AUTOIMMUNE PANCREATITIS
Dr.med.Brindusa Diaconu
2 TYPES

- Different clinical picture, different histopathology,

- Different evolution
Types of Autoimmune Pancreatitis

- Type 1 - Ig G4 related
  1. Diagnosis late in life
  2. 3:1 male predominance
  3. Other extrapancreatic organs may be involved
  4. High relapse rates

- Type 2 - IDCP
  1. Younger age, without sex bias
  2. Clinical presentations limited to the pancreas
  3. 15% association with IBD
  4. Low relapse rates
**Type 1 AIP**

- Ig G4 related pancreatitis
- Typical histology
- Frequent elevations in serum IgG4 levels
- Abundant IgG4 positive plasma cells in affected organs

- Dramatic response to corticosteroids
Pathogenesis of IgG4 related pancreatitis

- Genetic predisposition
- Possible immunologic triggers
- Subsequent immune reactions
CLINICAL PRESENTATION

- Painless jaundice - 60-70%
- Pancreatic mass without jaundice
- Pancreatic insufficiency
- Uncommonly acute pancreatitis
HISTOLOGY

- Periductal lymphoplasmacytic infiltrate without granulocytic infiltration
- Obliterative phlebitis
- Storiform fibrosis
- > 10 IgG4 positive cells/HPF
HISTOLOGY
IMAGING

- CT
- MRI & MRCP
- Endoscopic ultrasound
- ERCP
Ductal changes: MRCP vs ERCP

- Portions of the pancreatic duct may not be visible at MRCP:
  
  *MRCP is not a substitute for endoscopic retrograde cholangiography if ductal findings are to be used for diagnosis* (Recent advances in autoimmune pancreatitis, Gastroenterology 2015; 149:39-51)
IMAGING
ERCP-ductal changes
IMAGING-FUTURE PERSPECTIVES

- EUS: irregular narrowing of MPD in association with wall thickening: sensitivity of 93% and specificity of 98% against pancreatic cancer in one study

- PET-CT: possible role for the assessment of other organ involvement—further studies needed
SEROLOGY

- Elevation in IgG, IgG4 and ANA—but not specific!!!

- Only serum IgG4 recommended as serological marker

- False negative and false positive results of Ig G4

- Ig G4 is not useful as a single test for diagnosis of AIP or IgG4 related disease
**Ig G4 in tissue and blood**

- A small subset of AIP patients lack any evidence of tissue Ig G4 positivity or serum IgG4 elevations at presentation.....

- „Ig G4 abnormalities are at best characteristic but not essential for the diagnosis of AIP”

  *(Sah RP, Chari ST. Pancreas 2015; 31:387-394)*
FUTURE APPROACH

- Role of flow cytometry gating for Ig G4 positive plasma cells in blood in diagnosing and monitoring of the disease

Extrapancreatic involvement - IgG4 infiltration

- Biliary tree
- Salivary/lacrimal glands
- Retroperitoneum
- Kidney
- Lung
- Lymph nodes
- Prostate
- Aorta, pericardium
- Pituitary gland
## International Consensus Diagnostic Criteria

### Pancreas

#### Table 2. Diagnostic features in International Consensus Diagnostic Criteria (ICDC) and establishment of diagnosis of AIP (type 1) and IDCP (type 2)

<table>
<thead>
<tr>
<th>International Consensus Diagnostic Criteria (ICDC)</th>
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<tbody>
<tr>
<td><strong>A. Diagnostic features</strong></td>
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<tr>
<td><strong>Level 1 (strong)</strong></td>
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<tr>
<td>Histology (see text), H</td>
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<tr>
<td>IDCP: presence of GELs, and absent or scant IgG4 positive cells</td>
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<tr>
<td>Imaging (see text), I</td>
</tr>
<tr>
<td>IgG4 serology, S</td>
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<tr>
<td>Other organ involvement (OOI), O</td>
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<tr>
<td>(any one of the listed features)</td>
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<tr>
<td>Response to steroids, Rt (dramatic radiologic improvement at 2 weeks)</td>
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### Establishment of diagnosis

Diagnosis established when any one of the following meets:

- **AIP (type 1)**
  1. Characteristic (level 1) histology, or
  2. Typical (level 1) imaging with any collateral evidence (O or S), or
  3. Positive response to steroid in presence of supportive (level 2) imaging with
     (a) one strong (level 1) collateral evidence (O or S), or
     (b) only supportive (level 2) evidence (O or S or H) with consistent ductal imaging (ERP)

- **IDCP**
  1. Characteristic (level 1) histology, or
  2. Supportive (level 2) histology, absent S and O, presence of clinical IBD and positive response to steroids
TREATMENT

- Corticosteroids (after induction of remission different approaches according to the geographic regions regarding maintenance therapy)

- Treatment of relapse:
  1. corticosteroids
  2. Immunomodulators- azathioprine, 6 mercaptopurine, mycophenolate mofetil etc.
  3. Rituximab (monoclonal CD20 antibody)
RITUXIMAB

- Apart from corticosteroids it is the only agent that can induce remission for IgG4 related disease

- Reasonable to consider as first line therapy in
  1. Previous intolerance to high dose corticosteroids
  2. Patients at high risk of relapse: proximal biliary strictures or extensive multiorgan disease
PROGNOSIS

- Some develop pancreatic stones, pancreatic insufficiency

- Risk of cancer - contradictory data
**IG G4 related cholangitis**

- Commonest extrapancreatic manifestation of type 1 AIP (20-88%)  
- Jaundice is the most common presenting symptom  
- May be diagnosed asymptomatically in patients presenting with type 1 AIP
CLASSIFICATION OF IGG4 RELATED SCLEROSING CHOLANGITIS

<table>
<thead>
<tr>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
<th>Type 4</th>
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<tbody>
<tr>
<td><img src="image1" alt="Type 1" /></td>
<td><img src="image2" alt="Type 2a" /></td>
<td><img src="image3" alt="Type 2b" /></td>
<td><img src="image4" alt="Type 3" /></td>
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<tr>
<td><img src="image5" alt="Type 4" /></td>
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**Differential diagnosis**
- Pancreatic cancer
- Bile duct cancer
- Chronic pancreatitis
- Primary sclerosing cholangitis
- Bile duct cancer
- Gallbladder cancer

**Useful modalities**
- IDUS (bile duct)
- EUS-FNA (pancreas)
- Biopsy (bile duct)
- Liver biopsy
- Colonoscopy (R/O coexistence of IBD)
- EUS (bile duct, pancreas)
- IDUS (bile duct)
- Biopsy (bile duct)
DIAGNOSIS

- Cholangiography obtained by ERCP: specificity of 88%, sensitivity 45%

- OOI may provide powerful evidence for IgG4

- Raised serum IgG4 levels in 9% of patients with PSC and are unhelpful in differentiating IgG4-SC and PSC

- Possible role for cholangioscopy in diff. IgG4 from PSC—further data are needed
**DIAGNOSIS**

- ERCP with brush citology, endobiliary biopsies or ampullary biopsies
- Cholangioscopy
- If dominant stricture- stenting because of the risk of biliary sepsis

*Ig G4 should be considered only in conjunction with other diagnostic criteria*
**Differential diagnosis**

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<tr>
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<th>PSC</th>
<th>IgG4-SC</th>
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<tr>
<td><strong>Gender</strong></td>
<td>M:F 1.5:1</td>
<td>M:F 7:1</td>
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<tr>
<td><strong>Age of onset</strong></td>
<td>Young age (&lt;40 years)</td>
<td>Older (&gt;50 years)</td>
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<tr>
<td><strong>Presentation</strong></td>
<td>Cholestatic liver biochemistry</td>
<td>Obstructive jaundice</td>
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<td><strong>Biliary abnormalities</strong></td>
<td>Beading, band-like strictures, peripheral pruning</td>
<td>Long smooth strictures; low CBD stricture</td>
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<tr>
<td><strong>Raised serum IgG4 levels</strong></td>
<td>&lt;20%</td>
<td>&gt;70%</td>
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<td><strong>Pancreatic involvement</strong></td>
<td>&lt;5%</td>
<td>&gt;80%</td>
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<tr>
<td><strong>Multi-organ involvement</strong></td>
<td>No</td>
<td>Yes</td>
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<tr>
<td><strong>Association with IBD</strong></td>
<td>80%</td>
<td>Yes</td>
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<tr>
<td><strong>Response to steroids</strong></td>
<td>Rare (IgG4 +ve PSC)</td>
<td>Yes</td>
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Hepatic manifestations in Ig G4 related disease

- Inflammatory pseudotumor-lymphoplasmacytic
- Subtle lymphoplasmacytic IgG4 on liver biopsy
- Subtype of AIH characterised by infiltration of IgG4 expressing plasma cells-particularly responsive to corticosteroids
TYPE 2 AUTOIMMUNE PANCREATITIS

- Common presentations: acute pancreatitis and jaundice

- 15% associate IBD, predominantly UC

- The only means of definitely confirming dg-GEL on histology
**Histology in Type 2 AIP**

- Granulocytic infiltration of duct wall (GEL) with or without granulocytic acinar inflammation

- Absent or scant IgG4 positive cells
ACUTE PANCREATITIS IN PATIENTS WITH IBD

- Most are not AIP type 2

- Consider first other causes: gallstones, medication