IgG4 related Cholangiopathy and Pancreatitis

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PSC Meeting, Pittsburgh
April 26-28, 2013
Some publications from UPMC on this subject

Autoimmune Pancreatitis

- Autoimmune disorder
- First described as a distinct entity in 1995
- Rare disease
  - Exact prevalence in Western countries unknown
  - ~2500 cases in the US if we extrapolate from Japanese data
Autoimmune Pancreatitis

• Clinical presentation mimics Pancreas cancer
• Less common
  • Pancreatitis, persistent pancreatic mass, scarred or shrunken pancreas, malabsorption
• Elevation of serum IgG4 levels
• Typical appearance on imaging tests and biopsy
• Patients often have involvement of other organs
• Two forms have been recognized - Type I and II

GCNA 2008;37:439-60; Pancreas 2012;41:835-9; Pancreas 2011;40:352-8
Autoimmune Pancreatitis
Autoimmune Pancreatitis
Autoimmune Pancreatitis
Autoimmune Pancreatitis
IgG4-related Disease

IgG4-related sclerosing disease

Autoimmune pancreatitis

IgG4-related sclerosing sialadenitis

IgG4-related pseudotumors

IgG4-related sclerosing cholangitis

IgG4-related retroperitoneal fibrosis
### Organs involved in IgG4 related disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>Organ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mikulicz's syndrome</td>
<td>Salivary and lachrymal glands</td>
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<tr>
<td>Kuttner's tumour</td>
<td>Submandibular glands</td>
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<tr>
<td>Riedel's thyroiditis</td>
<td>Thyroid</td>
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<tr>
<td>Hashimoto's thyroiditis</td>
<td>Thyroid</td>
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<tr>
<td>Autoimmune pancreatitis</td>
<td>Pancreas</td>
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<tr>
<td>Eosinophilic angiocentric fibrosis</td>
<td>Orbit and upper respiratory tract</td>
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<tr>
<td>Multifocal fibrosclerosis</td>
<td>Orbit, thyroid, retroperitoneum, mediastinum</td>
</tr>
<tr>
<td>Inflammatory pseudotumor</td>
<td>Orbit, lungs, liver, kidneys</td>
</tr>
<tr>
<td>Mediastinal fibrosis</td>
<td>Mediastinum</td>
</tr>
<tr>
<td>Retroperitoneal fibrosis</td>
<td>Retroperitoneum</td>
</tr>
<tr>
<td>Interstitial pneumonitis</td>
<td>Lungs</td>
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<tr>
<td>Inflammatory aortic aneurysm</td>
<td>Abdominal aorta</td>
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<tr>
<td>Idiopathic hypocomplementemic tubulointerstitial nephritis</td>
<td>Kidney</td>
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<tr>
<td>Periaortitis and periarteritis</td>
<td>Aorta</td>
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<tr>
<td>Autoimmune hypophysitis</td>
<td>Hypophysity</td>
</tr>
<tr>
<td>Cutaneous pseudolymphoma</td>
<td>Skin</td>
</tr>
<tr>
<td>Rosai-Dorfman disease</td>
<td>Glands</td>
</tr>
</tbody>
</table>
IgG4 related disease

• Systemic disease - First recognized in 2003
• Can involve virtually any organ(s)
  (Pancreas, bile ducts, salivary glands, periorbital tissue, kidneys, lungs, lymph nodes, meninges, aorta, breast, prostate, thyroid, pericardium, skin)
• Elevation of serum IgG4 levels
• Pathology findings are characteristic
  • Dense lymphoplasmacytic infiltration; storiform fibrosis; mild-moderate eosinophil infiltration; rich in IgG4-positive plasma cells
• Excellent response to steroids

NEJM 2012;366:539-51
IgG4 related Sclerosing Cholangitis

- IgG4 related disease involving the bile ducts
- ~90% cases also have Autoimmune Pancreatitis
- Usually elderly male presenting with painless jaundice
- Elevation of serum IgG4 levels
- Imaging findings mimic PSC and cholangiocarcinoma
- Bile duct biopsies show IgG4-positive plasma cells
PSC and elevated serum IgG4
Elevated IgG4 are seen in ~10% PSC patients

No special features to identify them from patients with normal IgG4 levels

Have more aggressive and severe disease

Shorter time to transplantation

Show good response to steroids – however, the role of steroids and other immunosuppressive treatments still poorly defined
• IgG4 related disease is an increasingly recognized clinical entity
• Can involve multiple organs
• Elevations in serum IgG4 levels common
• Has typical pathology findings
• Excellent response to steroid treatment
Summary

- Autoimmune Pancreatitis is the most common manifestation of IgG4 related disease
- ~1 in 3 patients can have bile duct involvement
- Disease relapse often is seen in these patients and can require medications to suppress the immune system
- A subset of patients with PSC have elevations in serum IgG4 levels – signifies more aggressive disease