Gallbladder Polyps and Other Pre-Malignant Gallbladder Lesions

Jennifer Maranki, MD, MSc
Assistant Professor of Medicine
Director of Experimental Endoscopy and Therapeutics
Temple University School of Medicine

Disclosures

• Consultant, Boston Scientific Corp
Objectives

- Review epidemiology of gallbladder polyps
- Review categorization of benign polypoid lesions
- Provide overview of adenomyomatosis and cancer risk
- Discuss diagnostic and surveillance options

Epidemiology

- Overall prevalence is approximately 5 – 8%
- Observed in 0.004 to 13.8 percent of resected gallbladders
  - 1.5 to 4.5% of gallbladders assessed by ultrasound
- Not associated with traditional risk factors for gallstones
  - No association with age, sex, weight, pregnancy status
  - Average age of dx is 49 years

Park JY, J Gastro Hep, 2009
Classification of Benign Lesions

**Neoplastic**
- Adenoma  
  – Most common
- Leiomyoma
- Lipoma

**Non-neoplastic (Pseudotumors)**
- Cholesterol polyps  
  – “cholesterolosis”
- Adenomyomas
- Inflammatory polyps

---

**Adenomas**

- Most common benign tumor of gallbladder
  – Rare
  – Unlike in the colon, gallbladder adenocarcinoma is more common than gallbladder adenoma
- Incidence is < 0.5%
- Benign epithelial tumors
  – Comprised of biliary tract epithelium
  – Papillary vs non-papillary
Adenoma: Risk of cancer

- Unknown risk of progression
- Risk is related to the size
- 6% incidence among polyps less than 1 cm (Japanese data) Nihon Shokakibyo Gakkai Zasshi 1986
- 37.5% incidence among polyps 1 – 2 cm

Cholesterolosis

- Accumulation of lipids in the wall of the gallbladder
- Usually incidentally found, but can cause sxs
- Common
  - Autopsy results from 1300 cases: 12% Feldman, Gastro, 1954
  - Prevalence 9 to 26% from resected GBs
- Risk factors are similar to those for gallstones, but equal distribution among men and women
Cholesterolosis

Lipid accumulation creates yellow deposits in the background of hyperemic mucosa.
Fat-laden macrophages with elongated villi.

Adenomyomatosi

- Characterized by mucosal overgrowth, muscle wall thickening, and intramural diverticula
- Does NOT involve ADENOMATOUS change
- Not considered to be a premalignant condition
  - Has been found in GBs resected for cancer
  - Relationship is unclear
- Clear association with cholelithiasis
  - 89% of patients with segmental adenomyomatosis had stones
Adenomyomatosis

- Less common than cholesterolosis (1%)
- More common in women
- Three types:
  - diffuse
  - segmental
  - localized
Adenomyomatosis: Pathology

- **Diffuse**
  - Thickening and irregularity of the mucosal surface and muscle – cystic-like structures in GB wall and polypoid projections from the mucosa

- **Segmental**
  - Circumferential ring divides GB into separate but connected compartments

- **Localized**
  - Cystic structure forms a nodule involving the muscle layer, usually in the fundus, that appears to be a polyp

Adenomyomatosis and GB Cancer

**Data show increased risk**

- 3197 consecutive CCY: GB cancer in 6.4% of those with segmental adenomyomatosis vs 3.1% in other
- 4560 CCY: GB cancer in 6.6% with adenomyomatosis vs 4.3% in those without

**Data show no increased risk**

- 4704 CCY: adenomyomatosis in 2.4%, but no cancers
- In 30 patients with adenomyomatosis over 7 years, no GB cancer
- 1099 CCY: adenomyomatosis in 14.2%, but no cases of GB cancer

Zakko, UTDOL, 2014
Inflammatory Polyps

- Least-common non-neoplastic lesion
- Sessile or pedunculated
- Granulation and fibrous tissue with plasma cells and lymphocytes
- Usually less than 1 cm

Clinical Features

- Often incidentally found
- May be associated with biliary pain
- May be associated with pancreatitis
- Associated with chronic dyspepsia, as well as nausea and vomiting
- Mechanism: may lead to poor gallbladder emptying
Risk of Malignancy: Possible Factors

- Lesions > 10mm
- Solitary lesion
- Age > 50 – 60 years
- Polyp growth over time
- Concurrent gallstones
- Adenomatous polyps
- Sessile lesions
- Gallbladder wall thickening

Myers RP, Can J Gastro, 2002

Risk of Malignancy

- Biggest factor is size of the polyp
- Polyps > 2 cm are almost always malignant
- Polyps 1 – 2 cm in size could possibly be malignant
  - Incidence 43 to 77%
- Age
  - Older than 50 years is associated with a higher risk
Diagnosis

- Ultrasound
  - Contrast enhanced ultrasonography
  - Doppler US
- CT
- EUS
- PET

Radiologic Assessment

- Hyperechoic material protruding into the GB lumen
- Absence of shift with positional change
- May or may not cast an acoustic shadow
- Sensitivity of US in detecting precancerous lesions of the GB is between 32% and 90%  
  - Decreased by the presence of gallstones
  - Poor correlation between US and pathology
3mm echogenic polyp adherent to GB wall
Path: Cholesterolosis

12 mm polyp with adjacent GB wall thickening
Path: inflammatory polyp with focal adenomatous change

Images from Corwin et al, Radiology 2011

Radiologic Assessment

- EUS: better than transabdominal ultrasound?
  - Tiny echogenic spot or aggregation of echogenic spots and multiple microcysts: cholesterol polyps
  - Comet tail artifact: adenomyomatosis
  - Sugiyama et al: EUS more precise than TAUS (97% vs 76%) Sugiyama, Gut, 2000
  - Contrast enhancement further increases accuracy of depth of tumor invasion: 93% vs 79%
    Hirooka, GIE, 1998
Is EUS Alone Enough to Assess GB Polyps?

• Case series 365 pts with EUS for GB polyps < 2cm
• 94 went to CCY
• Neoplastic lesions in 19 (17 adenoma, 2 CA)
  – 10 had polyps 5 – 10 mm in size
• EUS 88.9% sensitive in dx neoplasia in lesions > 1 cm
• EUS 44.4% sensitive in dx lesions < 1 cm

Cheon et al, World J Gastro, 2009

What about Surveillance?

• Cairns et al, Archives Surgery 2012
  – Retrospective study of 986 patients with GBPs
  – Follow-up on 467
  – 6.6% of polyps grew over the surveillance period
  – Those that grew were initially bigger than those that did not progress in size (7mm vs 5mm)
  – Only 3.7% of resected polyps were malignant or had malignant potential
Surveillance

- Cairns et al, Arch Surg, 2012

Table 3. Predictors of Benign vs Neoplastic/Potentially Neoplastic Polyps

<table>
<thead>
<tr>
<th></th>
<th>Benign Median (Range)</th>
<th>Potentially Malignant/Malignant Median (Range)</th>
<th>Area Under Curve</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size of polyps, mm</td>
<td>5 (2-9)</td>
<td>10 (6-13)</td>
<td>0.81</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Follow-up, mo</td>
<td>8.1 (0.7-19.5)</td>
<td>21.1 (7.5-40.3)</td>
<td>0.79</td>
<td>.001</td>
</tr>
<tr>
<td>No. of polyps</td>
<td>1 (1-4)</td>
<td>1 (1-4)</td>
<td>0.59</td>
<td>.28</td>
</tr>
<tr>
<td>Age, y</td>
<td>53.6 (22-91)</td>
<td>62.6 (44-76)</td>
<td>0.63</td>
<td>.34</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Benign No. %</th>
<th>Potentially Malignant/Malignant No. %</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex progression</td>
<td>19 (14.7)</td>
<td>100</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Multiple</td>
<td>13 (10.1)</td>
<td>1 (50.0)</td>
<td>.39</td>
</tr>
<tr>
<td>Female</td>
<td>78 (60.5)</td>
<td>8 (40.0)</td>
<td>.87</td>
</tr>
</tbody>
</table>

Cost Effectiveness of Surveillance

Surveillance results in a net saving of > $200,000 annually

Cairns, Arch Surg 2012
Does Growth Rate Predict Neoplasia?

- Shin et al, J Clin Gastro, 2009
- Retrospective study 145 patients with GB polyps, at least 1 follow-up exam, and CCY
- 125 non-neoplastic and 20 neoplastic polyps found at CCY
  - Neoplastic more common in older (age > 60) and large polyps size (>10mm)
  - Growth rate was not related to neoplasia (0.6mm/month)

Management

- Cholecystectomy
  - Symptomatic
  - Prevention of malignancy
  - If polyps and PSC -> CCY
  - If adenomyomatosis and sx(s) or concern for obscuring a malignancy -> CCY
Management: Asymptomatic

- Lesions larger than 20 mm: CCY
- Lesions between 10 and 20 mm: CCY
- Lesions between 6 and 9 mm: surveillance US
  - Some suggest at 3 months, 6 months, and then yearly
  - ASGE recommends annual US
  - If increasing size -> CCY
- Lesions 5 mm or smaller: repeat x 1 in 12 months

Proposed Management Algorithm

Gallahan and Conway, Gastro Clin N Am, 2010
Summary

• Gallbladder polyps are frequently encountered, and usually incidentally found
• Difficult to discern neoplastic from non-neoplastic
• All polyps should be followed (if GB not removed)
  – If 5 mm or less, one follow-up exam may be enough
• Cholecystectomy is the one effective treatment

Thank You!