CASE STUDY

CASE STUDY: MAJOR DUODENAL PAPILLA CANCER COMPLICATED BY ACUTE PARACANCROTIC NECROTIZING PANCREATITIS

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ABSTRACT

The given paper describes a case of treating adenocarcinoma of the papilla of Vater diagnosed as the cause after an episode of acute pancreatitis. The etiology of acute pancreatitis was considered idiopathic until the onset of complaints caused by tumor growth. The volume of radical surgery has changed intraoperatively due to the detection of infected limited necrotic clusters, didn't diagnosed both laboratory and instrumentally. Pathomorphological conclusion: considering clinical data, low-grade (G3) adenocarcinoma of the major duodenal papilla, which developed from pre-existing tubular villous adenoma of the duodenum or intraampullary papillary neoplasia (IAPN). Predicting the early detection of MNPs after AP episode requires further research by improving imaging techniques, introducing new non-invasive techniques and investigating circulating biomarkers. The scope of surgery for patients with clinically significant complications of tumor growth and identified competing diagnosis at the target site should be individually decided and weighed. Infected pancreatitis in the late stages requires careful diagnosis.

KEY WORDS: pancreatitis, periampullary tumor, idiopathic pancreatitis

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INTRODUCTION

While the leading position in the etiology of acute pancreatitis (AP) is occupied by gallstones and alcohol, rarer causes of the disease, such as drugs, trauma, congenital features of the pancreatic duct, tumors, etc., require additional measures for achieving best clinical outcome and prevention in standard diagnosis and treatment. The frequency of detection of malignant neoplasms of the pancreas and periampullary zone (MNP) as a cause of pancreatitis according to various sources varies from 1 to 10% [1-9].

Analyzing the probable predictors of MNP development [5,6], the pathophysiology of AP development in patients with later detected MNP can be considered in two ways:

A) Already developed tumor tissue, being associated with the pancreatic duct, obstructively initiates the development of AP, with treatment and diagnosis being stopped at inflammatory changes, postponing the standard way of treatment and follow-up depending on the severity of AP. Kimura et al. [6] also reported the release of specific chemical mediators during the growth and development of tumor tissue that trigger inflammatory changes in the gland.

B) Damage to the tissue of the pancreas after the acquisition of inflammatory changes in the form of a single or recurrent episode of AP, or the development of chronic pancreatitis, which can be considered as oncogenetic changes. [10]

Peculiarities of acute pancreatitis (AP) manifestation in the presence of pancreatic tumors and anatomical structures located in the area of papilla of Vater has not been reliably studied. The main mechanism of AP is driven by tumor obstruction of the main pancreatic duct (MPD), which leads to the release of enzymes into the pancreatic tissue (PT), while Pelletie et al. argue that with slow growth of pancreatic tumors, compression of MPD does not occur, as a result, AP develops less common.

MNPs diagnosed a few months after the first episode of AP are manifested by a resectable stage of the disease. However, in some cases timely diagnosis of MNP is delayed due to initially incorrect diagnosis, which worsens survival.

AP in pancreatic cancer is more common in patients older than 40 years with no alcohol abuse and gallstones in past medical history (4). Published studies reveal an increase in the 5-year survival rate of patients with a history of pancreatic cancer and a primary episode of AP by 16-23% compared with patients without an epizode. (5) Predicting the early detection of MNPs after AP episode requires further research by improving imaging techniques, introducing new non-invasive techniques and investigating circulating biomarkers.

The given paper describes a case of treating adenocarcinoma of the papilla of Vater diagnosed as the cause after an episode of acute pancreatitis.

CASE REPORT

Female patient I, born in 1954, was hospitalized in the surgical department at the clinical base of the General Surgery Department №1, Bogomolets National Medical

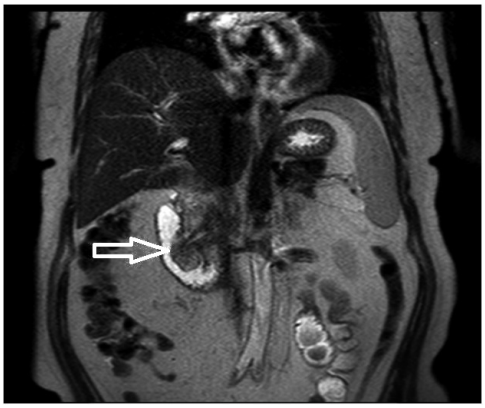

Fig 1. MRI of the patient's abdominal organs after temporary biliary stenting. The arrow highlights the tumor.

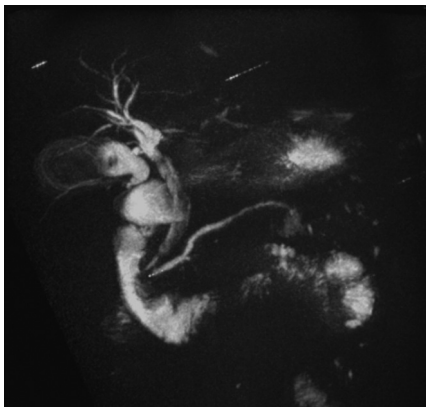

Fig 2. MRHPG after temporary biliary stenting.

Fig 3. CT scan three months after radical surgery.

University, due to urgent indications with complaints of skin yellowing and sclera and fever up to 38 C with moderate pain in the epigastrium with a previous diagnosis of mechanical jaundice and cholangitis.

From the anamnesis it was known that four months ago before the patient was hospitalized for acute pancreatitis for 17 days. Following the protocol volume of examinations, alimentary, biliary and hypertriglyceride genesis of the attack was then excluded. The diagnosis was: Acute idiopathic necrotizing pancreatitis, moderate severity; acute fluid collections. Conservative pancreatotropic therapy was performed according to the protocol and dosing regimens. Due to prolonged febrile fever and elevated levels of C-reactive protein (143.6 mg / l) and procalcitonin (1.7 IU) amid sonographic dynamic monitoring, the patient received two courses of antibiotic therapy with further improvement and reduction of C-reactive protein (CRP) and procalcitonin. After the treatment the patient's condition improved without invasive intervention and the patient was discharged for outpatient treatment with a predicted formation of walled-off necrosis. CT of the abdominal organs and FGDS were suggested among a number of other recommendations. Over the next four months before hospitalization with the mechanical jaundice, the patient was not examined for unknown reasons.

In reference to the episode of mechanical jaundice, at the time of hospitalization hyperbilirubinemia up to 258 μmol / l with elevated levels of transaminases (ALT - 480 U / l, AST - 425 U / l) was detected. The level of C-reactive protein was 114 mg / l.

Ultrasound examination of the abdominal cavity and pelvis revealed signs of ectasia of the common bile duct, enlarged pancreatic head, diffuse changes in the liver parenchyma and pancreatic tissue, without free fluid in the abdomen and pelvis.

According to the absolute indications for therapeutic and diagnostic purposes, after instrumental and laboratory examination with a diagnosis of mechanical jaundice and cholangitis endoscopic papillosphincterotomy, EPST were performed. Endoscopically - in the area of the mouth of the p.Vateri growth of the type of "cauliflower", the tumor-like formation extends to the distal choledochus. Choledoch stenting with 8.5 Fr plastic stent and p.Vateri biopsy were performed. The patient was diagnosed with p.Vateri tumor complicated by mechanical jaundice and cholangitis. According to morphological data after endoscopic biopsy villous adenoma p.Vateri was diagnosed.

Amid further therapy after normalization of bilirubin level the patient underwent MRI of the abdominal cavity (Fig. 1). Thus, in Vater's papilla there is a a formation of 23x17 mm, which exophytically penetrates into the lumen of the duodenum, moderately heterogeneous contrast. The distal segments of the choledochus and virsung duct are amputated in the thickness of the formation (Fig.2). The virsung duct is moderately ectasified to 4.5 mm.

After symptomatic treatment, the patient's condition improved; she was diagnosed with: Vater's papilla neoplasm. (Histologically villous adenoma P.Vateri). Mechanical jaundice. Acute cholangitis, Grade I (Tokyo Guidelines 2018). Partial obstruction of the duodenum. Acute necrotic pancreatitis, Walled-off necrosis. (disease duration - 4 months.) Aterosclerosis of the aorta and coronary vessels. Hypertension stage II, grade 1, risk 3, high. CI I. Diabetes mellitus, stage of compensation, insulin independent variant.

Then, surgical treatment was planned as the next stage in the treatment of the disease after one month of endobiliary stenting with general condition considered as satisfactory and normalization of C-reactive protein and procalcitonin. Due to inability to reliably exclude the malignant nature of the tumor and the description of MRI images, it was planned to perform pancreatoduodenal Whipple resection. However, the volume of surgery was changed intraoperatively due to the detection of infected limited necrotic clusters. The following procedures were performed: Papillectomy, cholecystectomy, hepaticojejunostomy on the Brown loop, pancreatic necrosectomy, sanitation and drainage of the abdominal cavity, drainage of the omental sac. Intraoperatively: a tumor of the major duodenal papilla was contoured through the duodenum, covering the duodenum and disrupting the passage through it. In the area of the distal part of the pancreas, a demarcated

cluster was revealed: pancreatic sequesters were removed, necrosis affected the body and tail of the pancreas.

Intraoperative culture of pancreatic sequestration detected K.oxytoca * 10^5, sensitive to gentamicin, ceftazidime, ceftazidime-avibactam, cefepime, amikacin, levofloxacin, meropenem. Intraoperative culture of bile and endobilar stent found E. coli * 10^6, E. faecalis * 10^5, Kl. pneumoniae * 10^5 sensitive to gentamicin, ceftazidime-aviabactam, meropenem.

Intraoperative express biopsy was performed: Vater's papilla adenocarcinoma.

Microscopic description of the surgical macropreparation: "Duodenal wall tissue with complexes of invasive tumor, formed by layers of epithelioid and focal elongated cells with signs of significant pleomorphism / atypia. In some areas, the formation of single glandular cribrous structures is determined by tumor cells, which corresponds to low-differentiated G3 adenocarcinoma. The tissue of invasive neoplasia directly borders on the exophytic epithelial formation of tubular-villi / papillary structure with the presence of intraepithelial neoplasia / dysplasia of the intestinal type of low and high degree, corresponding to tubular villous adenoma or intraampullary papillary neoplasia.

Pathomorphological conclusion: considering clinical data, low-grade (G3) adenocarcinoma of the major duodenal papilla, which developed from pre-existing tubular villous adenoma of the duodenum or intraampullary papillary neoplasia (IAPN).

During further inpatient treatment, the patient received antibiotic therapy with amikacin intravenously. The postoperative period was complicated by the development of gallbladder bed abscess: in 10 days after surgery, according to CT with intravenous amplification, there was visualized limited accumulation of fluid content 53x39mm in the gallbladder bed, which spread to the parenchyma of Sg4b \ Sg5 contrasting. Puncture and drainage of the abscess under ultrasound control were performed. According to the microbiological study, E. coli * 10^7, Kl.pneumoniae * 10^7, sensitive to meropenem were detected: sanation and antibiotic therapy were performed with further condition improvement.

Diagnosis: Cancer of the major duodenal papilla pT-3NxM0 G3 (low-grade adenocarcinoma amid IAPN) II stage cl.group 2, Partial duodenal obstruction. Cholangitis. Acute necrotic paracancrous infected pancreatitis. Walled-off necrosis. (The duration of the disease was 5 months). Gallbladder bed abscess (condition after ultrasound puncture and drainage) IHD: cardiosclerosis of the aorta and coronary vessels. Hypertension stage II, grade 1, risk 3, high. CI I. Type 2 diabetes mellitus, stage of compensation, non-insulin dependent variant.

After the treatment, the patient was discharged from the hospital in a satisfactory condition. The condition improved and complaints leveled. The postoperative period lasted 28 bed-days.

Further on, the patient received three cycles of adjuvant chemotherapy Gemcitabine / Capecitabine, further treatment was discontinued due to the development of toxic hepatitis. Three months and one year after radical surgical treatment, CT control was performed with no recurrence detected (Fig. 3).

Problems in the diagnosis and timely initiation of MNP therapy may be related to the simplified post-hospital management of patients with acute pancreatitis who have suffered from its mild form. Konur and co-authors [4] comparing the severity of Balthazar of AP in patients with and without MNP, reported a mild disease in more than 80% of patients with MNP. Similar conclusions can be drawn for patients with AP who did not undergo surgery or whose condition improved significantly during the minimally invasive procedure. However, in a study by Shaoyun et al. [1], 83% of patients with AP and MNP underwent surgery, including tumor biopsy. Even if there is no history of gallstone disease and alimentary genesis, hypertriglyceridemia or surgery, patients are rarely re-examined, being limited to such preventive measures as, strict adherence to prescribed diet and enzyme replacement therapy. And in the case of diagnosed gallstones or hypertriglyceridemia, subsequent treatment and follow-up examination after discharge from the hospital have certain limitations due to the focus on a particular metabolic pathology. The authors suggest a greater prevalence of AP on the background of MNP due to problems with additional examination of patients with AP in the anamnesis. The same features can explain variation in the prevalence of idiopathic pancreatitis, which occupies up to 10% in the etiology of AP [8]. Routine ultrasound during inpatient treatment of patients and after treatment of AP and assessment of pancreatic size without clear visualization of the tumor in some cases can distort the conclusion amid patients' absence of measured cancer markers and other instrumental research methods. Kimura et al. [6] report that MNP cannot be ruled out even if the main pancreatic duct does not dilate in patients with acute pancreatitis, and that induction of AP in patients with MNP is not limited to spread to the main duct / its obstruction. Accordingly, the pathophysiology of this etiological factor is considered today.

In a cohort study held in 2018 [9], among almost 50,000 patients with AP, only 1.1% were diagnosed with MNP after the disease, and more than half (56%) of them in the period from two months to five years. The characteristics of the patients in this study indicate the presence of concomitant pathology and alcohol abuse in most patients, and the etiology is not related to gallstones (58%). Among the patients studied, the number of recurrent episodes of AP was also indicated, and among them 99% of those with recurrence of AP in the next two years were diagnosed with MNP – i.e. undiagnosed MNPs caused recurrent episodes of "idiopathic" AP.

What are the ways of choosing the right amount of surgery for this group of patients, when periampullary malignancy and the consequences of necrotic infected pancreatitis are simultaneously diagnosed? Given that infected limited necrotic accumulations were detected in the patient only during surgery, with normal levels of CRP and procalcitonin, as well as absent in the description of preoperative MRI signs of infection, the amount of radical intervention was changed, i.e. limited. The

erroneous exclusion of infection of pancreatic necrosis in the preoperative period could be explained by lower body reactivity due to the age - normal values of CRP and procalcitonin were accompanied by a satisfactory assessment of the general condition. The lack of MRI data for infection can be explained by the incorrectly chosen method of instrumental diagnosis, when the primary task was to confirm the tumor process. Individual approach, vigilance in the initial diagnosis and weighted risk assessment [11] play a key role in this case.

CONCLUSIONS

The case study describes the experience in treatment of malignant neoplasms of the major duodenal papilla in the patient with previous paracancrotic pancreatitis.

In the given case, loss of one of the instrumental types of follow-up examination (endoscopy), not indicated to the patients with idiopathic acute pancreatitis on admission, emphasizes the importance of increased diagnostic attention during outpatient or inpatient management of patients with the most common pancreatic disease.

The question of absolute indications for endoscopic interventions in patients with acute pancreatitis remains open. In the absence of signs of choledochal obstruction and gallstone disease over the initial hospitalization, endoscopic examination would be crucial in the early detection of a major duodenal papilla tumor, and as it later became clear, the etiology of the acute pancreatitis attack.

Predicting the early detection of MNP amid AP requires further research by improving imaging techniques, introducing new non-invasive techniques, investigating circulating biomarkers, revising clinical strategy.

The scope of surgery for patients with clinically significant complications of tumor growth and identified competing diagnosis at the target site should be individually decided and weighed.

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