Pancreatitis of unknown aetiology

Irene Esposito
Morphological assessment is important:

- To assess the cause of CP

- For the differential diagnosis of pancreatitis vs tumor/malignancy

- For the identification of rare causes of pancreatitis-like damage/symptoms
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Consultation case
M, 50 y. Question: Malignancy? AIP?
Consultation case
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**Morphology**

- Paucicellular connective tissue
- Atrophy of acinar tissue
- Focal inflammation
Consultation case
M, 50 y. Question: Malignancy? AIP?

Morphology

• Paucicellular connective tissue
• Atrophy of acinar tissue
• Focal inflammation
• Prominent nerves
• Arteriitis

Diagnosis: „classical“ (alcoholic) CP
Consultation case
M, 72 y. Jaundice, weight loss. Question: PDAC?
Consultation case
M, 72 y. Jaundice, weight loss. Question: PDAC?

Morphology

• Highly cellular connective tissue
• Partial acinar atrophy
Trichrome staining (Van Gieson)
Consultation case
M, 72 y. Jaundice, weight loss. Question: PDAC?

Morphology

• Highly cellular connective tissue
• Partial acinar atrophy
• Phlebitis (venulitis)
Consultation case
M, 72 y. Jaundice, weight loss. Question: PDAC?

Morphology

- Highly cellular connective tissue
- Partial acinar atrophy
- Phlebitis (venulitis)
- IgG4-positive plasmacells

Diagnosis: AIP (type 1)
Type 1 and type 2 AIP

Table 1. Comparison of histological findings between type 1 and type 2 AIP.

<table>
<thead>
<tr>
<th>Histological findings</th>
<th>Type 1 AIP (n=37)</th>
<th>Type 2 AIP (n=15)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periductal lymphoplasmacytic infiltration</td>
<td>37 (100%)</td>
<td>3 (20%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Storiform fibrosis</td>
<td>37 (100%)</td>
<td>0 (0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obliterative phlebitis</td>
<td>18 (48.6%)</td>
<td>0 (0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IgG4-positive cells†</td>
<td>34 (91.9%)</td>
<td>0 (0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Granulocytic epithelial lesion</td>
<td>0 (0%)</td>
<td>15 (100%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lobular neutrophilic infiltration</td>
<td>3 (8.1%)</td>
<td>15 (100%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

†>10 cells/hpf in biopsy specimen or >20 cells/hpf in resection specimen.

Song TJ et al, J Hepatol Gastroenterol 2011
# Clinical correlations

<table>
<thead>
<tr>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Frequency</td>
</tr>
<tr>
<td>55-75% of all cases</td>
<td>25-45% of all cases</td>
</tr>
<tr>
<td>Gender &amp; Age (median)</td>
<td>Gender &amp; Age (median)</td>
</tr>
<tr>
<td>M 61-91%, 63y</td>
<td>M 48-73%, 44y</td>
</tr>
<tr>
<td>Initial presentation</td>
<td>Initial presentation</td>
</tr>
<tr>
<td>Painless jaundice (70%)</td>
<td>Abdominal pain (60%), AP (40%)</td>
</tr>
<tr>
<td>Imaging</td>
<td>Imaging</td>
</tr>
<tr>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Serum IgG4 ≥135mg/dl</td>
<td>Serum IgG4 ≥135mg/dl</td>
</tr>
<tr>
<td>90%</td>
<td>0-9%</td>
</tr>
<tr>
<td>Other organ involvement</td>
<td>Other organ involvement</td>
</tr>
<tr>
<td>50-70% (bile duct up to 80%)</td>
<td>12% (bile duct up to 9%)</td>
</tr>
<tr>
<td>IBD (UC)</td>
<td>IBD (UC)</td>
</tr>
<tr>
<td>0-5%</td>
<td>25-33%</td>
</tr>
<tr>
<td>Response to steroids</td>
<td>Response to steroids</td>
</tr>
<tr>
<td>Complete remission</td>
<td>Complete remission</td>
</tr>
<tr>
<td>Relapse after steroids</td>
<td>Relapse after steroids</td>
</tr>
<tr>
<td>40%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Zen et al, *Orphanet J Rare Dis*, 2011
Song TJ et al, *J Hepatol Gastroenterol* 2011
Klöppel et al, *J Gastroenterol* 2010
Consultation case
M, 34 y. Question: Diagnosis?
Consultation case
M, 34 y. Question:  Diagnosis?

Morphology

- Acinar tissue with increased cellularity
- Interlobular cellular fibrosis
Consultation case
M, 34 y. Question: Diagnosis?

Morphology

- Acinar tissue with increased cellularity
- Interlobular cellular fibrosis
- Granulocytic infiltration of acinar parenchyma

Diagnosis: AIP (type 2)
Diagnosis of AIP on biopsy

Fibrosis

Periductal Inflammation

GEL

IgG4

Detlefsen S et al. Virchows Arch 2009
Frequency of the individual histological features in pancreatic core needle biopsy specimens (mean length 16 mm)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Clinically suggestive of AIP</th>
<th>Clinically suggestive of Non-AIP CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granulocytic epithelial lesion (GEL)</td>
<td>48.3% (14/29)</td>
<td>0% (0/15)</td>
</tr>
<tr>
<td>&gt;10 IgG4 positive plasma cells/HPF</td>
<td>41.4% (12/29)</td>
<td>13.3% (2/15)</td>
</tr>
<tr>
<td>&gt;10 eosinophilic granulocytes/HPF</td>
<td>62.1% (18/29)</td>
<td>33.3% (5/15)</td>
</tr>
<tr>
<td>Cellular fibrosis with inflammation</td>
<td>96.6% (28/29)</td>
<td>40.0% (6/15)</td>
</tr>
<tr>
<td>Lymphoplasmacytic infiltration</td>
<td>93.1% (27/29)</td>
<td>33.3% (5/15)</td>
</tr>
<tr>
<td>Venulitis</td>
<td>65.5% (19/29)</td>
<td>26.7% (4/15)</td>
</tr>
</tbody>
</table>

Detlefsen S et al. Virchows Arch 2009
Microscopic features observed per specimen in 29 core needle biopsy specimens from 26 AIP patients and in 15 core needle biopsy specimens from 14 non-AIP CP patients

<table>
<thead>
<tr>
<th>Feature</th>
<th>AIP</th>
<th>Non-AIP CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0% (0/29)</td>
<td>33.3% (5/15)</td>
</tr>
<tr>
<td>1</td>
<td>0% (0/29)</td>
<td>13.3% (2/15)</td>
</tr>
<tr>
<td>2</td>
<td>0% (0/29)</td>
<td>26.7% (4/15)</td>
</tr>
<tr>
<td>3</td>
<td>24.1% (7/29)</td>
<td>26.7% (4/15)</td>
</tr>
<tr>
<td>4</td>
<td>48.3% (14/29)</td>
<td>0% (0/15)</td>
</tr>
<tr>
<td>5</td>
<td>24.1% (7/29)</td>
<td>0% (0/15)</td>
</tr>
<tr>
<td>6</td>
<td>3.5% (1/29)</td>
<td>0% (0/15)</td>
</tr>
</tbody>
</table>

Sensitivity 76%, Specificity 100%

Detlefsen S et al. Virchows Arch 2009
## Biopsies of other sites (type 1)

<table>
<thead>
<tr>
<th>Biopsy Type</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Usefulness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampullary biopsy</td>
<td>52-80%</td>
<td>91-100%</td>
<td>Correlates well with AIP</td>
</tr>
<tr>
<td>Liver needle biopsy</td>
<td>24-60%</td>
<td>100%</td>
<td>Only if intrahepatic changes are present</td>
</tr>
<tr>
<td>Bile duct biopsy</td>
<td>52%</td>
<td>97%</td>
<td>Operator dependent</td>
</tr>
</tbody>
</table>

Rebours et al, *Clin Gastroenterol Hepatol* 2012
Morphological assessment is important:

- To assess the cause of CP
- For the differential diagnosis of pancreatitis vs tumor/malignancy
- For the identification of rare causes of pancreatitis-like damage/symptoms
Consultation case
F, 79 y. Question: fibrotic pancreas. AIP? Malignancy?
Consultation case
F, 79 y. Question: fibrotic pancreas. AIP? Malignancy?

**Morphology**

- Cellular fibrosis
- Atrophy of acinar tissue
- "Naked" ducts
Consultation case
F, 79 y. Question: fibrotic pancreas. AIP? Malignancy?

**Morphology**

- Cellular fibrosis
- Atrophy of acinar tissue
- „Naked“ ducts
- Atypical ductal structures

Diagnosis: PDAC
Consultation case
F, 44 y
Tumor in the pancreatic head
Diagnosis: Myoepithelial neoplasia

Collagen-rich tumor with sharp demarcation from acinar tissue
Consultation case
F, 44 y
Tumor in the pancreatic head
Diagnosis: Myoepithelial neoplasia

**Morphology**

- Collagen-rich tumor with sharp demarcation from acinar tissue
pancytokeratin
Consultation case
F, 44 y
Tumor in the pancreatic head
Diagnosis: Myoepithelial neoplasia

Morphology

- Collagen-rich tumor with sharp demarcation from acinar tissue
- Entrapment of epithelial islands
- Cystically dilated pancreatic ducts in the duodenal wall/paraduodenal pancreatic tissue

Diagnosis:
Paraduodenal (groove) pancreatitis

Synonyms: cystic dystrophy of heterotopic pancreatic tissue
hamartoma of the pancreas
paraduodenal wall cyst
myoadenomatosis
Paraduodenal pancreatitis

58 resected cases

- 6.6% of all resected CP cases (n=882; 1990-2006)
- 93% men
- 44.7 years (38-51)
- 95% alcoholics and/or smokers
- Indication for surgery: 80% pain; 14% suspicion of malignancy; 5% jaundice
- Good outcome; 22% with persisting pain

Casetti et al, World J Surg 2009
Morphological assessment is important:

- To assess the cause of CP

- For the differential diagnosis of pancreatitis vs tumor/malignancy (AIP, groove pancreatitis)

- For the identification of rare causes of pancreatitis-like damage/symptoms
Consultation case
M, 52 y, tumor in the pancreatic head
Question: NET?

Fibrotic area with tryptic necrosis: CP?
Consultation case
M, 52 y, tumor in the pancreatic head
Question: NET?

**Morphology**

- Fibrotic area with tryptic necrosis
Consultation case
M, 52 y, tumor in the pancreatic head

Question: NET?

**Morphology**

- Fibrotic area with tryptic necrosis
- Intrapancreatic artery with intimal proliferation and hyperplasia of the media

**Diagnosis:** Ischemic necrosis of the pancreas due to hypertensive arteriopathy
Conclusions

Morphological assessment of CP is important and feasible:

In the pre-operative setting:
  to avoid unnecessary surgery (AIP)
  to set indication for resection in unclear cases (tumor vs CP)

In the post-operative setting:
  to establish/confirm the cause of CP
  to confirm the clinical diagnosis