ISCHEMIC CHOLANGITIS

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Keywords: ischemic cholangitis, cholestasis, jaundice *Abstract:* Biliary ducts present a high tendency to be affected by ischemia, due to the morphofunctional particularities of the blood pressure at this level. The ethiology of ischemic cholangitis is various, being represented by medical causes and by postsurgery conditions. Clinical subjective symptoms are nonspecific and scarce. Laboratory tests add up to the cholestasis and jaundice syndroms aspect. The diagnosis is confirmed by endoscopic cholangiography. Treatment resides in antibiotic theraphy, endoscopic interventional cure and in case of failure of these methods, liver transplantation.

Cuvinte cheie: colangită ischemică, colestază, icter **Rezumat:** Căile biliare prezintă o susceptibilitate ridicată de a fi antrenate în suferință în condiții de ischemie, datorită particularităților morfofuncționale ale circulației arteriale de la acest nivel. Etiologia colangitei ischemice este variată, fiind reprezentată de cauze medicale și de stări post intervenții chirurgicale. Manifestările clinice, subiective sunt nespecifice și sărace. Examinările biologice întregesc tabloul sindroamelor de colestază și icteric. Diagnosticul este confirmat de colangiografia endoscopică. Tratamentul constă în terapia antiinfecțioasă, cura intervențională endoscopică și, în caz de eșec al acestor metode, transplantul hepatic.

INTRODUCTION

Ischemic hepatitis, a probably underdiagnosed entity has been lately observed. Biliary ducts can also be affected in case of ischemia. Ischemic cholangitis generally has a more severe evolution and a more reserved diagnosis. The explanation resides in the particularities of the biliary system and the reduced regeneration capacity of the cholangiocytes.

The term ischemic cholangitis is used as a common label for all ischemia induced bile duct lesions (1).

As compared to hepatocytes which are capable of regeneration, when we refer to biliary duct cholangiocytes this capacity is far more reduced, being dependent on the persistence of a microcirculation in vasa vasorum.

Cholangiocytes are epithelial cells with a polarised growth, which line the lumen of the intra- and extrahepatic biliary ducts. They substantially contribute to the production and modification of the biliary flow. In the Canals of Hering proliferated hepatic stem cells have been emphasised which indicate adhesive molecules significant for the differentiation of adult cells (hepatocyte, cholangiocyte). Biliary epithelia actively participate to the formation of the bile. This ductular bile modifies the biliary flow excreted by hepatocytes. It is supposed that dysfunctions in the production of ductular bile contribute to the determinism of cholestatic biliary diseases (2, 3, 4, 5).

Due to the susceptibility of cholangiocytes to various aggressions, ischemic cholangitis and types of cholangitis determined by systemic septic disorders often develop severe progressive morphological lesions. In the case of ischemic cholangitis, the presence of bacterial cholangiocytes that generate other disorders is common (6).

ETHIOLOGY

The ethiology of ischemic cholangitis is various; some causes undergo evaluation (7, 8). K.P. Batts defines 3 categories

of ethiological conditions associated with biliary ischemia:

- definite causes (states of shock, massive haemorrhage, hepatic artery thrombosis following transplantation, lesions after hepatic intraarterial chemotherapy, vasculitis);
- probable causes (anastomotic strictures or posttransplantation ductopenia, ABO blood incompatibility associated to chronic rejection);
- possible causes (primary sclerosing cholangitis, paroxysmal nocturnal hemoglobinuria, extrahepatic portal vein obstruction, autoimmune hepatitis) (1).

The frequency of ischemic cholangitis is rising, due to the greater number of liver transplantation (9,10).

VASCULARISATION

Arterial vascularisation of the biliary system

Extrahepatic biliary ducts and a small part of the major intrahepatic biliary ducts depend on arterial vascularisation. The blood flow of the biliary system is produced by artery branches:

- hepatic,
- · retroduodenal,
- gastroduodenal,
- retroportal.

The vascularisation of the extrahepatic biliary system is classified into:

- biliary,
- supraduodenal,
- retropancreatic.

The common supraduodenal biliary duct has the poorest vascularisation. The right and left hepatic canals as well as the intrahepatic biliary ducts have a rich non-axial network of thin arteries. At a microscopic level, the vascularisation of the biliary epithelium is assured by a vascular plexus made up of arterioles, venules and capillaries, situated in the peribiliary branch (1).

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PATHOGENESIS

The pathogenetic mechanisms involved in ischemic cholangitis are complex, as related to ethiology. Subsequent to hepatic transplantion, ischemic cholangitis is determined by hepatic artery thrombosis, stenosis and occlusions of the parabiliary arteries through fibrointimal proliferation (probably post thrombosis) (11). The obstruction of the large arteries is rapidly compensated through the opening of the collateral intrahepatic arteries or transcapsular, thus avoiding ischemic aggression. However, ischemic ductular lesions become possible when the small hepatic arteries or the peribilary vascular plexus are affected, or in case of the interruption of any arterial blood flow, as it happens in case of liver transplantation with hepatic arterial thrombosis (7, 12, 13). Vasculitis (polyarteritis nodosa, giant cell arteritis, leukocytoclastic vasculitis) are rarer causes of ischemic cholangitis produced through vascular inflammation (13). The presence of biliary casts was underlined at patients with severe condition, assisted by intensive-care services, with respiratory failure (mechanically ventilated) and who needed catecholamine for hemodynamic stabilization. These elements obstruct the biliary ducts and are associated with ulcerations of the biliary epithelium and hemorrhagic exudates. The infections with multiresistant germs are favoured, the process ending with a sclerosing cholangitis (8, 14).

The biochemical bile test at patients suffering from hepatic post-trasplantation ischemic cholangitis showed a high level of phospholipids and cholesterol (15).

MORPHOPATHOLOGY

From a morphological point of view, ischemic cholangitis presents: biliary strictures, cholangiectases, the distruction of intrahepatic billiary ducts. Histological examinations frequently show atrophies and erosions of the biliary epithelium from the large biliary duct which regards a part of their whole circumference. At the level of the small biliary ducts epithelial atrophy and ductopenia appears. Biliary casts often appear and a microscopic aspect similar to primary sclerosing cholangitis (8,13).

Morphological manifestations of the arteries correlate with ethology: thrombotic occlusions, vasculitic lesions, foam cell arteriopathy, associated with chronical rejection. The histology of intramural capillaries, little researched, has emphasized in some cases the decrease of their number.

CLINICAL MANIFESTATIONS

Identifying ischemic cholangitis is difficult, because the clinical picture often develops after a period lasting weeks or months from the triggering event. The clinical presentation of patients with ischemic cholangitis is generally non-specific, comprising abdominal pain and fever. The picture of intrahepatic and obstructive cholestasis and jaundice syndromes is achieved (7). Accordingly, pathological values of cholestasis enzymes are observed (serum alkaline phosphatase, Y –GT) and bilirubin respectively.

Additionaly, during evolution a secondary infection of the biliary system, ascending cholangitis and cholangitic abcesses may arise.

Suppurative cholangitis may turn into multiple organ dysfunctions. (11,13).

ENDOSCOPIC CHOLANGIOGRAPHY

Endoscopic cholangiography may indicate primary sclerosing cholangitis or biliary duct carcinoma. The dominant aspect is shown by inflammatory strictures.

The early images are offered by intrahepatic biliary casts (exudative obstructive elements, probably determined by bacterial or fungal infections as well as biliary duct necroses.

Cholangiectases follow and sometimes large lobular cystic dilatations (8).

IMAGING

Imaging (ultrasound, CT scan, MRI and digital substraction angiography) may emphasize progressive hepatic atrophy inside the biliary lesions.

PROGNOSIS

The prognosis of ischemic cholangitis is often severe, even in the circumstances of adequate treatment. In 40% of cases cirrhosis of the liver rapidly develops. The main cause of death is secondary fulminant septicemia and hepatic insufficiency (6).

TREATMENT

The therapeutic strategy includes antibiotic treatment and endoscopic interventional cure.

Endoscopic treatment includes removal of the occlusive material, dilatation of stenoses and intermittent stent bridges or percutaneous transhepatic cholangiography.

When biliary drainage or reconstruction is not possible, liver transplantation is recommended (7, 8, 13).

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