Sclerosing cholangiitis

Sclerosing cholangitis is a chronic inflammatory disease of the intrahepatic and extrahepatic bile ducts with gradual fibrotization and stenotization of the bile ducts. It is a progressive disease, usually leading to liver cirrhosis and liver failure. Sclerosing cholangitis is divided into two basic groups:

- **primary** – there is no obvious cause,
- **secondary** – an obvious cause is evident.

Primary sclerosing cholangitis

Primary sclerosing cholangitis is a slowly progressive disease of unknown etiology, usually leading to liver cirrhosis and portal hypertension after 10 to 15 years. The first description dates back to 1924, originally it was considered extremely rare, but apparently it is more common.

The incidence varies from 0.41 to 16.1 per 100,000 inhabitants per year, depending on the location and also according to the study. The disease usually begins between the ages of 30 and 40, and men are more often affected. Primary sclerosing cholangitis is strongly associated with non-specific intestinal inflammation, approximately 30-80% of patients with primary sclerosing cholangitis suffer from non-specific intestinal inflammation, usually ulcerative colitis. Associations with non-specific intestinal inflammation vary quite dramatically geographically. In northern European countries it reaches values of up to 80%, while in southern European and Asian countries the association can drop to 30%. Interestingly, smoking is a protective factor.

Clinical manifestations

Common manifestations at the time of diagnosis are (frequencies vary in different studies):

- asymptomatic disease: 15-44% of cases
- fatigue: 43-75% of cases
- pruritus: 25-59% of cases
- Jaundice: 30-69% of cases
- hepatomegaly: 34-62% of cases
- abdominal pain: 16-37% of cases
- splenomegaly: 14-30% of cases
- hyperpigmentation: 25% of cases
- weight loss: 10-34% of cases
- variceal bleeding: 2-14% of cases
- ascites: 2-10% of cases

Diagnosis

In the serum, alkaline phosphatase (ALP) is usually elevated three to ten times the upper limit, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are usually increased two to three times. More than half of patients have normal bilirubin. More than half of the patients have a higher IgG value, the level is roughly 1.5 times the upper limit. Liver test values may be normal during the course of the disease.

Autoantibodies are often demonstrable in primary sclerosing cholangitis. The most common are ANCA, ANA, antibodies against smooth muscle, antibodies against endothelial cells, antibodies against cardiolipin, antibodies against thyroperoxidase and rheumatoid factor. The IgG4 fraction may be increased.

The gold diagnostic standard is cholangiography, which shows a segmental stricture of the bile ducts with proximal dilatation to saccation. Virtually all intrahepatic bile ducts are affected. An alternative is magnetic resonance cholangiography.

Biopsy and subsequent histopathological diagnosis is not necessary for establishing the diagnosis if there is a clear radiological finding. However, it can help rule out other causes. Histological findings in the case of primary sclerosing cholangitis will show ductal proliferation, periductal inflammatory infiltration and ductal obliteration; a characteristic sign is periductal fibrosis layered around the duct like the skin of an onion, but this finding can only be detected in approximately 15% of biopsies and therefore its absence definitely does not rule out the diagnosis.

Therapy

Primary sclerosing cholangitis cannot be influenced in its course by conservative therapy. The conclusions of the study with ursodeoxycholic acid in a dose of 13–30 mg/kg/day are contradictory, most likely this therapy is without effect. In the final stage, the patient is indicated for a liver transplant.

Subtypes

Primary sclerosing cholangitis can have three possible subtypes:

- **Primary sclerosing cholangitis of the small ducts:** Mainly the small ducts are affected, so the radiographic findings are practically normal. The disease is proven histologically. The disease sometimes also leads to a disorder of the large ducts. The disease appears to progress more slowly than typical
- **Overlap syndrome with autoimmune hepatitis:** Patients have radiological signs of primary sclerosing cholangitis and biochemical and histological signs of autoimmune hepatitis. In this group, the course of the disease can possibly be influenced by immunosuppressive therapy.
- **IgG4-associated primary sclerosing cholangitis:** This is a relatively newly described group with disease response to corticoid therapy. This form of primary sclerosing cholangitis is often associated with autoimmune pancreatitis. The radiological picture is similar to conventional primary sclerosing cholangitis. Because it is a conservative therapy-responsive and potentially reversible disorder, differentiation from conventional primary sclerosing cholangitis is extremely important.

Secondary sclerosing cholangitis

Secondary sclerosing cholangitis develops as a consequence of a known pathological process. The initial manifestations are not dramatic, usually only an increase in the values of liver tests. As the disease progresses, other symptoms such as pruritus, icterus and abdominal discomfort in the right upper quadrant begin to appear. Ascending bacterial infections of the biliary tract are relatively common. The radiological findings are similar to primary sclerosing cholangitis, but an ultrasound examination may point to a possible cause. The frequency of the disease is unknown, the reported incidence is very low, but underdiagnosis is likely. The progression of secondary sclerosing cholangitis appears to be somewhat faster compared to primary sclerosing cholangitis.

The pathogenetic basis of secondary sclerosing cholangitis is induction of cholangiocyte proliferation, disturbance of periductal circulation, alteration of transport and secretory functions of epithelial cells and fibroproduction.

Causes

There are many primary disorders responsible for secondary sclerosing cholangitis, they can be divided into several groups:

- **Chronic obstruction:** cholelithiasis, cholecystitis, inflammatory polyp, tumor, pancreatic disease, aneurysm of adjacent arteries, bile duct stricture after transplantation or surgery. The immediate cause is most likely recurrent suppurative cholangitis.
- **Infection:** Parasitic infection in immunocompromised patients incl. patients with AIDS (e.g. cryptosporidiosis). The immediate cause is probably chronic inflammation.
- **Effects of toxic substances:** Usually iatrogenic instillation of alcohol or formaldehyde with direct damage to the ducts.
- **Immune disorders:** Autoimmune disorders localized to the biliary tract. eg IgG4-associated sclerosing cholangitis is classified by some authors as a subtype of primary sclerosing cholangitis.
- **Ischemic cholangiopathy:** Impaired blood supply, e.g. in post-transplantation thrombosis, graft rejection, systemic vasculitis or arterial wall damage during intra-arterial administration of chemotherapy.
- **Secondary sclerosing cholangitis of critically ill patients:** A relatively new entity, it affects patients who have been rescued from critical condition by aggressive intensive therapy. It is mainly described in patients who have experienced extensive trauma, burns or extensive surgery for internal indications. These patients were originally without pre-existing primary sclerosing cholangitis and without a known background for secondary sclerosing cholangitis. The cause is unknown, e.g. ischemic or toxic damage is considered in patients with genetically determined higher sensitivity. The disease progresses very quickly.

Therapy

Therapeutic options are also limited in secondary sclerosing cholangitis.

Links

related articles

- Primary sclerosing cholangitis
- Secondary sclerosing cholangitis
- Autoimmune sclerosing cholangitis

References

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