Management of Indeterminate Biliary Strictures

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Indeterminate Biliary Strictures

- Common in clinical practice
- PSC is ideal model/testbed for indeterminate biliary strictures
- Combines inflammatory disease, biliary obstruction, and very real risk of malignancy
PSC and Malignancy

- PSC Strongly associated with cholangiocarcinoma
  - Often diagnosed at an advanced stage
  - Resection or OLTx only curative options
- PSC also associated with:
  - Gallbladder cancer 3-14%
  - Hepatocellular carcinoma (due to underlying cirrhosis)

Razumilava et al Hepatology 2011

Adler’s Definition

“A dominant stricture is the cholangiographic finding of a stricture that stands out amongst all others in a patient with primary sclerosing cholangitis.”

Pro: Immediately intuitive, universally applicable
Con: Subjective
Douglas G. Adler, MD, FACG, FASGE

Tissue Acquisition in PSC

- Brushings
  - Routine Cytology
  - FISH
- Forceps biopsy
- EUS guided FNA

Routine Brushings

- Three possible results:
  - Positive for malignancy
  - Negative for malignancy
  - Atypical cells (AARGHHH!!!)

- Brush cytology
  - Sensitivity 30-60%
  - Specificity 90-96%

- Pro - Cheap, easy, fast
- Con - May be less than helpful

Macken Acta Gast Belg 2000
Atypical Cells…

- A common result on biliary brush cytology in PSC
- Inflammation can influence cellular appearance
- Malignancy sometimes difficult to detect
- May warrant re-sampling or evaluation of stricture in full clinical context

ABBS Score

Score ≥4 statistically associated with malignancy

<table>
<thead>
<tr>
<th>Atypical Biliary Brushing Score (ABBS)</th>
<th>Score</th>
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<tbody>
<tr>
<td>Age ≥ 60</td>
<td>+1</td>
</tr>
<tr>
<td>Endoscopic impression malignant</td>
<td>+2</td>
</tr>
<tr>
<td>Procedure indication pancreatic mass</td>
<td>+1</td>
</tr>
<tr>
<td>Stricture in Common Hepatic Duct</td>
<td>+2</td>
</tr>
<tr>
<td>Stricture in Distal Common Bile Duct</td>
<td>+1</td>
</tr>
<tr>
<td>Presence of PSC</td>
<td>+2</td>
</tr>
<tr>
<td>CA 19-9 above 300 U/mL</td>
<td>+1</td>
</tr>
</tbody>
</table>

Witt, Adler et al Diagnostic Cytopathology 2012
FISH

- Originally developed to test for urothelial cancer
- Malignant PB cancers: 80% show aneuploidy
- Targets the pericentromeric regions of the chromosomes 3 (CEP 3), 7 (CEP 7), and 17 (CEP 17) as well as the chromosomal band 9p21 (LSI 9p21).
- Four or more morphologically abnormal cells with two or more chromosomes with polysomy constitutes a positive test.
- Fourteen or more nuclei with a single gain constitutes a positive test
- Isolated trisomy 7 is equivocal

Huddleston, Lamb, Gopez, Adler, Collins Diagnostic Cytopathology 2012

FISH can detect polysomic cells before other tests

- In one study, 69% of FISH-Positive patients with PSC ultimately had CCA

FISH Polysomy
  - Sensitivity: Specificity 46%:88%

FISH Trisomy/Tetrasomy
  - Sensitivity : Specificity 25%: 67%

Barr Fritcher AJG 2011, Bangarulingam Hepatology 2011
Cholangiocarcinoma

- Less than 2% of all cancer diagnoses
- 1.2/100,000 individuals per year
- 2/3 of cases in individuals >65 years old

Risk factors
- PSC
- Chronic parasitic infections
- Recurrent pyogenic cholangitis

Patel T et al Cancer 2002

Cholangioscopy

- Mother-Baby ERCP scope system
- Allows direct visualization of biliary tree
- Allows more targeted brushings and biopsies
- May facilitate detection of cholangiocarcinoma in PSC
- Once rarely performed
  - Practice now widespread
Peroral cholangioscopy facilitates targeted tissue acquisition in patients with suspected cholangiocarcinoma

R. Liu 1, K. Cox RN 1, A. Siddiqui 2, M. Feuer 1, T. H. Baron 3, D. G. Adler 1

Cholangioscopy and CCA

- **PSC**
  - S/S/PPV/NPV: 75/55/23/92
- **Non-PSC**
  - S/S/PPV/NPV: 100/25/50/100
- **Overall**
  - S/S/PPV/NPV: 86/50/32/93

Liu, Adler Minerva 2014
If cholangiocarcinoma

- If unresectable
  - Uncovered SEMS
- If pre-op for resection or OLTx:
  - Plastic stents or PTC only

FCSEMS for Benign Indications

- Post-surgical
  - CCY injury
  - Anastomotic stricture following OLTx
- Inflammatory
  - Chronic Pancreatitis
  - Stones
- Intractable bile leaks
- Extrinsic compression
  - Pseudocysts
  - Pancreatic necrosis
Biliary Strictures in CP

- Typically distal biliary strictures
- Can mimic pancreatic adenocarcinoma
- Options
  - Multiple Plastic Stents
  - FCSEMS
  - Surgery*
  - * Look for calcifications around stricture

CSEMS for Benign Indications

- Wagh M et al Dign Ther Endo 2013
  - 23 patients with benign biliary strictures
  - Long term success: 83%
- Irani et al DDS 2014
  - 145 patients with benign biliary strictures
  - Stricture resolution in 66% of patients
    - Median stent dwell time of 26 weeks
  - 17% complication rate
    - Cholangitis
    - Pancreatitis
    - Migration
Conclusions

- Stricture evaluation changing
  - Cholangioscopy
  - EUS

- Stricture management changing
  - FCSEMS for benign and malignant strictures
  - FISH testing