Cytological Analysis of Choledochal Mucosa in Acute Cholangitis in Patients with Mechanical Jaundice

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Changes in bile ducts in cholestasis are characterized by activation of proliferation and hypertrophy of cholangiocytes and degenerative and necrobiotic changes in ductal epithelium. Long-term cholestasis led to massive necrosis of cholangiocytes. Inflammatory changes in the choledochal mucosa were most pronounced in patients with choledocholithiasis.

Key Words: *cytology; cholangiocytes; cholestasis; cholangitis*

Cholestasis is a severe complication of bile duct diseases. It results from obstruction of extrahepatic bile ducts. Bile duct obstruction is often associated with acute cholangitis, the most severe complication of bile duct pathologies. Mechanical jaundice is associated with purulent cholangitis in 20-30% cases, the postoperative mortality of this category of patients is 15-45% [1,2].

Histologically cholestasis is characterized by accumulation of bile components in the liver parenchyma and reactive changes, which are most pronounced in extrahepatic cholestasis. This can be explained by the combined alterating effects of increasing hydrostatic pressure of the bile on epithelial lining of terminal bile ducts and by damage to epitheliocytes caused by bile components and bacterial toxins present in the bile in case of infection [5].

Changes in ductal epithelium during cholestasis are characterized by proliferation and hypertrophy of cholangiocyte and degenerative and necrobiotic processes in ductal epitheliocytes due to disturbances in water metabolism. Cholangiocytes are sharply enlarged, hyperplasia of the endoplasmic reticulum and free ribosomes and hyperplasia and hypertrophy of mitochondria are seen in their cytoplasm. The presence of light vesicles diffusely spread in the cytoplasm and hyperplasia of the Golgi complex indicated changes in water metabolism. The cells lose microvilli, the remaining microvilli are edematous. Electron microscopy reveals hypertrophy of typical cells; however there are also initial signs of dehydration. Long-term (more than 2-3 weeks) cholestasis leads to massive necrosis of cholangiocytes, they undergo karyopyknosis and karyolysis [3,4].

We analyzed changes of choledochal mucosa in cholestasis of different etiology and their dynamics in the early postoperative period.

MATERIALS AND METHODS

Patients with mechanical jaundice of different origin were included in the study (n=51). In 32 patients cholestasis was caused by choledocholithiasis (group 1) and in 3 patients choledocholithiasis was associated with stenosis of the major duodenal papilla (MDP; group 2). In 12 patients mechanical jaundice was associated with clinical laboratory and endoscopic manifestations of acute cholangitis without signs of pronounced suppurative inflammation of the choledochal mucosa (n=4; group 3) and with signs of such inflammation (n=8; group 4). In 8 patients mechanical jaundice was caused by isolated stenosis of the terminal portion of the choledoch and in 8 by MDP stenosis and stenosing papillitis (group 5). Blastomatous chole-

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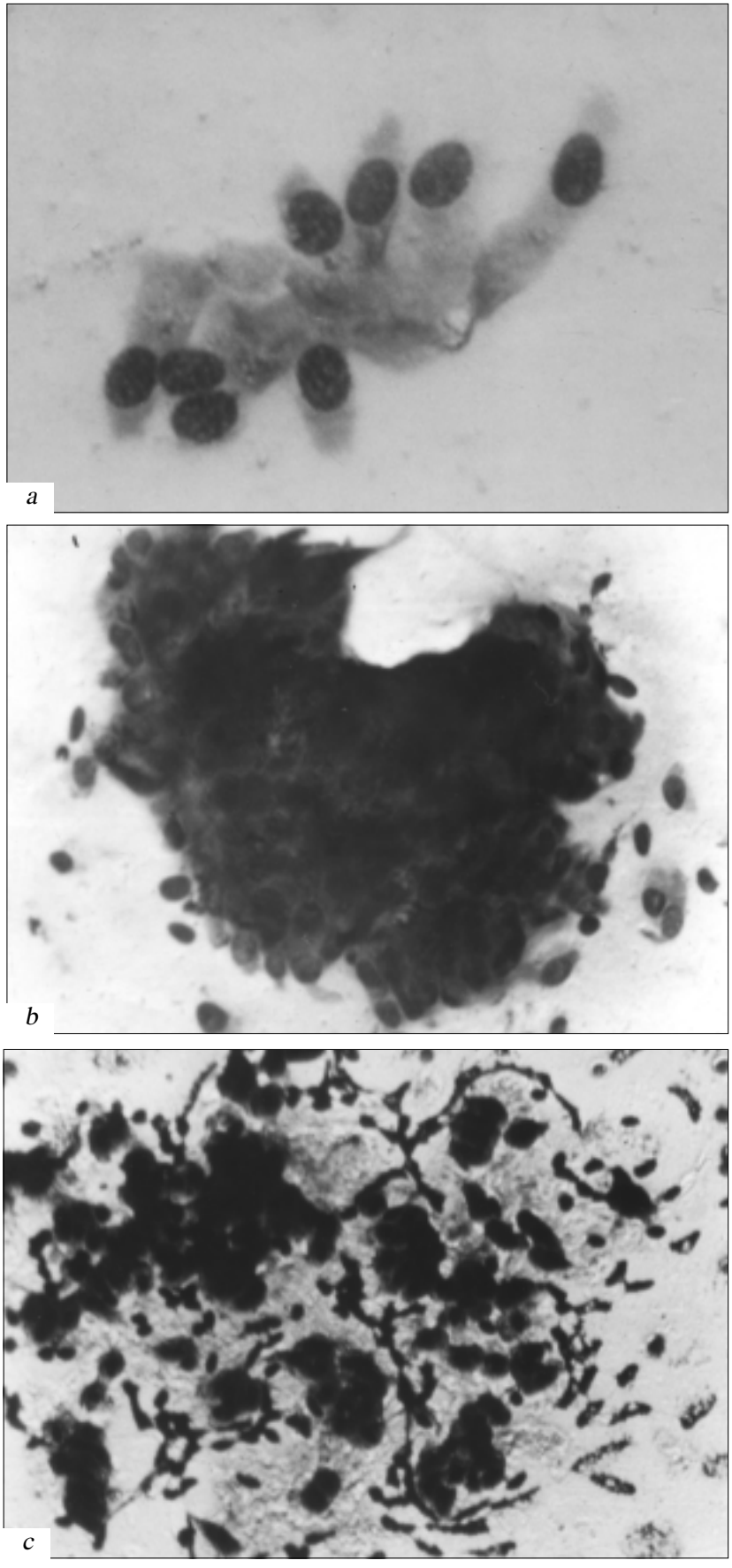

Fig. 1. Morphological picture of the common bile duct in patients with mechanical jaundice. Romanowskii—Giemsa staining, ×400 (*a*,*c*), ×200 (*b*). *a*) degenerative and necrotic changes in epitheliocytes (type A); *b*) massive desquamation and solitary epithelial cells with degenerative and necrotic changes (type B); *c*) desquamation (type C).

TABLE 1. Cytological Changes in the Choledochal Mucosa after Treatment

Group	Type of changes in the choledochal epitheliocytes	
	before treatment	after treatment
1	Type B changes	Type C changes (*n*=3); type B changes with decreased number of desquamation layers (*n*=1)
2	Type B changes	Type B changes (*n*=2)
3	Type B changes	Type C changes (*n*=1)
4	Type B changes	Type C changes (*n*=1); type B changes with decreased number of desquamation layers (*n*=2)
5	Type B changes	Type B changes with decreased number of desquamation layers (*n*=1)
6	Type B changes	Type C changes (*n*=1)

dochal strictures were detected in 3 patients (group 6). Biochemical tests of the blood on admission showed bilirubinemia (38.3-347.7 mmol/liter) in all patients. At the moment of endoscopic retrograde cholangiopancreaticography the level of total blood bilirubin was 38.8-298.7 mmol/liter due to bound fraction.

Choledochal mucosa for cytological analysis was collected during and after endoscopic intervention with a special cytological brush opening into the choledochus. The cells were transferred onto slides, dried, fixed with methanol, and stained by the method of Romanowskii—Giemsa.

RESULTS

The changes in choledochal mucosa revealed by cytological methods can be divided into 3 types. Type A were dystrophic and necrotic changes in epitheliocytes (Fig. 1, *a*) and the presence of numerous polymorphonuclear leukocytes. Type B changes were necrotic changes and desquamation of epithelial cells (Fig. 1, *b*). The samples presented by massive layers of desquamated epithelium were referred to type C (Fig. 1, *c*). The incidence of these changes depended on the cause of cholestasis (Fig. 2).

Inflammatory changes in the common bile duct mucosa were the most pronounced in patients with choledocholithiasis associated with clinical, laboratory, and endoscopic signs of acute cholangitis (Fig. 2). Differences in the cytological picture were determined by the presence of choledocholithiasis (foreign body in the choledochal lumen) inducing (apart from cholestasis) inflammatory degenerative process in the choledochal mucosa.

Cytological study of the choledochal mucosa was repeated after endoscopic decompression of bile ducts, local and systemic treatment of acute cholangitis in 12 patients (7-10 days after the first endoscopy).

Aggravation of inflammation in the common bile duct during the early postoperative period was observed in 6 (60%) patients (Table 1). This can be explained by two factors. First, damaged epitheliocytes die (which is confirmed by control cytological analysis) and second, pronounced edema of the mucosa at the site of endoscopic papillosphyncterotomy aggravates inflammation.

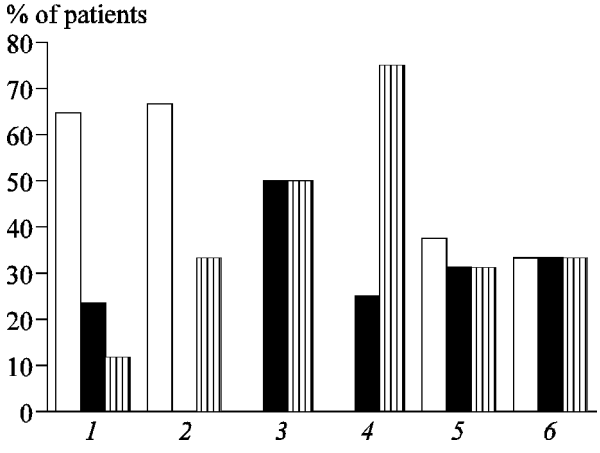

Fig. 2. Cytological changes in the choledochal mucosa in patients with mechanical jaundice. Light bars: type A changes; dark bars: type B changes; cross-hatched bars: type C changes. *1-3*) patients with choledocholithiasis without visual signs of acute cholangitis, in combination with MDP stenosis without visual signs of acute cholangitis, and with visual signs of acute cholangitis, respectively; *4*) patients with choledocholithiasis concomitant with clinical and visual signs of purulent cholangitis; *5*) patients with MDP stenosis and stenosis of the terminal portion of the choledoch; *6*) patients with blastomatous choledochal strictures.

In our opinion, cytological analysis of the choledochal mucosa in various bile duct diseases can be included in the diagnostic complex for verification of acute cholangitis, particularly at subclinical stages of the process. This method will help to determine the severity of inflammatory reaction of the bile duct mucosa and to start rational therapy at the early stages of the disease. This will improve the results of treatment by decreasing the incidence of complications of acute cholangitis.

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