CHAPTER 1

Liver, Biliary Tract, and Pancreas

A 44-year-old female presents with worsening jaundice over the last 3 days. On questioning, she admits to vague right upper quadrant pain on and off for the last several years, but states this is mild and never necessitated medical attention. In ER, she was found to be hemodynamically stable with a benign abdominal examination. Labs revealed a normal CBC, but elevated total bilirubin, ALP, and GGT. ALT, AST, and BMP were all normal. The patient's medical history includes anxiety and hypothyroidism. Her only past surgical history is a C-section and tonsillectomy. How do you manage her?

Differential

Choledocholithiasis, cholecystitis, Mirizzi syndrome, periampullary tumor, biliary stricture, pancreatitis, choledochal cyst, bile metabolism disorder, cholangiocarcinoma, brown primary bile duct stones, PSC, hepatic dysfunction

Priorities

- Full history and physical exam
  - Nature/timing of symptoms
  - Personal or family history of cancer, B symptoms, medications
  - Is the patient of Asian descent?
- Labs (CBC, metabolic panel, LFTs, lipase/amylase, coagulation studies)
  - Tumor markers (especially CA19-9) if any suspicion of a possible tumor after imaging

Imaging: US abdomen

The US shows a normal gallbladder and CBD dilation of 21 mm with no obvious etiology.

- MRCP

MRCP is the gold standard for noninvasive imaging of the biliary tract.

MRCP again shows the CBD dilation with no masses, gallstones, strictures, or other obvious etiology.

- Review images with the radiologist
- Morphology of dilation (saccular, bead-like, outpouching), does it taper off or abruptly end
- Level of dilation, any intrahepatic involvement
- Any masses or abnormalities noted in the pancreas or liver?
- Any evidence of pancreatitis or pancreatic duct dilation?
- Any suspicious lymph nodes?

On careful review of the MRCP images with the radiologist, an anomalous pancreaticobiliary junction is identified. No other new information. What is your next step?

- ERCP

Why perform an ERCP when an MRCP has already been done?

- The suspicion so far is that this is a choledochal cyst. This entity carries an elevated risk of harboring cholangiocarcinoma, especially when diagnosed in adulthood
- ERCP enables cytology brushings from the bile duct, further defines the dilation and anatomy, and rules out any possible intracholedochal abnormalities, which may have been missed by MRCP (strictures, masses)

Choledochal Cyst Types

- *Type I: fusiform dilation of the CBD, CBD excision proximally to nondilated and as distal as possible*
- *Type II: saccular diverticulum diverticulectomy*
- *Type III: choledochocele (within the wall of the duodenum) Sphincterotomy*
- *Type IVa: intrahepatic and extrahepatic bile duct dilation, extrahepatic duct excision, partial hepatectomy if confined to one lobe*
- *Type IVb: extrahepatic bile duct dilation, extrahepatic duct excision, and hepaticojejunostomy*
- *Type V: Caroli's disease (intrahepatic bile duct dilation) observation, liver transplant if progresses to portal hypertension or cirrhosis*

Surveillance is required following surgery due to the risk of cholangiocarcinoma in the remaining biliary ductal system.

Why is surgical excision recommended for most types of choledochal cysts?

- Risk of cholangiocarcinoma
- Biliary stasis leading to cholangitis or pancreatitis

A 42-year-old female presents with sharp, constant right upper quadrant pain radiating to the back. Vital signs are normal. The patient states she has had two similar but much milder attacks over the last year, which spontaneously resolved after 5–10 minutes. This pain has been constant for 10 hours.

Differential

Cholecystitis, cholelithiasis, gallbladder cancer, gallbladder polyp, PUD, GERD

Priorities

- Full history and physical exam
  - Abdominal pain details, weight loss, B symptoms, personal/family history of cancer, alcohol/smoking, liver disease, PMH/PSH
  - Jaundice, cachexia, ascites, lymphadenopathy, BMI (NASH), DRE
- Labs (CBC, metabolic panel, LFTs, lipase/amylase, coagulation studies)
- Imaging: Review the US with the radiologist. Rule out cholecystitis if possible, and characterize the gallbladder wall thickening if possible

US shows acute calculous cholecystitis.

- Antibiotics and fluids intravenously
- Laparoscopic cholecystectomy

The procedure goes well, and the patient is sent home the next day. The pathology, however, comes back 1 week later as consistent with stage T1a gallbladder carcinoma.

- Review the operative and pathology reports
  - Are margins negative (including cystic duct margin)?
  - Any LNs in the specimen? Are they positive or negative?
  - Bile spillage at the initial operation increases the risk of metastases
- CT chest/abdomen/pelvis and serum tumor markers (CEA, CA19-9, CA125)
- Discuss the result with the patient

Gallbladder Cancer

- *T1a lamina propria (intramucosal) cholecystectomy only as long as margins are negative*
- *T1b muscularis propria*
- *T2 perimuscular connective tissue*
- *T3 perforates serosa and/or invades liver and/or other adjacent structures*
- *T4 portal vein or hepatic artery, or 2 or more extrahepatic organs*

Any gallbladder cancer that is beyond the T1a stage and resectable should get at least a radical cholecystectomy and portal lymphadenectomy in medically fit patients

- More extensive resection may need to be done for stages T3 and T4
- Always start with a diagnostic laparoscopy
  - If any suspicious nodules are found on laparoscopy biopsy, send for frozen section
    - If positive, terminate the procedure and treat as stage 4
- Refer to hepatobiliary surgery
- Routine laparoscopic port site excision is not indicated

If there is no evidence of metastatic disease, but there is lymphadenopathy in the porta hepatis, or the patient presents with jaundice, neoadjuvant chemotherapy may be indicated.

What is a radical cholecystectomy?

- Resection of gallbladder with limited resection of liver segments 4b and 5 to get 2 cm margins

What is a portal lymphadenectomy?

- *Remove all LNs along the porta hepatis, hepatoduodenal ligament, and retroduodenal area*
  - *Skeletonize the common hepatic artery starting at the common hepatic node and moving distally down the artery, resecting all fibrofatty tissue off the vessels. Skeletonize the portal vein and resect lymphatic tissue around the CBD, taking extreme care not to devascularize it*

When is extrahepatic bile duct excision and reconstruction indicated?

- Positive cystic duct margin

What if there is a suspicious LN on imaging outside of the porta hepatis, hepatoduodenal ligament, and retroduodenal areas?

- This is considered stage 4 disease. Image-guided FNA biopsy to confirm malignancy, then refer to Medical Oncology/discuss at multidisciplinary tumor board

What chemotherapeutic agents are usually used in stage 4 gallbladder adenocarcinoma?

- Gemcitabine and Cisplatin

What is the appropriate surveillance after treatment of gallbladder cancer?

- CT chest/abdomen/pelvis q 3 months for 2 years, q 6 months to complete 5 years, annually after 5 years

A 36-year-old female presents with right upper quadrant pain radiating to the back. She is hemodynamically stable and afebrile with a WBC of 14, total bilirubin/ALP/ALT/AST are all elevated, but the lipase is normal. The US abdomen shows cholelithiasis, CBD dilated to 1.4 cm, and no evidence of cholecystitis. You get called by ER to manage this patient.

Differential

Choledocholithiasis, pancreatitis, cholecystitis, Mirizzi syndrome, periampullary tumor, choledochal cyst, biliary stricture, PSC, cholangiocarcinoma

Priorities

- Full history and physical exam
- Labs (CBC, metabolic panel, LFTs, lipase/amylase, coagulation studies)
- Imaging
  - US done
  - MRCP will help delineate the etiology of CBD obstruction, but it is not mandatory unless US findings are unclear, or this is a suggestion (clinical and/or radiologic) of malignancy

MRCP is not available at your institution at this time. What are the possible treatment options?

- Laparoscopic cholecystectomy and intraoperative cholangiogram
- Laparoscopic cholecystectomy and postoperative ERCP

- ERCP first, followed by laparoscopic cholecystectomy
  - If ascending cholangitis
  - If choledocholithiasis is definitively diagnosed preoperatively
- MRCP followed by laparoscopic cholecystectomy
  - May delay treatment
  - Necessitates ERCP if positive for choledocholithiasis

Which option do you choose?

- Since the patient has ongoing symptoms and there is no evidence or suspicion of ascending cholangitis, I will take her to the OR for a laparoscopic cholecystectomy and intraoperative cholangiogram.

Intraoperative Cholangiogram in Laparoscopic Cholecystectomy

Standard cholecystectomy dissection, dissect the structures of the cystic triangle and obtain the critical view of safety, perform a partial transection in the cystic duct after clip is placed on the gallbladder side of the cystic duct, gently guide the cholangiocatheter through the cystic duct transection and secure it in place with a clip (not too tight so as to occlude the cholangiocatheter and prevent injection), inject contrast through the cholangiocatheter (50% contrast, 50% normal saline), fluoroscopy through the C-arm for cholangiogram images.

Describe your criteria for a normal cholangiogram of good quality?

- Contrast seen in the duodenum
- CBD without filling defects
- Visualization of both hepatic radicals

What do you do if the cholangiogram shows a CBD filling defect?

- This is concerning for a CBD stone
- Have anesthesia administer 1 mg of Glucagon, wait 3–5 minutes, then flush the duct with saline and reshoot the cholangiogram
  - If the CBD stone persists, it may repeat one more time
- Laparoscopic transcystic CBD exploration and stone clearance
  - Cystic duct diameter >4 mm
  - Stone size <6 mm
- If unsuccessful, either postoperative ERCP or transcholedochal CBD exploration
  - ERCP has a risk of ERCP-induced pancreatitis and technical failure (5–20%)

What if the cholangiogram showed a complete nonvisualization of the hepatic ducts?

- Repeat cholangiogram with more contrast volume and/or cautiously more pressure
- Ensure the catheter is properly placed and there are no air bubbles or leaks in the system

You do this, and there is still no filling of the hepatic ducts.

- This is concerning for a common hepatic duct injury
- Consult hepatobiliary surgery intraoperatively
  - Ideally, repair of any injured duct would be performed immediately

Hepatobiliary surgery is not available at your institution.

- Consult a hepatobiliary surgeon at the nearest center over the phone
- Leave drains, close, and transfer to hepatobiliary surgery

What is the critical view of safety?

- Dissection of the hepatocystic triangle with exposure of at least one-third of the cystic plate and visualization of only two tubular structures connecting to the gallbladder (cystic duct and cystic artery) after
  - Hepatocystic triangle: cystic duct, hepatic duct, inferior edge of the liver
  - Cystic plate: the liver bed of the gallbladder

What if inflammation and/or fibrosis preclude an adequate critical view of safety?

- Subtotal cholecystectomy and JP drain in the gallbladder fossa

Would you continue the procedure laparoscopically or convert to open?

- Continue laparoscopically as long as it is safe to do so and progress is being made

What are the options for operative management of a difficult gallbladder?

- Laparoscopic retrograde cholecystectomy (top-down approach) with partial cholecystectomy and drain
  - Divide across Hartmann's pouch with an endoscopic stapler
- Open cholecystectomy and drain

You successfully perform an outpatient elective laparoscopic cholecystectomy on an otherwise healthy 34-year-old female. She presents back to ER 3 days later with abdominal pain and nausea. Her vital signs are normal, but there is mild generalized tenderness to deep palpation of her abdomen. Her WBC is 14.1, but the rest of her CBC and BMP are normal.

Differential

Bile leak, common bile duct injury, gastrointestinal leak/injury

Priorities

- Full history and physical exam
  - Exact character and timing of pain
  - Review operative and pathology reports
  - Associated symptoms: fevers, jaundice, etc.
- Further labs: liver function tests, lipase, lactate

Imaging

- CT abdomen/pelvis
- May also start with US abdomen +/− CT

CT shows intraperitoneal fluid, no biliary dilation, and no concern for GI perforation.

- IR guided drainage

Fluid comes back as bile.

- Ask for urgent ERCP with sphincterotomy and stent across the cystic duct opening

What if fluid comes back as succus?

- Initiate broad-spectrum antibiotics
- Emergency laparotomy

What if fluid comes back as serosanguinous?

- This is reassuring as long as the patient remains hemodynamically stable and with no peritonitis
- Will admit the patient for observation with vital signs monitoring, serial clinical exams, and serial labs (including liver enzymes)
- Consider biliary imaging to rule out leak or obstruction
  - US abdomen if not already done *or*
  - HIDA scan

What if the same patient had been presented with tachycardia and hypotension?

- ABCs
- IV fluids and broad-spectrum antibiotics
- Fast exam
- Formal imaging if transiently responds to resuscitation
- Laparotomy

A 53-year-old male presents to ER with a 3-day history of worsening central abdominal pain and nausea. He denies having similar episodes in the past. Today, the pain is a constant, sharp 9/10 intensity pain, which prompted him to come to ER. The patient has a history of hypertension and atrial fibrillation. Family history is noncontributory.

Differential

Pancreatitis, peptic ulcer disease, gastritis, mesenteric ischemia, bowel obstruction, early appendicitis, biliary colic/cholecystitis/choledocholithiasis

Priorities

- Stabilize first (ABCs, two large-bore IVs) while sending labs and stool studies
  - ECG always (especially if tachycardia) for SMA embolus or cardiac source of upper abdominal pain, abdominal X-ray
  - Give 1 L Ringer's lactate if sinus tachycardia while working up
- Full history and physical after a quick assessment of his vital signs and overall clinical status
  - Details of symptoms, previous episodes, medical/surgical history
- Labs: CBC, BUN/Cr, lytes, coags, LFTs, Lipase, lactate
- Imaging: CT Abdomen and pelvis with IV contrast
  - Must ensure the patient is hemodynamically stable first

- If renal function is impaired, hydrate first, then re-evaluate before CT
- Useful to grade pancreatitis and assess perfusion of the gland, rule out complications, and assess biliary dilation

Clinical and laboratory results are consistent with acute pancreatitis.

- Priority is fluid resuscitation and hemodynamic stability
- Identify the cause (gallstones, alcohol, calcium, triglycerides, drugs, chronic pancreatitis, mass, etc.)
- Diligent pain control
- Nutrition
  - Guided by what the patient can tolerate and their clinical status/stability
- If the clinical situation worsens after stabilization, repeat imaging to rule out pancreatic necrosis with infection
  - Look for malperfusion, air bubbles, and fluid collections

Gallstone pancreatitis

- ERCP in the acute phase is indicated for patients with concomitant ascending cholangitis
  - If ERCP or PTC cannot be done, surgical decompression is necessary
- ERCP is also indicated if there is evidence of ongoing obstruction from a stone impacted at the ampulla
  - Best to verify this first with MRCP
- Cholecystectomy should be performed on the same admission for mild pancreatitis
- If cholecystectomy is contraindicated (due to medical comorbidities), ERCP with sphincterotomy should be done

What if ERCP/PTC is unavailable or unsuccessful in ascending cholangitis?

- If the patient is stable, laparoscopic CBD exploration can be attempted
- If the patient is sick, open CBD exploration should be done
  - Open CBD drainage and stone clearance, closure over T tube

How aggressively do you hydrate someone with dehydration and AKI due to acute pancreatitis?

- Manage in ICU and insert a Foley catheter
- Give a total of 2 L bolus of Ringer's lactate
- After boluses, keep on crystalloid infusion at 200 cc/hour and titrate to a urine output of 1 cc/kg/hour
- Repeat Cr and BUN every 6 hours

Possible complications of acute pancreatitis

- Sterile pancreatic necrosis
  - Continue conservative treatment and watch closely in the ICU
- Infected pancreatic necrosis
  - Suspect with worsening clinical status, fever, tachycardia
  - Diagnosed by air bubbles on CT or CT-guided aspiration C&S
  - Start antibiotics immediately (Carbapenem + Vancomycin)
  - Percutaneous drainage of any fluid collections

- Abdominal compartment syndrome
  - Suspect if respiratory difficulties arise, lowering urine output, tense abdomen, and large positive fluid balance
  - Diagnose with bladder pressure >20 mm Hg + clinical picture
  - Emergency decompression laparotomy

What are the possible longer-term complications of acute pancreatitis?

- Pseudocyst
- Chronic pancreatitis
- Pancreatic fistula
- Exocrine or endocrine insufficiency

A 62-year-old female with a history of COPD, depression, and hypertension presented to ER with dyspepsia and a small asymptomatic incisional hernia at the umbilicus from a previous laparoscopic cholecystectomy. ER ordered a CT scan, which showed a small fat-containing hernia at the umbilicus and a 2.5 cm cystic lesion in the tail of the pancreas. She is referred to your office for further management of the incidental pancreatic lesions.

Differential

Serous cystadenoma/carcinoma, mucinous cystadenoma/carcinoma, IPMN, pseudocyst, adenocarcinoma, cystic neuroendocrine tumor, solid pseudopapillary tumor, congenital cyst, cystic metastases, cystic acinar cell carcinoma

Priorities

- Full history and physical exam
  - Abdominal pain, back pain, pancreatitis, diabetes, exocrine insufficiency, B symptoms, personal/family history of cancer, alcohol/smoking
- Labs (CBC, metabolic panel, LFTs, lipase/amylase, coagulation studies), CA19-9
- Imaging: MRCP
  - Better than CT for cystic lesions
  - Better at determining the connection of the cyst with the pancreatic ductal system

What are you looking for in imaging?

- Lesion characteristics: size, location, enhancement pattern
- Cyst characteristics: loculations, solid component, mural nodules, debris, central scar, calcifications
- Duct dilation: main versus side branch, extent within the gland
- Lymphadenopathy
- Evidence of liver or extrahepatic metastases
- Features of acute or chronic pancreatitis

When is tissue diagnosis not required?

- History and imaging features consistent with serous cystadenoma
- History and imaging features consistent with pseudocyst

Imaging features

- Serous: stellate scar, honeycomb pattern, microcysts, central calcification
- Mucinous: single cyst, wall calcifications

Criteria for EUS-FNA biopsy

- The diagnosis is unclear
- Possible mucinous lesion
- Possible malignancy
  - Based on either clinical or radiological data
    - History, jaundice, high serum CA19-9
    - Solid component, mural nodule, duct dilation (>5 mm), change in duct caliber with upstream, atrophy, size >3 cm
- The biopsy result will change management
  - Usually requires that the patient is a surgical candidate
- IPMN with
  - Cyst >3 cm in size
  - Main pancreatic duct 5–9 mm
  - Enhancing mural nodule <5 mm
  - Thick, enhancing cyst wall
  - Abrupt change in caliber of pancreatic duct with distal atrophy
  - Lymphadenopathy
  - High CA19-9
  - Cyst growth >5 mm over 2 years

EUS-FAN fluid analysis

- Cytology, mucin, CEA, CA 19-9, amylase, glucose, K-RAS mutation, cytopathology (atypia)
- Serous: no mucin, CEA<192, glucose >50, low amylase
- Mucinous: mucin positive, CEA>192, glucose <50, low amylase, K-RAS mutation
- Malignant: cytology positive, CA19-9 >37
- Pseudocyst: high amylase

KRAS mutation predicts mucinous lesion (complements CEA level)

Indications for surgical resection

- Symptomatic cysts
- Mucinous cysts
- Significant growth in size with surveillance
- IPMN with
  - Obstructive jaundice
  - Main pancreatic duct dilation 1 cm or more
  - Mural nodule >5 mm
- Patient must be a good surgical candidate, ideally <75 years of age (if older, discuss with them)

Should the spleen be removed or preserved with distal pancreatectomy?

- Should be removed if there is confirmation or high suspicion of malignancy

- Can be safely preserved in surgery for a premalignant lesion
- Administer spleen vaccinations anyway for all those getting a distal pancreatectomy
  - Ideally, 2 weeks prior to surgery
  - 14 days postoperatively or before discharge (whichever is earliest)

What if there is likely a mucinous or indeterminate lesion, but the patient is not an ideal surgical candidate (has some comorbidities), 76 years or older, or hesitant to agree to surgery (because of possible complications)?

- Close surveillance with MRCP or EUS (alternating) every 6 months
- Serum CA19-9 every 6 months

Laparoscopic Spleen-preserving Distal Pancreatectomy for IPMN

Patient supine in reverse Trendelenburg with left side up, camera port at umbilicus and four additional ports triangulating toward the LUQ, explore the peritoneal cavity to rule out metastatic disease, enter lesser sac by dividing the gastrocolic ligament, retract stomach to expose pancreas and retroperitoneum, identify splenic artery coursing on superior border of the pancreas, open a plane along inferior border of pancreas with energy device, mobilize the splenic flexure of the colon by dividing the splenocolic ligament to expose the full length of the pancreas, dissect the splenic vein away from overlying pancreas out to the splenic hilum using a combination of energy device and clips to divide the splenic vein branches to the pancreas, dissect the splenic artery away from the pancreas, after both vessels are mobilized off the pancreas the pancreatic neck is transected with a laparoscopic stapler, remove specimen with a specimen bag, get intraoperative frozen section of proximal margin to ensure there is no high-grade dysplasia at the margin (if proximal margin is positive re-resect proximally and send again for frozen section), leave a drain (since gland is soft and duct is small).

Laparoscopic Distal Pancreatectomy and Splenectomy

With the patient supine and in steep reverse Trendelenburg with left side up, mobilize the stomach and transect the short gastric vessels, suspend the stomach away, then fully mobilize the splenic flexure to expose the inferior edge of the pancreas and create a retro-pancreatic tunnel 2 cm to the patient's right of the tumor, transect the pancreas at this location using gradual compression with a blue load stapler, dissect out the splenic artery at the same area and transect the area and bring the lymph nodes and artery with the specimen, then dissect out and transect the splenic vein with a vascular load stapler, dissect the pancreas out of the retroperitoneum in a plane outside the pancreatic fat taking that tissue with the specimen, lastly mobilize the spleen off its lateral attachments, remove the specimen in a bag, and place a drain in the splenic fossa.

How do you manage the drain postoperatively?

- Send drain amylase levels on POD 1 and 3
- Remove prior to discharge if output <30 cc daily, amylase level normal and no signs or symptoms of a pancreatic fistula or leak

A 71-year-old male presents to ER with abdominal pain and nausea that has been slowly worsening over the last 4–6 months. He has a history of hypertension, dyslipidemia, and depression. No past surgical history. In ER, the patient is noted to be jaundiced with an otherwise benign abdominal examination.

Differential

Cholecystitis, periampullary tumor, pancreatitis, choledocholithiasis, biliary strictures, Mirizzi syndrome, PSC, hepatic dysfunction

Priorities

- Full history and physical exam
- Labs (CBC, metabolic panel, LFTs, lipase/amylase, coagulation studies)
- US abdomen

US shows a normal liver, distended GB without stones, CBD 1 cm diameter, no choledocholithiasis

- US shows distal CBD obstruction not likely caused by choledocholithiasis
- Suspect periampullary tumor given the patient's age and history of weight loss
- Order CT pancreas protocol
- Triple phase (arterial, venous, and portal venous phases)
- Less than 1 cm slices through the pancreas
- MRCP is a possible alternative

CT shows a pancreatic mass and again notes the biliary dilation. There are no other lesions suspicious for metastasis, and the liver is otherwise clear.

- Review the CT with the radiologist to determine
  - Size and location of mass
  - Signal intensity (for example, hypodense concerning cancer)
  - Double duct sign (dilation of both CBD and PD)
  - Lymphadenopathy
  - Liver lesions
  - Involvement or abutment of SMV/SMA/PV/HA
  - Other lesions suspicious for possible extrahepatic metastases

Which pancreatic cancers are anatomically resectable (based on imaging)?

- No arterial contact of the tumor (celiac axis, common hepatic, SMA)
- Less than 180° contact with SMV/PV with no contour irregularity

Which pancreatic cancers are borderline resectable?

- Arterial abutment
- Vein encasement

Which pancreatic cancers are unresectable?

- Arterial encasement

Any arterial involvement is a contraindication to upfront surgical resection.
Abutment = <180° tumor contact with the vessel
Encasement = >180° tumor contact with the vessel

When is preoperative biliary drainage indicated?

- Ascending cholangitis
- Pruritis
- Significant malnutrition
- Coagulopathy
- Very high bilirubin levels (>12) and prolonged preoperative workup/optimization (>2 weeks) secondary to patient comorbidities – *to reduce risk of postop cholestatic liver failure*
- Neoadjuvant chemotherapy planned

The degree of hyperbilirubinemia and/or CBD dilation is generally not an indication on its own.

- *Preoperative biliary drainage may increase the risk of infectious complications of surgery*

When is a preoperative tissue biopsy for diagnosis indicated?

- When upfront surgery is not possible (*and chemotherapy is planned*)
  - Anatomically unresectable
  - Borderline resectable
  - Suspicion of metastases

Biopsy through ERCP and brushings for cytology is safest to prevent tumor dissemination, but may also be the lowest yield.

Other options include EUS-FNA, percutaneous FNA, and image-guided biopsy of suspected metastasis (most commonly liver).

Considerations for surgery in seemingly resectable nonmetastatic pancreatic cancer

- Anatomic resectability
- Biologic resectability (risk of occult metastatic disease)
- Patient status (medical comorbidities)

What needs to be done before surgery?

- Stage with CT chest
- CA19-9 (baseline best obtained after biliary decompression if that is going to be done preoperatively)
- Discuss the case in a multidisciplinary tumor board
- Genetic testing (for anyone with pancreatic cancer)
- Start with a diagnostic laparoscopy for all pancreatic cancer cases
  - Not strictly mandatory if patient is a candidate for upfront surgery (anatomically resectable on imaging, good functional status, no biological resectability red flags, no evidence of metastases), but may reveal previously undetected peritoneal or other metastases in >20% of cases

CA19-9 requires Lewis blood antigen expression (absent in 5–10% of the population)

Biologic resectability: factors that increase the risk of metastases

- Tumor size >5 cm
- CA19-9 >150
- Borderline resectable tumor

- Low-volume ascites
- Suspicious lymph nodes on imaging

Patients with one or more of these may be considered for neoadjuvant chemotherapy.

Complications of Whipple: pancreatic leak or fistula, delayed gastric emptying, GDA pseudoaneurysm and bleed

What chemotherapy regimen is used for Pancreatic cancer?

- Folfirinox (Leucovorin, 5-FU, Irinotecan, Oxaliplatin)
- All pancreatic cancer patients get chemotherapy
  - Patients with upfront resection get 6 months of adjuvant chemotherapy
  - Patients who get neoadjuvant chemotherapy usually get adjuvant therapy to complete 6 months of total chemotherapy

Whipple Procedure

Start with a diagnostic laparoscopy ad examine the surfaces of liver/peritoneal and mesenteric surfaces/intestinal surfaces for any occult metastatic lesions, if negative proceed with midline laparotomy, enter lesser sac by dividing the attachments between the greater omentum and transverse colon, trace the middle colic vein up to SMV at inferior border of pancreas, bluntly develop a plane behind the neck of pancreas and encircle the pancreas with umbilical tape, (check for resectability of plane between pancreas neck and PV), mobilize the hepatic flexure and perform a complete Kocher maneuver to palpate course of SMA (check resectability of SMA interface with pancreas), perform a cholecystectomy with portal dissection and divide the common hepatic duct, identify and ligate the GDA, transect the distal stomach, divide the small bowel distal to ligament of Treitz mobilizing the distal duodenum from the mesentery, transect the pancreatic neck and send the distal pancreatic duct margin for frozen section, divide the uncinate process attachments freeing it from the SMA adventitia, once froze section confirms the margin is clear proceed with reconstruction with a tension-free duct to mucosa hand-sewn pancreaticojejunostomy/hepaticojejunostomy/gastrojejunostomy, leave closed suction drains near pancreatic and biliary anastomoses.

How long before you remove the drains?

- Check amylase/lipase levels from the drains daily
- Remove drains prior to discharge if output <30 cc/day, amylase/lipase levels not elevated, and no clinical suspicion of leak or pancreatic fistula

How does a postoperative pancreatic leak or fistula present?

- May present with abdominal pain, nausea and vomiting, fever, low urine output, tachycardia, and/or hypotension

How do you manage a suspected pancreatic leak or fistula?

- Immediate management: ABCs (fluid bolus), abdominal X-ray, labs, send drain fluid for amylase levels
- Nasogastric tube if stomach distention, start broad-spectrum antibiotics once leak is suspected (ongoing signs and symptoms + leukocytosis), CT abdomen and pelvis for diagnosis

What is your follow-up plan after completing treatment of pancreatic cancer?

- History and physical/serum CA19-9/CT chest abdomen pelvis 3–6 months for 2 years, then yearly thereafter

A 62-year-old male presents to ER with acute generalized abdominal discomfort, nausea, and diarrhea. CBC, electrolytes, and BUN/Cr are normal in ER. CT abdomen and pelvis without contrast show a mass in the pancreatic tail but otherwise normal study. The ER physician had a mild episode of gastroenteritis but consulted you for the incidental finding in the pancreas.

Differential

Pancreatic adenocarcinoma, pancreatic neuroendocrine tumor, metastatic malignancy, benign pancreatic lesion, lymphoma, chronic pancreatitis, pseudocyst, aneurysm or pseudoaneurysm, solid pseudopapillary tumor, acinar cell carcinoma

Priorities

- Focused history and physical exam
- Labs (including LFTs, amylase/lipase, CA19-9)
- Further imaging with either the CT pancreas protocol or MRCP
  - US (either transabdominal or EUS) if cyst

CT pancreas protocol is performed and shows a 1.8 cm hyper-enhancing lesion on the arterial phase

Hypervascular pancreatic lesions on the arterial phase on CT

- *Pancreatic neuroendocrine tumors*
- *Metastatic lesion (melanoma, renal cell carcinoma, thyroid cancer)*
- *Aneurysm*
- *Intrapancreatic accessory spleen*
- *Focal pancreatitis*
- *IPMN*
- *Solid pseudopapillary tumor*
- *Acinar cell carcinoma*

What would you like to know about history based on this CT finding?

- Symptoms of functional neuroendocrine tumors
  - Gastrinoma: recurrent or resistant severe peptic ulcers
  - Insulinoma: hypoglycemia, Whipple triad, obesity
    - Fatigue, headache, lightheadedness, palpitations, sweating, tremors
  - Glucagonoma: glucose intolerance, necrolytic migratory erythema, glossitis/stomatitis, weight loss, anemia, venous thrombosis
  - Somatostatinoma: hyperglycemia/diabetes, cholelithiasis, steatorrhea, achlorhydria
  - VIPOMA: watery diarrhea, hypokalemia, achlorhydria
- Family history of MEN syndrome, VHL, NF-1, Tuberous sclerosis
- Personal or family history of cancer, B symptoms, smoking/alcohol

What labs would you order?

- CBC, metabolic panel, LFTs, lipase/amylase, coagulation studies

- Chromogranin A
  - Also useful for follow-up, especially in nonfunctional tumors
- Tumor-specific labs *based on symptoms*
  - Insulinoma: low fasting glucose, high insulin, high C-peptide
  - Glucagonoma: serum glucose, glucagon >500
  - VIPOMA: fasting VIP >200
  - Gastrinoma: fasting serum gastrin >500, Secretin stimulation test
  - PPOMA: pancreatic polypeptide

What imaging tests do you normally consider for suspected neuroendocrine tumors of the pancreas?

- Primary imaging is CT Abdomen and pelvis Pancreas protocol or MRCP
- EUS for tumors <1 cm
- Rarely, angiography with selective arterial calcium stimulation to localize the tumor to a general area in the pancreas (head, body, tail)
- EUS-FNA biopsy in all tumors to confirm diagnosis with IHC staining and to determine grade, differentiation, KI-67, and mitotic count
- DOTATATE CT-PET to rule out metastatic disease
  - Only effective in well-differentiated neuroendocrine tumors

Malignancy rate for neuroendocrine tumors

- *Gastrinoma 75%*
- *Insulinoma 10%*
- *Glucagonoma 75%*
- *Somatostatinoma >70%*
- *VIPOMA 50%*
- *Nonfunctional 50%*

Conditions that elevate serum gastrin: PPI, chronic atrophic gastritis, GOO, post-vagotomy, chronic renal failure, H. Pylori infection, gastrinoma or MEN1, gastric carcinoid type I, short gut syndrome

Criteria for surgery for pancreatic neuroendocrine tumors

- *Nonfunctional <2 cm and low grade: observe*
  - *CT in 6 months, and if no growth, yearly MRI thereafter*
  - *Surgery if significant growth over 6–12 months observation*
- *Nonfunctional >2 cm or intermediate/high grade*
- *Surgery if localized or metastatic with completely resectable primary + >90% resectable metastases*
  - *Octreotide if metastatic and unresectable*
- *Functional*
  - *Surgery if localized or metastatic with completely resectable disease*
  - *Octreotide if metastatic and unresectable*

You are performing surgery on a pancreatic neuroendocrine tumor with liver metastases. You realize during the metastectomy phase of the operation, however, that you are unable to achieve R0 resection. What do you do next?

- Debulk the metastatic disease in the liver (cytoreductive surgery) if it is possible to debulk 90% of the disease in the liver
- If there is extensive liver disease (where 90% debulking is not possible), then abandon the metastectomy

Does your surgery for a pancreatic neuroendocrine tumor include a regional lymphadenectomy?

- Only if there is suspicion that the neuroendocrine tumor is malignant
  - 2 cm or greater in size
  - Symptoms or
  - Imaging suggestive of malignancy (invasion, lymphadenopathy, metastasis)
  - High grade histology or Ki-67 index >3% on biopsy
  - Gastrinomas (60–90% malignancy) or MEN I

What if a 1 cm pancreatic neuroendocrine tumor is diagnosed as an Insulinoma, shows no evidence of lymphadenopathy or metastasis on imaging, and FNA showed low-grade histology and a Ki-67 index <3%? You are planning for surgery given the symptoms produced by the lesion. Would you also perform a regional lymphadenectomy?

- No

In the above tumor, what surgery would you perform?

- It depends on the location of the tumor within the pancreas
  - Head: enucleation
  - Tail: spleen-preserving distal pancreatectomy

Enucleation is safe if tumor is at least 3 mm away from the pancreatic duct (the center of the pancreas), and far enough from the vasculature; otherwise, resection.

Enucleation should be avoided if the lesion is 2 cm or larger, malignant or likely malignant, high-grade or Ki-67 index, within 3 mm of the pancreatic duct or very close to vasculature, gastrinomas or MEN 1, or lymphadenopathy.

What is your surgical approach for a symptomatic Gastrinoma?

- Open surgical exploration
  - High likelihood of submucosal lesions in the duodenum and regional lymphadenopathy

What if you had a ZES or MEN-1 with a CT pancreas protocol and an MRCP failed to localize the lesion?

- EUS, SSR scan, DOTATE PET/CT
- Selective arterial Secretin injection (by IR)
- Open surgical exploration +/− intraoperative US
  - Gastrinoma triangle: cystic duct and CBD junction, second and third duodenum junction, pancreas body, and neck junction

What if the patient is a poor surgical candidate?

- Multidisciplinary tumor board discussion
- Palliation with Octreotide if a functional tumor
- Referral for possible endoscopic or percutaneous ablation

Medical management of neuroendocrine tumors

- VIPOMA: Octreotide
- Glucagonoma: Octreotide
- Gastrinoma: PPI, possible Octreotide
- Insulinoma: Diazoxide (suppresses insulin secretion), Octreotide

A 23-year-old male presents to ER with nausea, fevers, chills, and upper abdominal pain of 2 days' duration. He recently suffered a liver injury secondary to an MVC, which necessitated a laparotomy, packing, and angiographic embolization. He was discharged 12 days ago from the hospital. He is hemodynamically stable and has benign abdominal examination. He is otherwise healthy.

- Labs: CBC, electrolytes, BUN/Cr, PTT/INR, LFTs
- CT abdomen and pelvis with IV contrast

WBC 22, Hb 10, ALT 265, AST 250, ALP 300, total bilirubin 1.6, Cr 1.1, INR1

- Blood cultures, start broad-spectrum antibiotics, await CT result

CT scan shows liver necrosis with air locules in segments 6 and 7.

- Consult IR for percutaneous image-guided drainage

IR places the drain successfully, which produces small amounts of purulent material. After 12 hours, the patient becomes tachycardic and hypotensive with persistent spiking temperatures despite antibiotic therapy. What do you do next?

- Open exploration for drainage or possible resection of the necrotic liver segments
- Consult a hepatobiliary surgeon to help with the surgery
- Consider concomitant gallbladder resection
  - Delayed gallbladder ischemia may occur following major liver trauma or angioembolization

A 64-year-old male is referred to your office after a CT abdomen was done after minor trauma, which revealed an incidental mass in the liver.

Differential

Benign (adenoma, hemangioma, FNH, hamartoma), HCC, metastatic, cyst, benign vs malignant, solid vs cystic

Priorities

- Full history and physical exam
  - Abdominal pain, prior EGD or colonoscopy, lower GI symptoms, B symptoms, personal/family history of cancer, alcohol/smoking, liver disease, IVDU, OCP, anabolic steroids
  - Jaundice, cachexia, ascites, lymphadenopathy, BMI (NASH), DRE
- Labs (CBC, metabolic panel, LFTs, lipase/amylase, coagulation studies), hepatitis panel, AFP, CEA, CA19-9, CA-125

- Imaging: triple phase CT liver
  - MRI is a good alternative
    - Preferred over CT if suspicion of cholangiocarcinoma

What are you looking for in imaging?

- Lesion characteristics: enhancing on arterial phase with rapid washout on portal or venous phase (HCC), and a capsule, a peripherally enhancing lesion indicates adenocarcinoma or mixed type cholangiocarcinoma
- Evidence of liver cirrhosis
- Portal hypertension (splenomegaly, recanalized umbilical vein, varices)

LIRADS Score

- Benign: *Return to Surveillance (US and AFP q 6 months)*
- Probably benign: *Repeat imaging in 6 months*
- Intermediate: *Biopsy or further imaging*
- Probably HCC: *Biopsy or further imaging*
- Definitely HCC: *Multidisciplinary discussion for management*

LIRADS

- *For the diagnosis of HCC on CT and MRI*
- *Should only be used in cirrhosis or chronic HBV*

Indications for biopsy

- Indeterminate diagnosis
- Possible metastatic lesion
  - Any lesion that has characteristics of an adenocarcinoma on imaging with peripheral enhancement requires a biopsy for diagnosis
- Low LIRADS score (indeterminate for HCC)
  - Usually LIRADS 3 (intermediate) and 4 (probably HCC)
- Likely HCC on imaging but suspicious lymphadenopathy
  - Metastases to lymph nodes are uncommon in HCC and indicate a worse prognosis but require biopsy of the lymph nodes preoperatively

The only malignant liver lesion that can be diagnosed by imaging alone is HCC.
LIRADS score alone is not an automatic indication for biopsy

- *The decision to obtain tissue diagnosis should be subject to the consideration of how it will change management, the patient's clinical condition, as well as multidisciplinary discussion*

Surgical resection versus transplantation for HCC

- Adequate liver function to tolerate major resection favors surgical resection
  - Child class A, normal bilirubin, no signs of portal hypertension
- Transplantation for Child class B and C who meet the Milan criteria
  - Single lesion 5 cm or less
  - Three lesions, each 3 cm or less
  - No vascular invasion

In patients with extrahepatic metastases, both surgical resection and transplantation are contraindicated.

In a patient with limited HCC disease (for example, one main nodule) who is neither a candidate for surgical resection (due to poor hepatic reserve) nor transplantation (due to social factors, medical comorbidities, etc.), locoregional techniques such as ablation (RF or microwave) or TACE may be considered.

Surgical resection for HCC

- Partial hepatectomy with 1 cm margins, formal anatomic segmentectomy if tumor is close to the segmental portal pedicle (PV, HA, Bile duct)
- Surgical resection has lower short-term operative risks compared to transplantation but a higher risk of recurrence
- If the future liver remnant is expected to be <20% in a normal liver or <40% with Child class A, preoperative portal vein embolization should be considered
  - Portal vein embolization can also be combined with TACE, but this should be subject to a multidisciplinary discussion

What if the biopsy shows metastatic adenocarcinoma, and the primary is unknown?

- Gastroscopy and colonoscopy
- If negative, capsule endoscopy
- If GI search is negative, treat as a primary hepatic cholangiocarcinoma

Treatment for metastatic adenocarcinoma to the liver from the colon or small bowel

- *Neoadjuvant chemotherapy followed by resection*

Treatment for metastatic adenocarcinoma to the liver from esophagus or stomach

- *Palliative chemotherapy (these are much more aggressive, and resection is classically contraindicated)*

Primary liver cholangiocarcinoma

- *Rule out metastatic disease and satellite lesions, then resect with 1 cm margins*