for cholangiocarcinoma
 - Liver transplant is only therapy once cirrhosis develops. 37% recurrence of PSC in transplanted liver in 3 years – especially in men with intact colon

Gallbladder Cancer

- Aggressive adenocarcinoma with poor prognosis unless detected early, usually incidentally at the time of cholecystectomy
- 5th most common GI malignancy
- Females > males
- 75% of patients are older than 65
- 2.5cases/100,000, more common in Native Americans and in Chile
- Risk factors: gallstones, anomalous pancreatobiliary duct junction, porcelain gallbladder, choledochal cysts, PSC
- 1% of elective cholecystectomies for stones have an occult cancer
- At diagnosis, 25% are localized to GB wall, 35% have metastases to lymph nodes or adjacent organs, 40% have distant metastases
- Diagnosis
 - Ultrasound: mass in GB lumen and irregular GB wall, Sensitivity 70-100%
 - CT/MRI: shows mass in GB and extension in to liver, vascularity
 - Cholangiography: long stricture in common hepatic duct
 - CT/sono guided biopsy if unresectable disease is seen on imaging

- Management
 - T1a – found after cholecystectomy, 100% 5yr survival
 - T1b or higher – extended cholecystectomy(lymphadenctomy of the cystic duct, pericholedochal, portal, right celiac, and posterior pancreatoduodenal LNs, 2cm margin into liver parenchyma beyond extent of tumor
 - Chemo/radiation have not been shown to improve survival

- Survival
 - T1a – 100% 5 yr survival
 - T1b – 72% 5yr survival
 - Most pts have advanced unresectable disease - <15% of all pts are alive in 5 years

TNM Staging of Gallbladder Cancer – AJCC

T1	Tumor invades lamina propria (T1a) or muscular (T1b) layer
T2	Tumor invades perimuscular connective tissue, no extension beyond the serosa or into the liver
T3	Tumor perforates the serosa (visceral peritoneum) and/or directly invades into liver and/or one other adjacent organ or structure such as the stomach, duodenum, colon, pancreas, omentum, or extrahepatic bile ducts
T4	Tumor invades main portal vein or hepatic artery or invades multiple extrahepatic organs and/or structures
N0	No lymph node metastases
N1	Regional lymph node metastases
M0	No distant metastases
M1	Distant metastases
Stage	Stage Grouping
IA	T1 N0 M0
IB	T2 N0 M0
IIA	T3 N0 M0
IIB	T1 N1 M0
	T2 N1 M0
	T3 N1 M0
III	T4 Any N M0
IV	Any T Any N M1

Gallbladder polyps Lee et al. *Polypoid lesions of the gallbladder*. Am J Surgery 2004(188)

- Cholesterol polyps most common (60%) – other types: inflammatory, hyperplasia, adenoma
- 3-8% of polyps are malignant
- Risk factors: polyps >1cm, age >50, solitary polyps, symptomatic polyps, associated stones, hypervascularity
- Sonographic surveillance for polyps <1cm every 3-6months
- laparoscopic cholecystectomy for polyps >1cm. Open cholecystectomy for polyps >1.8cm or suspicion of malignancy

Gallbladder Polyps + PSC: Buckles, et al. *In primary sclerosing cholangitis, gallbladder polyps are frequently malignant*. Am J Gastroenterology 2002 vol 97(5)

- Of 102 pts with PSC s/p cholecystectomy, 14(13.7%) had a GB mass
- 8/14(57%) had adenocarcinomas – 7 primary, 1 metastatic cholangiocarcinoma
- 6 benign lesions – 5 adenomas, 1 cholesterol polyp
- Recommend early cholecystectomy in pts with PSC found to have GB polyps or frequent ultrasound surveillance
- Some authors recommend prophylactic cholecystectomy at time of laparotomy for UC or other reasons

Laparoscopic vs Open Cholecystectomy for GB polyps

- *Weiland et al. Journal of Gastrointestinal Surgery 2002(6)*
- 16 pts with T1 or T2 GB cancer s/p laparoscopic cholecystectomy
- 12 re-explorations, 7 radical resections
- 69% had recurrences or died at follow up of 4-39 months
- 3 port site recurrences
- 5/7 pts with bile spillage at laparoscopic cholecystectomy died or recurred
- Conclusions: patients with suspected cancer should undergo open resection, bile spillage is likely cause of recurrences.

Kim et al. J Hepatobiliary Pancreatic Surgery 2002(9)

- Retrospective review of 31 patients with GB cancer diagnosed after laparoscopic cholecystectomy
- 10 pts with pT1a – no recurrences after laparoscopic cholecystectomy 100% 5 year survival
- 9 pts with pT1b – 3 conversions to open, 2 recurrences 100% 5 year survival
- 7 pts with pT2 – 4 conversions to open, 3 recurrences 68% 5 year survival
- Recommended laparoscopic cholecystectomy for all T1a lesions on frozen section; open cholecystectomy with radical resection for >T1b lesions on frozen, use of bag for removal of specimen, avoiding bile spillage

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