Endoscopic Evaluation and Management of Unexplained Acute Recurrent Pancreatitis

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Etiologies of Acute Pancreatitis

- Autoimmune
- Drug-induced
- Iatrogenic
- IBD-related
- Infectious
- Inherited
- Metabolic
- Neoplastic
- Structural
- Toxic
- Traumatic
- Vascular

10-30%
What is Idiopathic Acute Recurrent Pancreatitis (IARP)?

**History**
- Alcohol
- Medications
- Trauma
- Family history

**Laboratory**
- Calcium
- Triglycerides
- Liver tests
- Genetics

**Imaging (CT, US)**
- Tumors
- Pancreas divisum
- IPMN
- Stone, Stricture

**No cause for AP**

Objectives/Questions

- Discuss role of ERCP in IARP
- Where does EUS fit in the algorithm
- Can s-MRCP be use to triage
- Prove that endoscopy has a critical role in the diagnosis and therapy of IARP
Potential Causes of IARP Diagnosed by ERCP and Ancillary Techniques

- Occult gallstones
- Abnormalities/anomalies of the pancreatic and bile duct
- Sphincter of Oddi dysfunction
- Pancreatic and ampullary tumors

Techniques Applied at ERCP to Diagnose Cause of IARP

- Screening endoscopy
  - Ampullary and IPMN
- Ductography
  - Bile duct stones
  - Anomalies/abnormalities of PD/BD
  - Chronic pancreatitis
  - Tumors
- Sphincter of Oddi Manometry
  - Sphincter of Oddi dysfunction
- Aspiration of bile for crystals
  - Microlithiasis
Why Evaluate

- The patient has an underlying disease which will predispose to further attacks unless the cause is adequately treated.
- The pancreatitis may be due to a tumor.

When to Evaluate by ERCP

- Limited data
- Our approach:
  - > 40 years: after first episode
  - < 40 years: after second episode unless first episode is severe
### IARP: Yield of ERCP ± SOM ± Bile Microscopy Correlated with Age (n=225)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>&lt;20 yr n=15</th>
<th>20-40 yr n=53</th>
<th>40-60 yr n=95</th>
<th>&gt;60 yr n=62</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplasm</td>
<td>0%</td>
<td>4%</td>
<td>23%</td>
<td>25%</td>
</tr>
<tr>
<td>Benign*</td>
<td>93%</td>
<td>75%</td>
<td>71%</td>
<td>64%</td>
</tr>
<tr>
<td>Normal</td>
<td>7%</td>
<td>21%</td>
<td>6%</td>
<td>11%</td>
</tr>
</tbody>
</table>

Choudari. AJG 1998;93:1654A
* SOD, pdiv, chr panc, misc

### Occult Gallstone Disease
(Gallstone Pancreatitis)
**Subtle Gallbladder Disease Causing IARP**

- Two prospective studies* suggested that 67-75% of patients had microlithiasis as the cause for IARP
- Diagnosis based on microscopic examination of bile, usually confirmed at CCx or follow-up ultrasonography

*Ros. Gastro 1991;101:1701
Lee. NEJM 1992;326:589

**Cholesterol Crystals**
Microlithiasis

Results

- Therapy with UDCA prevented ARP in 11 of 12 with cholesterol crystals during a mean follow-up of 42 months
- Cholecystectomy prevented ARP in 17 of 18 during a mean follow-up of 36 months
- Endoscopic sphincterotomy is an option for high-risk surgical patient

Ros. Gastroenterology 1991;101:1701
Conclusions

• Microscopic examination of bile for crystals in patients with gallbladder in situ is recommended. Crystals appear to predict the presence of microlithiasis.

• A variety of therapies effective – cholecystectomy, biliary sphincterotomy, UDCA

Sphincter of Oddi Dysfunction
Sphincter of Oddi

Triple Lumen Catheter
Sphincter of Oddi Manometry

SO Manometry Tracing
### Sphincter of Oddi Dysfunction Causing IARP (9 series 1985-2010)

<table>
<thead>
<tr>
<th>No. patients</th>
<th>Frequency SOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1757</td>
<td>698 (40%)</td>
</tr>
</tbody>
</table>

### Does Biliary Sphincterotomy Alone “Cure” Pancreatitis in SOD?

<table>
<thead>
<tr>
<th>Therapy</th>
<th># Pts.</th>
<th>F/U</th>
<th>Asymptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biliary ES</td>
<td>16</td>
<td>5 yr</td>
<td>44%</td>
</tr>
</tbody>
</table>

*Sherman. GIE 1993;39:331A*
Pancreatic Sphincterotomy

IARP and Increased Pancreatic Sphincter Pressure: Need for Ablation of Both Biliary and Pancreatic Sphincters

<table>
<thead>
<tr>
<th>Therapy</th>
<th>N</th>
<th>Number Pts Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>BD ES</td>
<td>18</td>
<td>5 (28%)</td>
</tr>
<tr>
<td>BD ES + PD balloon dilation</td>
<td>24</td>
<td>13 (54%)</td>
</tr>
<tr>
<td>BD ES + PD ES</td>
<td>27</td>
<td>22 (81%)</td>
</tr>
</tbody>
</table>

p < .001

Guelrud. GI Endosc 1995;41:398A
IARP – RCT of BDES vs. BDES + PDES for Pancreatic SOD (f/u 7 years)

Recurrent Pancreatitis

\[
\begin{array}{c|c|c}
 & BDES (n=33) & BD + PDES (n=36) \\
\hline
49\% & 47\% & p = 1 \\
\end{array}
\]

Coté. DDW 2012

Conclusions: IARP Due to SOD

- SOD is the most common cause of IARP when detailed endoscopic evaluation performed
- Sphincter of Oddi manometry is the gold standard for diagnosing SOD
- The best therapy awaits further study
  - At present, the role of sphincter therapy remains unclear
Congenital Anomalies of Pancreatic Duct and Bile Duct

Pancreas Divisum

- Most common congenital variant of PD anatomy
- Occurs when dorsal and ventral ducts fail to fuse
- With duct nonunion, the major portion of the exocrine juice drains into the duodenum via the dorsal duct and minor papilla
- Common cause of IARP
Pancreas Divisum

Minor Papilla
Pancreas Divisum: Endoscopic Therapy

• Aim to alleviate the outflow obstruction
• Methods: dilation, ES, stenting

Dorsal Duct Stent
Minor Papilla ES

Minor Papilla Rx for Pancreas Divisum and IARP
12 studies 1986-2009

<table>
<thead>
<tr>
<th>No. pts.</th>
<th>Follow-up (mos)</th>
<th>Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>241</td>
<td>30</td>
<td>76%</td>
</tr>
</tbody>
</table>
## Pancreas Divisum and IARP: Results for Minor Papilla Stenting

<table>
<thead>
<tr>
<th>Therapy</th>
<th>F/U (mo)</th>
<th>Hosp.</th>
<th>ER</th>
<th>Number w/panc.</th>
<th>Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent (n=10)</td>
<td>29</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>9 (90%)</td>
</tr>
<tr>
<td>Control (n=9)</td>
<td>32</td>
<td>5*</td>
<td>2</td>
<td>7*</td>
<td>1 (11%)*</td>
</tr>
</tbody>
</table>

*P*<.05; *Lans. GI Endosc* 1992;38:430

## Conclusion: IARP Due to Pancreas Divisum

- Patients with pancreas divisum and acute recurrent pancreatitis are good candidates for minor papilla therapy
- Long-term outcome studies of endoscopic therapy are needed
Choledochocele
(Type III Choledochal Cyst)

- Cystic dilation of the CBD most often involving the intramural segment
- High incidence of pancreatitis
Choledochocele – Endoscopic Rx

Endoscopic Rx of Choledochoceles: Pancreatitis

<table>
<thead>
<tr>
<th>Author (yr)</th>
<th>N</th>
<th># Pancreatitis</th>
<th># Improved # Panc Treated at ERCP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venu (1994)</td>
<td>8</td>
<td>5</td>
<td>2/3</td>
</tr>
<tr>
<td>Martin (1992)</td>
<td>10</td>
<td>7</td>
<td>7/7</td>
</tr>
<tr>
<td>Ladas (1995)</td>
<td>15</td>
<td>1</td>
<td>1/1</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>13 (39%)</td>
<td>10/11 (91%)</td>
</tr>
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</table>
Conclusions: IARP Due to Choledocholeces

- Choledocholeces are an uncommon cause of IARP but commonly present with pancreatitis
- Diagnosis made on endoscopy and ERCP
- Endoscopic therapy effective in large majority of patients

Tumors
Tumors Causing IARP

• Malignant and pre-malignant lesions are an uncommon cause of IARP in patients <40 yrs but should be considered in patients >40 yrs
• Most common tumors reported in IARP series
  – IPMN/cystic tumors
  – Ampullary tumors
  – Pancreatic adenocarcinoma
  – Islet cell
• May be missed on standard abdominal imaging

IARP: Yield of ERCP ± SOM ± Bile Microscopy Correlated with Age (n=225)

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</thead>
<tbody>
<tr>
<td>Pancreatic Ca</td>
<td>0%</td>
<td>0%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Amp tumors</td>
<td>0%</td>
<td>2%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>IPMN</td>
<td>0%</td>
<td>2%</td>
<td>17%</td>
<td>23%</td>
</tr>
<tr>
<td>Benign</td>
<td>94%</td>
<td>78%</td>
<td>72%</td>
<td>65%</td>
</tr>
<tr>
<td>Normal</td>
<td>7%</td>
<td>21%</td>
<td>6%</td>
<td>11%</td>
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*Choudari. AJG 1998;93:1654A*
IPMN

Ampullary Tumor Resection
## Endoscopic Resection of Ampullary Tumors (21 series 1993-2011)

<table>
<thead>
<tr>
<th>No. pts.</th>
<th>Complete resection</th>
<th>Complications</th>
<th>Recurrence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>967</td>
<td>82%</td>
<td>25%*</td>
<td>14%</td>
</tr>
</tbody>
</table>

* Pancreatitis 14%, bleeding 4%, perforation 2%, cholangitis 6%

## IARP: ERCP, SOM, Bile Microscopy (4 series, 522 patients)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOD</td>
<td>179 (34%)</td>
</tr>
<tr>
<td>P.Divisum</td>
<td>70 (13%)</td>
</tr>
<tr>
<td>Panc/pap tumor</td>
<td>46 (9%)</td>
</tr>
<tr>
<td>GB/Duct stones</td>
<td>37 (7%)</td>
</tr>
<tr>
<td>PD stricture/ chronic panc</td>
<td>37 (7%)</td>
</tr>
<tr>
<td>Choledochocele</td>
<td>12 (2%)</td>
</tr>
<tr>
<td>Total abnormal</td>
<td>381/522 (73%)</td>
</tr>
</tbody>
</table>
Outcome of Therapy (n=100)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N</th>
<th>F/U (mos)</th>
<th>Asymptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOD</td>
<td>67</td>
<td>33</td>
<td>79%</td>
</tr>
<tr>
<td>GB/Duct Stones</td>
<td>18</td>
<td>31</td>
<td>89%</td>
</tr>
<tr>
<td>Pancreas Divisum</td>
<td>9</td>
<td>24</td>
<td>89%</td>
</tr>
<tr>
<td>Tumor</td>
<td>2</td>
<td>28</td>
<td>50%</td>
</tr>
<tr>
<td>Choledochoccele</td>
<td>2</td>
<td>18</td>
<td>100%</td>
</tr>
<tr>
<td>PD Stricture</td>
<td>2</td>
<td>31</td>
<td>50%</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>30</td>
<td>81%</td>
</tr>
</tbody>
</table>

*Kaw. GIE 2001;55:157*

Role of EUS in Idiopathic Acute Recurrent Pancreatitis

- Minimally invasive endoscopic procedure
- Highly accurate for detecting gallbladder sludge/microlithiasis, bile duct stones, pancreas divisum, chronic pancreatitis, and pancreatic neoplasms when other imaging tests were negative
Gallstones

Small BD Stone
## 15 mm Pancreas Cancer

![Image of 15 mm Pancreas Cancer](image)

## Selected Studies Evaluating the Yield of EUS in IAP and IARP

<table>
<thead>
<tr>
<th>Author (yr)</th>
<th>N</th>
<th>Biliary</th>
<th>Neoplasm</th>
<th>Cause identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frossard ('00)</td>
<td>168</td>
<td>61%</td>
<td>7%</td>
<td>78%</td>
</tr>
<tr>
<td>Yusoff ('04)</td>
<td>370</td>
<td>19%</td>
<td>4%</td>
<td>59%</td>
</tr>
<tr>
<td>Tandon ('01)</td>
<td>31</td>
<td>16%</td>
<td>3%</td>
<td>68%</td>
</tr>
<tr>
<td>Norton ('00)</td>
<td>44</td>
<td>59%</td>
<td>2%</td>
<td>72%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>613</td>
<td>33%</td>
<td>4%</td>
<td>65%</td>
</tr>
</tbody>
</table>
Mild Chronic Pancreatitis
s-MRCP Demonstrating a Multifocal Side Branch IPMN

Remember Other Investigations

- Genetic testing
  - CFTR, PRSS 1, SPINK-1

- Autoimmune pancreatitis
  - ANA, IgG 4

- Metabolic
  - Serum triglyceride, calcium on admission
Idiopathic Acute Pancreatitis (standard evaluation negative)

1 attack
- young
  - observe
- older
  - EUS and/or s-MRCP

≥ 2 attacks
- young or older
  - Sample bile for crystals when GB in situ
  - ERCP or surgery by providing detailed images of the ductal and parenchymal structures

Conclusions

- IARP is an endoscopic disease
- Techniques applied at ERCP and EUS have an important role in identifying the cause of IARP
- s-MRCP can assist in triaging patients to ERCP or surgery by providing detailed images of the ductal and parenchymal structures
- Microscopic examination of bile for crystals in patients with the GB in situ is recommended. Crystals predict the presence of microlithiasis
- The majority of diseases uncovered appear to be treatable by endoscopic and/or surgical techniques