Cholangiocarcinoma (Klatskin tumor)

Epidemiology: 2000-3000 cases per year. Accounts for 3% of GI malignancies. Usually presents between ages 50-70 but can present earlier in pts with primary sclerosing cholangitis (PSC) and in pts with choledochal cysts. Slightly higher incidence in men.

Pathogenesis: From the intrahepatic and extrahepatic epithelial cells. Some thought that related to mutation in tumor suppressor gene.

Risk factors:
- Primary sclerosing cholangitis: Recall that incidence of ulcerative colitis is 90% in pts with PSC. 30% of cholangiocarcinomas are diagnosed in pts with PSC and UC, and lifetime risk in these patients is 10-15%. Unclear why these patients are at greater risk but smoking and alcohol may contribute.
- Choledochal cysts: Risk is related to duration of disease. May be as high as 15% per year after first two decades.
- Parasitic infections: Liver flukes (Clonorchis and Opisthorchis) are associated with intrahepatic cholangiocarcinoma; may be due to inflammatory response.
- Hepatolithiasis (also called Oriental cholangiohepatitis) is rare in US but present in up to 50% in Taiwanese and other Asians with gallstones.
- Toxin exposures: auto, rubber, chemical, and wood-finishing occupations
- Genetics: “cancer family” syndromes (eg, Lynch, Li-Fraumeni), Caroli’s syndrome (congenital dilation of intrahepatic ducts), multiple biliary papillomatosis

Clinical presentation:
- Symptoms: pruritis 60%, abdl pain 30-50%, weight loss 30-50%, fever 20%, fatigue, clay stools, dark urine. Classic triad for hepatobiliary or pancreatic cancer is cholestasis, abdl pain, weight loss.
- Signs: jaundice (often intermittent) 90%, hepatomegaly 25-40%
- Lab test: increased bilirubin, increased alkaline phosphatase.
  --CEA elevated in some but not sensitive or specific. Best if level obtained directly from bile.
  --CA 19-9 elevated in 80% and most helpful in pts with PSC. Combining the two tests is more helpful.

Radiographic imaging:
--Ultrasound: see segmental dilatation or nonunion of R and L ducts, polypoid intraluminal masses, nodular smooth masses with mural thickening. Should do Doppler, as this is helpful to assess vascular invasion (unresectable)
--CT: A contracted gallbladder is more typical of a Klatskin tumor whereas a dilated GB is suggestive of a common bile duct tumor.
--Cholangiography (ERCP or PTC): ERCP has benefit of obtaining cells for biopsy
--MRCP: similar to CT, cholangiography, and angiography combined. Early studies show PPV 86% and NPV 98%

Treatment and prognosis:
- Prognosis: 5 year survival without surgery 5-10%. With surgery 10-30% or higher.
- Treatment:
  --Surgery is best option if resectable (no liver or systemic mets, no lymph node invasion, no vascular invasion
  --Adjuvant therapy: post-operative radiation may provide benefit in incomplete resections. Chemotherapy combined with radiation therapy may improve survival time by up to 10 months in pts with unresectable tumors.
- Palliative therapy: 50-90% of patients will need this. Stenting of biliary tree relieves obstruction but increases risk of cholangitis. Partial hilar resection, chemo/radiation therapy, bypass surgery have all been tried with mixed results. Photodynamic therapy (administering drug that gets activated with light and forms free radicals at site of activation where neoplastic cells have preferential uptake) is a work in progress.