Gallbladder and Biliary Tract Pathology: Reactive vs. Neoplastic

Mucosa
Muscularis Propria
Perimuscular Connective Tissue
Serosa or Liver
Layering of the GB is very different than that of the luminal GI tract.

- Stomach
  - Mucosa
  - Submucosa
  - Muscularis Propria
  - Subserosa

- Duodenum
  - Mucosa
  - Submucosa
  - Muscularis Propria
  - Subserosa
Non-Neoplastic Gallbladder Polyps

• Seen in 3% of cholecystectomy specimens
• Most are incidental microscopic lesions with a mean size of 0.4 cm
• Only 7% are clinically significant (> 1 cm)
• When all clinically significant (> 1 cm) polyps are considered, non-neoplastic polyps constitute ~5% of this group
The Gallbladder has a LOT of Bumps

<table>
<thead>
<tr>
<th>Granulation Tissue</th>
<th>Lymphoid Aggregates</th>
</tr>
</thead>
</table>

- **Granulation Tissue**
- **Lymphoid Aggregates**

**Cholesterolosis**

(60% occur in the absence of cholesterolosis)
Fibromyoglandular Polyp (< 0.5 cm)

Inflammatory Conditions of the Gallbladder (Cholecystitis)

Rokitansky-Aschoff Sinus
Metaplasia: Pyloric Gland Metaplasia

Metaplasia: Polypoid PG Metaplasia (Not Pyloric Gland Adenoma)
Metaplasia: Intestinal Metaplasia

Xanthogranulomatous Cholecystitis

Xanthogranulomatous Cholecystitis
Eosinophilic Cholecystitis

Lymphocytic Cholecystitis

Reactive or Neoplastic?
Reactive or Neoplastic?

Hyalinizing Cholecystitis
• Surface mucosa is often denuded/sloughed.
• Uncommon to have Rokitansky-Aschoff sinuses.
• If glands are present, suspect gallbladder adenocarcinoma.
Gallbladder Dysplasia

- **Incidence**: Parallels high gallbladder cancer-risk areas: >15% in Mexico & Chile; in the U.S. <2%
- **Association**: Injury/inflammation
  - Gallstones
  - Long h/o sclerosing cholangitis
  - Anomalous union of ducts
  - Choledochal cysts

Gallbladder Dysplasia

- **Anatomic Location**: Most common in the fundus and body where carcinoma is most common
- **Invasive Cancer**: Dysplasia is found in 2/3 of gallbladders with invasive carcinoma
- **Molecular**: Frequent alterations in *TP53* and *CDKN2A*, while *KRAS* mutations are often restricted to carcinoma
Gallbladder Dysplasia

- **Architecture**: Spectrum of complexity (denuded/flat to papillary)
- **Low-grade Dysplasia**: Stratified, cigar-shaped nuclei (analogous to a colonic tubular adenoma)
- **High-grade Dysplasia**: Apical/budding nuclei, prominent nucleoli and nuclear contour irregularities

Low-Grade Dysplasia
Low-Grade or High-Grade Dysplasia?

High-Grade Dysplasia: Spectrum
Reactive Atypia

High-Grade Dysplasia
HGD vs. Early Invasion (pT1a/pT1b)?

- Connection to Surface Epithelium
- Lobular arrangement

HGD vs. Early Invasion (pT1a)?

- Lack of Desmoplasia
Invasion: Growth Near Musc. Vessels

Vascular and Perineural Invasion

pT Staging

- Mucosa (pT1a)
- Muscularis Propria (pT1b)
- Perimuscular Connective Tissue (pT2a and pT2b)
- Serosa (pT3)
**pT Staging**

- **pT2b**: Tumor invades perimuscular connective tissue on the hepatic side, with no extension into the liver

- **pT4**: Tumor invades main portal vein, hepatic artery, or 2 or more extrahepatic organs/structures

**pN Staging**

- **pN1**: Lymph node involvement near the gallbladder (e.g., cystic duct, common bile duct, hepatic artery and portal vein)
- **pN2**: Lymph node involvement of the periaortic, pericaval, SMA and celiac artery lymph nodes

- **7th**
  - pN1: Metastases to 1 - 3 regional lymph nodes
  - pN2: Metastases to ≥ 4 regional lymph nodes
Neoplastic Gallbladder Polyps

Pyloric Gland Adenoma

Pyloric Gland Adenoma
Pyloric Gland Adenoma

High-Grade Dysplasia (PGA > 1 cm)

Pyloric Gland Adenoma

Other Polyps/Adenomas
**Premalignant Lesions**

**Literature:**
- Pyloric gland adenoma
- Biliary adenoma
- Intestinal adenoma
- Tubular adenoma
- Tubulopapillary adenoma
- Papillary adenoma
- Papillary neoplasm
- Papillary carcinoma

**WHO (2010):**
1. Adenoma
   - Tubular
   - Papillary
   - Tubulopapillary
2. Intracystic papillary neoplasm
   - Pancreatobiliary
   - Intestinal

---

**Pancreatic Head**

- Ampulla
- Bile Duct
- IPMN
- PDAC

**Intraductal Papillary Mucinous Neoplasm (IPMN)**
Intracholecystic Papillary-Tubular Neoplasm (ICPN) of the Gallbladder
Background: High-Grade Dysplasia

Intraductal Papillary Neoplasm (IPN) of the Bile Duct