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Study of Etiological Factors of Chronic Pancreatitis Complicated by Biliary Hypertension

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Abstract.

During the 2009-2015 time period, 127 patients with complicated forms of chronic pancreatitis (CP) underwent surgical treatment at the Department of General Surgery of the Ivano-Frankivsk Regional Clinical Hospital. CP was accompanied by biliary hypertension (BH) in 39 (30.7%) patients. 14 (11.1%) patients developed BH with concomitant chronic duodenal obstruction (CDO), and in 4 (3.1%) patients a combination of BH+CDO and local venous hypertension (VH) of the vessels in the pancreatobiliary area was found. The analyzed group included 36 (92.3%) men and 3 (7.7%) women at the age of 21 to 60 years. In all 39 patients tubular stenosis of the intrapancreatic part of the choledoch was the morphological substrate of BH due to fibrose-degenerative changes in the pancreatic head; in 9 (23.1%) patients it was combined with cysts of the pancreatic head. In 28 (71.7%) patients, BH had clinical signs (ochrodermia and mucosal icterus, hyperbilirubinemia), and in 11 (28.9%) patients BH was asymptomatic and was diagnosed only by means of ultrasonography (USG) and computed tomography (CT) (tubular stenosis and dilation of the suprapancreatic segment of the common bile duct 0.7 cm to 1.3 – 1.5 cm). In 3 (7.6%) patients, BH was accompanied by the manifestations of cholangitis. All patients with CP complicated by BH underwent surgical treatment. Drainage, resection, and combined surgical interventions were used. In 17 (43.5%) patients CP complicated by BH was the result of acute pancreatitis (1 to 10 years ago), 14 of them underwent surgeries: 2 patients – laparoscopic drainage of the enzymatic peritonitis, 5 patients – laparotomy, drainage of the peritoneal omental sac, abdomen and retroperitoneal space, 5 patients – endoscopic retrograde cholangiopancreatography (ERCP) with drainage of biliary ducts, 2 patients – endoscopic stenting of the pancreatic ducts. In 4 (10.2%) patients, CP was associated with previous surgeries on the organs of the pancreatobiliary area: 2 patients underwent cholecystectomy due to cholelithiasis, and 2 patients underwent Bilroth II gastrectomy due to duodenal ulcer. In 14 (35.9%) patients their condition was probably caused by cigarette smoking. In 8 (20.5 %) patients, a direct connection between CP and regular alcohol consumption was established. In 7 patients, the causes of CP complicated by BH were not found, and in these cases CP was qualified as idiopathic. Acute destructive pancreatitis is often an etiological factor in the development of CP complicated by BH. BH in case of CP is one of the absolute indications for surgical treatment, and the method of BH correction should be determined individually.

Keywords: chronic pancreatitis; biliary hypertension

Problem statement and analysis of the recent research

Chronic pancreatitis is a group of chronic diseases of the pancreas of different etiology (mostly of inflammatory origin) that are characterized by phase-progressing segmental or diffuse degenerative, destructive changes in the exocrine pancreas; atrophy of glandular elements and their replacement by connective tissue (fibrosis), the development of which determines the rate of progression of the disease in general; changes in the pancreatic duct system with further formation of cysts and concrements; different degrees of decline in exocrine and endocrine function of the pancreas; development of complications at any stage of the disease (early, middle, and late) [10].

According to autopsy data, the incidence of CP is 0.01 to 5.4%, on average – 0.3–0.4%. The incidence of this pathology is constantly growing due to alcohol consumption, and frequency of its detection is increasing due to the improvement of the diagnostic methods; the percentage of alcohol-induced pancreatitis increased from 40% to 75% [2]. According to N. B. Gubertrits et al. [2], early complications of CP develop in 30% of cases, and late complications

develop in 70-85% of cases. 6.3% of patients with CP die within 5 years, 30% of patients with CP die within 10 years, and 50% of patients with CP die within 20 years.

CP is a pluricausal disease; many factors are involved in its development. They include acute pancreatitis, long-term alcohol abuse, smoking, high-fat and protein diets, disorders of the gall bladder and bile ducts, diseases of the papillary and peripapillary areas, duodenum, hereditary factors, etc.

In 65-70% of cases CP is associated with alcohol abuse. The total mortality rate due to CP among patients with alcohol-induced pancreatitis suffering from this disease for over 20 years is 28.8% to 35.0% [18]. Long-term heavy alcohol consumption (prolonged daily intake of 80g of pure ethanol at a dose of 80g or more) is an important etiological factor. However, consumption of less amount of alcohol may also contribute to the development of CP, especially when other risk factors are present [2]. The combination of smoking and heavy drinking increases the risk for the disease. However, there is no absolute link between alcohol drinking and CP. It remains unclear why only 10% of alcohol addicts develop clinical signs of CP [2]

An important independent risk factor in the development of CP is smoking, which contributes to pancreatic calcification and exocrine insufficiency [5, 8, 12].

The development of CP is often a result of acute pancreatitis, the transition of which into chronic stage is due to pancreatic duct obstruction (stenosis, calculi, and pseudocysts) and fibrotic process in the pancreas. Recurring and severe acute pancreatitis cause approximately 6% of CP cases [13]. The research published in scientific journal "Pancreas" (2011) [16] analyzed transition of acute pancreatitis into CP in 352 patients. The findings showed that acute pancreatitis transformed into CP in 85 (24%) patients, whereas in 48% of patients the genesis of the disease was found to be alcoholic, in 47% of patients it was idiopathic, and in 5% of patients rare forms were detected. Mortality rate in this group of patients was 2.7 times higher than in patients without similar transition.

An important role in CP development is played by a high-fat and high-protein diet [5, 8, 11, 12]. Disorders of the gall bladder and bile ducts, mainly gallstone disease in the form of choledocholithiasis, are of etiological importance primarily in women [1, 4]. Diseases of the papillary and peripapillary areas of the duodenum (sphincter of Oddi dysfunction, posttraumatic cicatrical strictures of the pancreatic ducts, papillitis, diverticula, etc.) are also frequent causes of CP development [10].

Hereditary factors also play an important role in CP development. There are three types of genetic variations associated with mutations. They include cystic fibrosis gene (CFTR), cationic trypsinogen gene (PRSS1), pancreatic secretory trypsin inhibitor (SPINK1) gene [7, 9, 18]. Genetically determined hereditary CP takes up approximately 1% in the general structure of this nosology [14]. This CP type is determined on the basis of researching mutations of PRSS1, SPINK 1, PRSS2, and CFTR genes in persons, whose family members (two or more) had or have CP in more than one generation [15]. The main distinction of hereditary CP is its manifestation in patients under 20 years and in many cases even in childhood [18].

In other cases CP is classified as idiopathic (20-25%) including factors such as tropical pancreatitis, which is the main cause of CP development in children in tropical regions, metabolic imbalance, autoimmune disorders, etc. [17].

Most often, CP is accompanied by functional disorders of the biliary tract with further development of manifestative or non-manifestative BH which occurs in 25-40% of cases. A common cause of jaundice in CP is tubular stenosis of the bile duct caused by pancreatic fibrosis and inflammation in the head of the pancreas [17]. Common bile duct obstruction is found in 56.3% of patients with CP, jaundice is detected in 22.2%, and 6% of patients develop jaundice with co-existent cholangitis [3]. A significant role in the development of obstructive jaundice in CP is also played by constriction of the distal part of the common bile duct by fibrotically changed pancreatic lingula [6].

The objective of the research was to study the causes of the development of chronic pancreatitis complicated by biliary hypertension.

Materials and methods

During the 2009-2015 time period, 127 patients with complicated forms of chronic pancreatitis (CP) underwent surgical treatment at the Department of General Surgery of the Ivano-Frankivsk Regional Clinical Hospital. CP was accompanied by BH in 39 (30.7%) patients. 14 (11.1%) patients developed BH with concomitant CDO, and in 4 (3.1%) patients a combination of BH+CDO and local venous hypertension (VH) of the vessels in the pancreatobiliary area was found. The dilatation of the portal vein diameter by over 1.1-1.3 cm during US indicated VH; additional VH signs included megalosplenia (2 patients) and gastric varices (1 patient). There were 36 (92.3 %) men and 3 (7.7 %) women at the age of 21 to 60 years.

Except laboratory data, US, ERCP, and contrast-enhanced CT were of most practical importance for diagnosing changes in the pancreas, pancreatic duct, and adjacent organs. In the course of research, the classification of CP suggested by academician O. O. Shalimov (1997) was used.

Results and discussion

In all 39 patients tubular stenosis of the intrapancreatic part of the choledoch was the morphological substrate of BH due to fibrose-degenerative changes in the pancreatic head; in 9 (23.1%) patients it was combined with cysts of the pancreatic head. In 28 (71.7%) patients, BH had clinical signs (ochrodermia and mucosal icterus, hyperbilirubinemia), and in 11 (28.9%) patients BH was asymptomatic and was diagnosed only by means of USG and CT (tubular stenosis and dilation of the suprapancreatic segment of the common bile duct 0.7 cm to 1.3-1.5 cm). In 3 (7.6%) patients, BH was accompanied by the manifestations of cholangitis.

The results of USG indicated local or diffuse enlargement of the head of the pancreas from 3.5 to 5.7 cm in all patients with BH and heterogeneity of pancreatic tissue in 25 (64.1%) patients. Calcifications in glandular tissue were found in 11 (28.2%) patients. Dilatation of the pancreatic duct by over 5 mm was detected in 12 (30.7%) patients, and Lithiasis of Wirsung's duct was found in 5 (12.8%) patients.

All patients with CP complicated by BH underwent surgical treatment. The development of BH in CP was considered to be a certain indication for surgical treatment. Drainage, resection, and combined surgical interventions were used. The method of BH correction was determined for each individual case.

General characteristics of performed surgeries are presented in Table 1.

Table 1

General characteristics of surgical interventions in patients with chronic pancreatitis complicated by biliary hypertension

Surgery	Number	%
Pancreaticoduodenal resection (Whipple procedure)	**5**	**12.8**
Frey's procedure	**11**	**28.3**
including choledochoenteroanastomosis	2	5.1
including insertion according to V. Kopchak and choledochoenteroanastomosis	2	5.1
Bern modification of Beger procedure	**2**	**5.1**
Longitudinal pancreaticojejunostomy	**8**	**20.5**
including choledochoenteroanastomosis	3	7.7
including insertion according to V. Kopchak and choledochoenteroanastomosis	1	2.6
Cystoenterotomy	**3**	**7.7**
including choledochoenteroanastomosis	2	5.1
Endoscopic cystoduodenostomy	**2**	**5.1**
Application of biliodigestive bypass anastomoses	**2**	**5.1**
External drainage of pancreatic cyst	**1**	**2.6**
ERCP with endobiliary stenting	**5**	**12.8**
Total	**39**	**100.0**

In 17 (43.5%) patients CP complicated by BH was the result of acute pancreatitis (1 to 10 years ago), 14 of them underwent surgeries: 2 patients – laparoscopic drainage of the enzymatic peritonitis, 5 patients – laparotomy, drainage of the peritoneal omental sac, abdomen and retroperitoneal space, 5 patients – endoscopic retrograde cholangiopancreatography (ERCP) with drainage of biliary ducts, 2 patients – endoscopic stenting of the pancreatic ducts. Other 3 patients were treated conservatively.

In 4 (10.2%) patients CP was associated with previous surgeries on the organs of the pancreatobiliary area: 2 patients underwent cholecystectomy due to cholelithiasis, and 2 patients underwent Bilroth II gastrectomy due to duodenal ulcer. These patients did not abuse alcohol and smoke.

In 14 (35.9%) patients their condition was probably caused by regular tobacco use. In 8 (20.5 %) patients a direct connection between CP and regular alcohol consumption was determined. However, not all patients were honest when answering this question. In 7 patients heavy alcohol consumption was combined with smoking. The majority of these patients did not have a permanent place of work.

In 7 patients, the causes of CP complicated by BH were not found. There were determined neither hereditary factors, nor connection with consumption of greasy food or other factors. Therefore, CP in these cases was qualified as idiopathic.

Conclusions

1. Acute destructive pancreatitis is the most often etiological factor in the development of CP complicated by BH.

2. BH in case of CP is one of the absolute indications for surgical treatment, and the method of BH correction should be determined individually.

Prospects for further research

The prospects for further research consist in further study of causes of the development of CP complicated by BH, and elaboration of measures of its prevention.

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