	Autoimmune hepatitis	Hepatitis B or C associated
Proportion of all cases of CAH in the UK*	50–80%	20–50%
Sex	Female > male (6 : 1)	Male > female (9 : 1)
Age at onset	10–30 years 40–60 years	Elderly
Associated autoimmune disease	Common	Rare
Smooth-muscle antibodies	Positive 70% High titre	Low titre or absent
Antinuclear antibodies	Positive in 80%	Negative
Anti-DNA antibodies	May be positive	Negative
Antimitochondrial antibodies	Positive 25%	Negative
Antibodies to liver and kidney microsomes	Positive 4% (especially children)	Negative
Serum immunoglobulins	IgG ↑↑	Normal or IgG ↑
HLA type	HLA-B8, -DR3	?
Response to steroids	Good	?
Risk of hepatoma	Low	High

Lecture No. 9

Primary Biliary Cirrhosis

Primary biliary cirrhosis (PBC) is an autoimmune disease of the liver that results in chronic injury to the intrahepatic bile duct epithelium. The gradual inflammatory destruction of the bile ducts causes cholestasis with the subsequent retention of toxins, inciting further hepatic injury and resulting in fibrosis, cirrhosis, and eventual liver failure. It is most common in women over the age of 50. The ratio of affected women to men has been reported to be as high as 9:1.

Causes

The cause of the disease is unknown, but research indicates that there is immunological basis for the disease, making it an autoimmune disorder. Most of the patients (>90%)seem to have anti-mitochondria antibodies (AMAs) against pyruvate dehydrogenase complex (PDC-E2), an enzyme complex that is found in the inner mitochondria membrane. Molecular mimicry is the most widely proposed explanation as to the induction of autoimmunity in PBC. Briefly, a host is infected with a microorganism that contains antigens similar to antigens present in the host. These microbial antigens induce an immunologic response when presented to the immune system of the host. As a result, what began as a pathogen-specific response then cross-reacts with the host antigens and results in tissue injury and disease.

The predisposing role of the HLA system to the disease has not been fully clarified, although a weak but significant association with HLA-DR8 has been reported.

The pathogensis of the bile duct damage in PBS is unclear. Bile ducts in PBS patients express increased densities of adhesion molecules, MHC classII antigens, IL-2 and pyruvate dehydrogenase compared with normal ducts, and so represent potential targets for the infiltrating activated T cells ($CD4^+$ and $CD8^+$).

Symptoms

The most common presenting symptoms include pruritis and fatigue. Jaundice, darkening of the skin in exposed areas and manifestations resulting from impaired bile excretion follow.latter range from steatorhoea to impaired absorption of lipid soluble vitamins , leading to osteomalacia (from vitamin D malabsorption), bruising (vitamin K) and occasionally night blindness (vitamin A).

Diagnosis

The diagnostic criteria for PBC include an elevation in liver enzymes (most notably alkaline phosphatase) for a duration of six or more months, histologic findings, and the presence of antimitochondrial antibodies in the serum. The presence of two criteria is highly suggestive of the disease while a definite diagnosis requires all three.

Involvement of the liver is heterogeneous, so a biopsy may demonstrate different stages of disease

- Stage I is characterized by portal inflammation comprised of predominantly lymphoplasmacytic infiltrates. The pathognomonic lesion of PBC, the florid duct lesion, represents focal duct obliteration by granuloma formation.
- Stage II there is extension of inflammation to theperiportal areas.
- Stage III. There is formation of fibrous septa that link adjacent portal triads and bile duct loss (ductopenia).
- Stage IV is defined by frank cirrhosis.

Primary Sclerosing Cholangitis

Primary Sclerosing Cholangitis(PSC) is a chronic liver disease that is characterized by chronic inflammation and fibrosis leading to narrowing and dilatation of the intrahepatic or extrahepatic bile duct, or both.

PSC typically presents in the fourth to fifth decades of life. Men are affected more often than women.

Although the exact cause of PSC is unknown, it is considered autoimmune due to the presence of autoantibodies.The condition is associated in the majority of cases with chronic inflammatory bowel disease, particularly ulcerative colitis.

Patient may present with clinical, biochemical, immunological and histological features indistinguishable from those of type I autoimmune hepatitis, though they have more frequently an atypical peri-nuclear anti-neutrophil cytoplasmic antibody. This pANCA is atypical in that its target antigen appears to be nuclear and not cytoplasmic.

The correct diagnosis can be made only by demonstrating the characteristic bile duct abnormalities by specialized imaging such as endoscopic retrograde cholangio-pancreatography or magnetic resonance cholangiography.

Lecture No. 10-11

Renal diseases

Many renal diseases have underlying immunological mechanisms. Antibody-mediated effects are primarily involved, whereas cellular mechanisms are less important. Immunological diseases of the kidney mainly affect the glomerulus, which is most likely due to its filter function. Circulating antibody-mediated renal diseases are induced in three mechanisms, circulating performed immune complexes accumulate subendothelially on the capillary aspect of the basement membrane, alternatively antibodies may react in situ with the glomerular basement membrane or with antigens of the visceral epithelial cells.

Antibody deposits can cause direct damage to epithelial or endothelial cells of glomerulus due to complement activation and pore formation. On the other hand, the antibodies can also bind to the FC receptors of monocytes, macrophages, granulocytes and platelets. This leads to the activation, or in the case of platelets aggregation of the cells. The glomerular damage can cause two distinct symptom complexes: the nephrotic syndrome and the nephritis syndrome.

Differentiation Between Nephrotic Syndrome and Nephritic Syndrome

Typical Features	Nephrotic	Nephritic
Onset	Insidious	Abrupt
Edema	++++	++
Blood pressure	Normal	Raised
Jugular venous pressure	Normal/low	Raised
Proteinuria	++++	++
Hematuria	May/may not occur	+++
Red blood cell casts	Absent	Present
Serum albumin	Low	Normal/slightly reduced