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Features of Liver and Pancreas Pathomorphological Pattern in Case of their Combined Alcohol-Induced Injury

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Abstract.

The level of alcohol consumption has significantly increased in recent years. Liver and pancreas are both directly and indirectly affected by its negative impact. Fibrosis-producing cells (stellate cells) are activated in these organs leading to cirrhosis and fibrotic changes in the pancreas.

The objective of the research was to study the features of morphologic changes in the liver and pancreas in case of their combined alcohol-induced injury. Multiple clinical anatomicopathological and morphological investigation of liver and pancreas was conducted using autopsied specimen. Alcohol-induced cirrhosis is micronodular manifesting in degenerative changes of hepatocytes, capillarization of the sinusoids and significant stage of fibrosis. Atrophic changes in acini, necrosis of exocrine pancreatic cells, enlargement of stromal and peryductal components by means of neoplasms and proliferation of connective tissue were found in pancreas in cases of the alcohol induced disorder. There were also presented signs of chronic inflammation of the excretory pancreatic ducts wall. Fibrosis was established to be more severe and the number of stellate cells was significantly higher in the case of combined alcohol induced pathology. Areas of hepatocytes necrosis were wider in liver, Mallory bodies in hepatocytes were larger and more numerous. Sclerogenic hyaloid necrosis, severe fibrosis with steatotic injury of hepatocytes in portal areas of the lobule was detected in two-thirds of deceased. Acini of the pancreas were deformated, metaplasia of exocrine pancreas cells, proliferation of epithelial cells in the ducts and accumulation of thick secret in duct's lumen were observed. Thus, it can be concluded, that morphological changes in the liver and pancreas in case of comorbidity are more severe than in case of separate diseases and therefore combined injury require individualized approach to their correction and further studies.

Keywords: alcohol induced cirrhosis, chronic alcohol induced pancreatitis, fibrosis, Mallory bodies.

Problem statement and analysis of the resent research

Alcohol consumption in the past 20 years continues to be high and depends on different factors. First of all, toxic liver damage is a result of alcohol effect as it is liver where alcohol metabolism occurs [13]. Increasingly, alcoholic hepatitis is transforming into cirrhosis and combined with pathological changes in other organs, including the pancreas [14]. Disorders of redox potential with following necrosis in the cells of these organs occur at the same time, fibrosis producing cells (stellate cells primarily) are activating leading to cirrhosis and fibrotic changes in the pancreas.

Histopathological changes in the liver in case of its separate alcoholic injury are studied rather thoroughly. [9] Stellate cells [2], fibroblasts and their transformation into myofibroblasts [11] are activating, peryacinal, intralobular and periductal fibrosis is progressing in case of alcohol-induced pancreas injury [7,13].

At the same time combined toxic effects of alcohol on the pancreas and the liver require researchers' attention in order to clarify diagnosis and select appropriate corrective therapy [12].

The objective of the research was to study the peculiarities of morphological changes of the liver and pancreas in case of their combined alcohol-induced injury.

Materials and methods of the research

Complex clinical, pathomorphological and autopsy study of liver and pancreas (22 cases) was conducted. 7 patients were diagnosed with alcoholic cirrhosis within their life, alcoholic pancreatitis was diagnosed in 6 patients, combined disease was diagnosed in 9 patients. Sections of organs were fixed in 10% buffered formalin solution, poured with paraffin, stained with haematoxylin and eosin and by Van-Gieson's stain. Pathologic diagnosis confirmed the clinical diagnosis.

Results of the research and their discussion

The left lobe of liver was hypertrophied and had tuberous surface in most patients with alcoholic cirrhosis. Liver architectonic was abnormal. Inflammatory changes were characterized by mild intralobular lymphocytic infiltration. Small nodules 1.0 - 3.0 - 4.0 mm in size were found in parenchyma. Hepatocytes in a state of ballooning and adipose degeneration were found in small nodules; however, steatosis signs were less severe in bigger nodes. Dystrophic changes were in varying degrees in hepatocytes. One and the same patient could have small and large vacuole dystrophy of hepatocytes, focal necrosis. Hepatocytes were tightly located and had a significant number of Mallory cells inside. Deformed sinusoids with areas of dilatation and constriction to almost complete overlap were determined between them. Hypoxic injury of hepatocytes was identified in these areas as a result of disorganization of liver acinus blood-stream. Areas of perycapillary sclerosis occurred in the acini due the violation of blood flow (sinusoid capillarization). As indicated [4] significantly increased in size Mallory bodies appeared in case of progressing of the large occlusive changes.

Lymphocytic and plasmocytic infiltration was also observed in the portal tracts on the background of thickened collagen fibers that had a tendency to spread from the periphery to the center of liver acinus, in other words, from the first to the third zone of liver acinus, indicating hepatocellular necrosis. Connective tissue between the nodules had an uneven thickness. Fibrotic septums were located around false lobules and were infiltrated by lymphocytes and plasmocytes. Bundles of collagen fibers tightly adjoined to the walls of blood vessels in hepatic triads. They interrupted blood flow to the liver parenchyma in the arteries and made hypoxic changes in hepatocytes more severe. Difficulty in passing the blood through the venous vessels also contributed to portal hypertension syndrome [8].

At autopsy pancreas was decreased in size, tight and light grey color in deceased patients with chronic alcoholic pancreatitis. Its capsule was sclerosal. Gland surface was tuberous, and pseudocysts with clear content (retention cysts) were found under the capsule. Wide areas of connective tissue proliferation in the parenchyma were observed. Significant changes in the excretory ducts of gland were noted on this background. The lumens had areas of dilatation and constriction.

Microscopic examination identified that almost all parts of the pancreas were injured. First of all, atrophic changes in acini with flattening of exocrine pancreatic cells, their necrosis were observed. Amount of collagen fibers increased around acini, somewhere forming wide strands and extending stromal component of pancreas. Collagen fibers caused local constriction of the excretory ducts, above which dilatation areas appeared. Intralobular proliferation of connective tissue was found and even separation of parenchymal structures in the form of pseudolobules. Signs of chronic inflammation were detected in the ducts walls of all levels (inserted, intralobular, interlobular and main pancreatic duct), duct epithelium was thinned and in some areas it was absent. Periductal connective tissue was thickened, infiltrated by lymphocytes, macrophages, plasmocytes. Thus, all signs of fibro-sclerotic pancreatitis were observed.

Histopathological pattern of combined alcohol-induced pathology (cirrhosis and chronic pancreatitis), is mainly characterized by the same morphological changes that are typical for each separate nosological form and that other researchers have marked out [4]. At the same time, it should be noted that in case of combined hepato-pancreatic pathology more severe fibrosis was found in liver, especially great accumulation of collagen fibers was detected in perysinusoidal areas, this data were also indicated by other scientists [5]. Hepatocytes necrosis took wider areas, and Mallory bodies were larger and more numerous in hepatocytes. Sclerosing hyaline necrosis was observed in micropreparations of two-thirds of patients – in 3 zone of the liver acinus was significant collagen accumulation around dystrophic changed hepatocytes (ballooning degeneration) and sinusoids. There was identified severe fibrosis with steatic hepatocytes injury in the acinus portal area l (1 zone of liver acinus). The number of stellate cells was increased, which contributed not only to fast transformation of hepatitis into cirrhosis, but also to its progression [6, 8].

In case of comorbidity, pancreas was also reduced in size, with a tuberous surface, with solid, thickened capsule. The degree of intraorganic fibrotic changes was high. Acini were deformed, metaplasia of exocrine pancreatic cells into the ducts cells was observed. Exocrine pancreatic cells were decreasing in their height and resembled flat cells of inserted exocrine ducts. However, accumulation of lipid granules was observed in zymogenic area of these cells. Cells of acini are able to metabolize alcohol. Direct toxic effects of alcohol and/or its metabolites on these cells can lead to gland

damage if the trigger factor is presented. Probably, this factor is the liver damage under the influence of alcohol as the liver and pancreas are functionally closely related. In sections, we found that the number of stellate cells was increased playing an important role in the progression of the pancreas fibrosis [1].

At the same time, proliferation of epithelial cells of ducts and accumulation of viscous secret were determined in their lumen in patients with comorbidity. Periductal sclerosis was more marked – the thickness of the connective tissue around the ducts was considerably higher compared to chronic pancreatitis without liver injury.

Conclusions

1. Histopathological alcoholic cirrhosis is micronodular, degenerative changes of hepatocytes (steatosis, ballooning degeneration) were found, capillarization of the sinusoids and significant degree of fibrosis were detected.
2. The main pathological features of the alcoholic pancreatitis are diffuse injury of all components of the gland: atrophic changes in the acini, necrosis of exocrine pancreatic cells, enlargement of stromal and periductal components of the pancreas through the formation and proliferation of connective tissue, signs of chronic inflammation in the wall of exocrine ducts.
3. In case of combined alcohol-induced liver and pancreas injury we identified more severe fibrosis, increased number of stellate cells in these organs. Hepatocytes necrosis was wider in the liver areas, Mallory bodies in hepatocytes were larger and more numerous, sclerosing hyaline necrosis was detected in two-thirds of the deceased. Severe fibrosis with steatic injury of hepatocytes was identified in the portal area of lobules. Acini of the pancreas were deformed, metaplasia of exocrine pancreatic cells, proliferation of epithelial cells in ducts, accumulation of viscous secret in their lumen were observed.
4. Based on these results, we can state the fact that the morphological changes in the liver and pancreas in case of comorbidity are more severe than in case of separate diseases and therefore combined injury require individualized approach to their correction.

Prospects for further research involve the search for effective treatment of combined alcohol-induced liver and pancreas injury.

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