Hépatopathies auto-immunes

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Autoimmune Liver Diseases

- Autoimmune hepatitis
- Primary biliary cholangitis
- Primary sclerosing cholangitis
- Overlap syndromes
- IgG4-associated cholangitis

Autoimmune Hepatitis

- Prevalence 15-25/100'000
- $\varphi : \varphi = 3 : 1$
- Clinical manifestations highly variable (asymptomatic - acute liver failure - chronic hepatitis - cirrhosis)
- May be associated with other auto-immune diseases
- Overlap syndromes (AIH-PBC, AIH-PSC)


Autoimmune Hepatitis

Diagnosis

- Exclusion of other liver diseases
- Autoantibodies
  - ANA, SMA (anti-actin) Type 1
  - anti-LKM1 Type 2
  - Others: SLA/LP, anti-LC1
- $\gamma$-globulins (IgG) ↑
- Liver biopsy
- Response to treatment

Autoimmune Hepatitis

Simplified Diagnostic Criteria

<table>
<thead>
<tr>
<th>Points</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 points</td>
<td>Probable AIH (sens. 88%, spec. 97%)</td>
</tr>
<tr>
<td>≥ 7 points</td>
<td>Definite AIH (sens. 81%, spec. 99%)</td>
</tr>
</tbody>
</table>

Autoimmune Hepatitis

Treatment

- Prednisolone 0.5-1 mg/kg/d
  - reduction to 10 mg/d by 10-12 wks
  - and to 5 mg/d by 6 months
  - if possible, withdrawal by 1 year
- Azathioprine 50 mg/d → 1-2 mg/kg/d
- Goal: complete remission
  (ALT, IgG, histology)
- Duration at least 3 years

Alternative treatment options
- Budesonide (only in non-cirrhotic pts)
- Intolerance to azathioprine: MMF
- Insufficient response: i.v. corticosteroids, CsA, tacrolimus, infliximab, ...
- Regular follow-up and treatment adherence are essential

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Primary Biliary Cholangitis

- F.k.a. primary biliary cirrhosis
- Autoimmune disease with progressive destruction of small bile ducts
- Prevalence 2-40/100'000
- ♀ : ♂ = 9 : 1, peak age 40-60 years
- May be associated with other autoimmune diseases (Sjögren's syndrome, thyroiditis, celiac disease, RA, ...)
Primary Biliary Cholangitis

Clinical Manifestations
- Initially asymptomatic (AP ↑, γ-GT ↑)
- Pruritus
- Fatigue
- Jaundice represents a late manifestation
- Xanthomas, osteopenia / osteoporosis, ...
- Complications of cirrhosis

Primary Biliary Cholangitis

Diagnosis
- Alkaline phosphatase ↑, γ-GT ↑
- Antimitochondrial antibodies (AMA) (anti-M2 = E2 subunit of pyruvate dehydrogenase complex)
  Sensitivity and specificity > 95%
- IgM ↑
- Liver biopsy (not mandatory)

Primary Biliary Cholangitis

Histological Stages

Ludwig's classification

Primary Biliary Cholangitis

Management
- Ursodeoxycholic acid 13-15 mg/kg/d
- Second line: obeticholic acid 5 → 10 mg/d
- Treatment of pruritus
  (cholestyramine, rifampicin, naltrexone, sertraline, phototherapy, ...)
- Prevention / therapy of osteoporosis
- Liver transplantation
- Investigational: fibrates, ...

Autoimmune Liver Diseases
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Primary Sclerosing Cholangitis

- Chronic fibrosing inflammatory process of medium- and/or large-size, intra- and/or extrahepatic bile ducts
- Prevalence 5-10/100,000
- $\varphi : \Omega = 2 : 1$, median age at diag. 40 yrs
- 80% associated with IBD (UC > CD)


Clinical Manifestations

- Initially asymptomatic (AP ↑, γ-GT ↑)
- Pruritus, pain, fatigue, jaundice
- Complications:
  - bacterial cholangitis
  - cholangiocarcinoma (1.5% per year)
  - complications of chronic cholestasis
  - complications of cirrhosis
  - colorectal cancer

Diagnosis

- Alkaline phosphatase ↑, γ-GT ↑
- MRCP
- "Atypical" pANCA pos. in 50-80% but not sufficiently specific
- Evtl. ERCP (antibiotic prophylaxis!)
- Evtl. liver biopsy (staging)
- Colonoscopy
**Primary Sclerosing Cholangitis Management**

- Ursodeoxycholic acid 13-15 mg/kg/d (?)
- Endoscopic dilation of dominant stenoses
- Treatment of pruritus
- Prevention / therapy of osteoporosis
- CCA and CRC surveillance
- Liver transplantation

**DD PSC-PBC**

<table>
<thead>
<tr>
<th>PSC</th>
<th>PBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Medium and large BD</td>
<td>- Small bile ducts</td>
</tr>
<tr>
<td>- ♂ &gt; ♀</td>
<td>- ♂ &gt; ♀</td>
</tr>
<tr>
<td>- ~ 40 years</td>
<td>- 40-60 years</td>
</tr>
<tr>
<td>- Association with IBD</td>
<td>- No association with IBD</td>
</tr>
<tr>
<td>- MRCP</td>
<td>- AMA (M2)</td>
</tr>
<tr>
<td>- Recurrent bacterial cholangitis</td>
<td>- Progressive cholestasis, pruritus</td>
</tr>
<tr>
<td>- Cholangiocarcinoma</td>
<td>- No cholangiocarcinoma</td>
</tr>
<tr>
<td>- UDCA 13-15 mg/kg/d ?</td>
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**Overlap Syndromes**

- PBC
- AIH
- PSC

**IgG4-Associated Cholangitis**

- Steroid-responsive sclerosing cholangitis
- ♂ > ♀, median age ~ 60 years
- Associated with autoimmune pancreatitis and diverse fibrosing conditions
- Often presents with obstructive jaundice; no association with IBD and CCA
- Serum IgG4 ↑
- IgG4-positive plasma cells
- Corticosteroids, evtl. azathioprine

Boberg KM et al. on behalf of the IAIHG. J Hepatol 2011;54:374-385.
Take Home Messages

- Consider autoimmune liver disease in the differential diagnosis of elevated LFTs
  - ANA, AMA, SMA, IgG
  - MRCP
- Regular follow-up and treatment adherence are crucial
- Collaboration between GP and specialist
- Progress in the understanding of the pathogenesis and management to be expected