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Mixed Serous-Mucinous Cystic Neoplasm of the Pancreas

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Abstract

A 47-year-old male presented to the clinic with complaints of general weakness, decreased appetite, and non-specific pain in the right upper quadrant of the abdomen, which had persisted for the past 3 months. The patient had experienced weight loss (approximately 7 kg). The complaints were progressive in nature.

The patient's medical history included hypertension, which was controlled with medication. He had undergone cholecystectomy 8 years prior due to cholelithiasis. Family history was significant for gastrointestinal malignancies (father - gastric cancer, mother - pancreatic cancer). The patient was a non-smoker and consumed alcohol moderately.

Physical examination revealed mild tenderness in the right upper quadrant of the abdomen, without palpable masses. Laboratory studies showed mild elevation of amylase and lipase levels, while liver function tests were within normal limits. The CA 19-9 tumor marker was slightly elevated.

Contrast-enhanced computed tomography revealed a 6.5 cm diameter cystic lesion at the junction of the pancreatic body and tail, with heterogeneous density and internal septations. Magnetic resonance cholangiopancreatography (MRCP) confirmed the cystic lesion, which was not connected to the pancreatic ductal system. Endoscopic ultrasound with fine-needle aspiration (EUS-FNA) revealed high-viscosity fluid containing mucin and atypical cells.

The differential diagnosis included:

1. Mixed serous-mucinous cystic neoplasm
2. Intraductal papillary mucinous neoplasm (IPMN)
3. Mucinous cystic neoplasm (MCN)
4. Solid pseudopapillary neoplasm
5. Pancreatic pseudocyst

Cytological examination results, radiological findings, and clinical characteristics suggested a diagnosis of mixed serous-mucinous cystic neoplasm with malignant potential.

Laparoscopic distal pancreatectomy with splenectomy was planned and performed. During the operation, it was found that the cystic lesion had not invaded adjacent tissues. Complete resection of the lesion was performed with negative surgical margins. Histopathological examination confirmed mixed serous-mucinous cystic neoplasm without signs of invasion; however, foci of dysplasia were identified, indicating malignant potential. Lymph nodes were negative for malignancy.

The patient's condition was assessed at 3, 6, and 12 months post-surgery. Control CT studies at 6 and 12 months showed no signs of recurrence or metastasis. Glucose tolerance testing revealed mild glucose metabolism impairment, which was controlled with diet. Annual CT surveillance and tumor marker monitoring are recommended for the next 5 years.

This case represents an example of successful surgical treatment of a rare pancreatic cystic neoplasm, where timely diagnosis and a multidisciplinary approach in developing the treatment strategy were crucial.
Key words: Mixed serous-mucinous cystic neoplasm, pancreatectomy, splecectomy, laparoscopy.

Introduction

Pancreatic cystic neoplasms represent a heterogeneous group of lesions with varying malignant potential. While serous cystadenomas are typically benign and mucinous cystic neoplasms carry significant malignant risk, mixed serous-mucinous cystic neoplasms represent a rare intermediate category that combines morphological and biological features of both entities. These lesions pose unique diagnostic challenges and require careful evaluation to determine appropriate management strategies. The incidence of pancreatic cystic lesions has increased significantly with the widespread use of cross-sectional imaging, with studies reporting detection rates of 2.6% to 13.5% in asymptomatic populations. Among these, mixed serous-mucinous cystic neoplasms account for less than 1% of all pancreatic cystic lesions, making them extremely rare entities in clinical practice. The classification and understanding of these mixed lesions have evolved considerably over the past decade. Initially described as variants of serous cystadenomas, recent molecular and histopathological studies have demonstrated distinct characteristics that warrant separate classification and management approaches. The presence of both serous and mucinous components within the same lesion raises important questions about oncogenesis, malignant potential, and optimal treatment strategies.

Case Presentation Patient Demographics and Clinical History

A 47-year-old male presented to gastroenterology clinic with a 3-month history of progressive symptoms. The patient complained of generalized weakness, decreased appetite, and non-specific pain

localized to the right upper quadrant of the abdomen. The pain was described as dull, continuous, and gradually worsening over time. Associated symptoms included significant unintentional weight loss of approximately 7 kilograms over the 3-month period. The patient's past medical history was significant for hypertension, which was well-controlled with antihypertensive medications (amlodipine 5 mg daily). He had undergone laparoscopic cholecystectomy 8 years prior for symptomatic cholelithiasis without postoperative complications. The patient denied any history of diabetes mellitus, pancreatitis, or previous abdominal trauma. Family history was particularly concerning, revealing a strong predisposition to gastrointestinal malignancies. His father had been diagnosed with gastric adenocarcinoma at age 62 and died from complications related to the disease. His mother had been diagnosed with pancreatic ductal adenocarcinoma at age 58, also with a fatal outcome. This family history raised immediate concerns about hereditary cancer syndromes and increased surveillance needs. Social history revealed that the patient was a lifelong non-smoker and consumed alcohol moderately (approximately 2-3 drinks per month). He worked as an office administrator with no known occupational exposures to carcinogens. The patient maintained an active lifestyle and had no known drug allergies.

Physical Examination

Physical examination revealed a well-appearing middle-aged male in no acute distress. Vital signs were stable with blood pressure of 138/82 mmHg, heart rate of 76 beats per minute, temperature of 98.4°F (36.9°C), and oxygen saturation of 98% on room air. The patient appeared mildly cachectic, consistent with his reported weight loss. Abdominal examination was notable for mild tenderness in the right upper quadrant and epigastric region on deep palpation. No palpable masses, organomegaly, or lymphadenopathy were detected. Bowel sounds were normal, and there were no signs of peritoneal irritation. The surgical scar from previous cholecystectomy was well-healed without evidence of hernia formation. Cardiovascular and pulmonary examinations were unremarkable. Neurological examination showed no focal deficits, and the patient was alert and oriented in all spheres.

Laboratory Investigations

Initial laboratory workup revealed several abnormalities suggestive of pancreatic involvement. Serum amylase was elevated at 152 U/L (normal range: 30-110 U/L), and lipase was similarly elevated at 198 U/L (normal range: 10-140 U/L). These elevations, while modest, suggested pancreatic inflammation or obstruction. Liver function tests were within normal limits, including alanine aminotransferase (ALT) 28 U/L, aspartate aminotransferase (AST) 31 U/L, alkaline phosphatase 89 U/L, and total bilirubin 0.9 mg/dL. This pattern helped rule out biliary obstruction or significant hepatic involvement. Complete blood count showed mild anemia with hemoglobin of 11.8 g/dL (normal range: 13.5-17.5 g/dL for males), likely secondary to chronic disease and weight loss. White blood cell count and platelet count were within normal ranges. Tumor markers revealed an elevated CA 19-9 level of 58 U/mL (normal range: <37 U/mL). While this elevation was modest, it raised concerns about malignant potential given the clinical presentation and family history. Carcinoembryonic antigen (CEA) levels

were normal at 2.1 ng/mL. Additional metabolic panels including comprehensive metabolic panel, thyroid function tests, and inflammatory markers (ESR, CRP) were within normal limits, helping to rule out other systemic conditions.

Imaging Studies

Contrast-Enhanced Computed Tomography (CT) Initial imaging with contrast-enhanced CT of the abdomen and pelvis revealed a well-defined cystic lesion measuring 6.5 cm in maximum diameter located at the junction of the pancreatic body and tail. The lesion demonstrated heterogeneous density with multiple internal septations of varying thickness. No solid enhancing components were identified within the cyst. The pancreatic parenchyma surrounding the lesion appeared normal without signs of ductal dilatation or parenchymal atrophy. No evidence of local invasion into adjacent structures was observed. The splenic vessels were in close proximity to the lesion but appeared uninvolved. No regional lymphadenopathy or distant metastases were detected. The liver showed no focal lesions, and the peritoneal cavity was free of ascites. Magnetic Resonance Cholangiopancreatography (MRCP) MRCP was performed to better characterize the relationship between the cystic lesion and the pancreatic ductal system. The study confirmed the presence of a multilocular cystic lesion with no communication with the main pancreatic duct or secondary ductal branches. The main pancreatic duct appeared normal in caliber throughout its course, and no strictures or filling defects were identified. The lesion demonstrated heterogeneous signal intensity on T2-weighted images, with some locules showing high signal intensity consistent with simple fluid, while others showed intermediate signal intensity suggesting proteinaceous or mucinous content. Endoscopic Ultrasound with Fine-Needle Aspiration (EUS-FNA) Given the size of the lesion, concerning clinical presentation, and family history, EUS-FNA was performed for tissue diagnosis. The procedure was performed under conscious sedation using a linear echoendoscope. The cystic lesion was easily visualized and demonstrated multiple septations with varying echo characteristics. The aspirated fluid was viscous and slightly turbid, with high viscosity suggestive of mucinous content. Cytological examination of the aspirated fluid revealed the presence of mucin and atypical epithelial cells. While frank malignancy was not identified, the presence of atypical cells raised concerns about dysplastic changes. Fluid analysis showed elevated amylase levels (>5000 U/L) and CEA levels (>192 ng/mL), supporting the diagnosis of a mucinous cystic neoplasm.

Differential Diagnosis

The combination of clinical presentation, imaging characteristics, and cytological findings led to consideration of several differential diagnoses: 1. Mixed Serous-Mucinous Cystic Neoplasm This rare entity combines features of both serous and mucinous cystic neoplasms. The heterogeneous appearance on imaging, presence of both serous and mucinous components on cytology, and lack of ductal communication supported this diagnosis. The potential for malignant transformation made surgical resection the preferred treatment approach. 2. Intraductal Papillary Mucinous Neoplasm (IPMN) IPMNs arise from the pancreatic ductal system and can present as cystic lesions with mucinous content.

However, the lack of communication with the pancreatic duct system on MRCP made this diagnosis less likely. IPMNs typically show ductal dilatation and may have visible papillary projections, which were not observed in this case. 3. Mucinous Cystic Neoplasm (MCN) MCNs are typically unilocular or oligolocular cystic lesions that occur predominantly in middle-aged women. While the mucinous content and cellular atypia were consistent with MCN, the patient's gender and the mixed cytological findings made this diagnosis less probable. 4. Solid Pseudopapillary Neoplasm These rare neoplasms typically occur in young women and can have cystic components due to internal degeneration. However, the lack of solid components and the patient's demographic profile made this diagnosis unlikely. 5. Pancreatic Pseudocyst Pseudocysts typically develop following acute pancreatitis or pancreatic trauma. The patient's lack of history of pancreatitis, the presence of internal septations, and the cytological findings of atypical cells made this diagnosis improbable. Based on the comprehensive evaluation, the clinical team concluded that mixed serous-mucinous cystic neoplasm was the most likely diagnosis, with significant malignant potential warranting surgical intervention.

Treatment After thorough discussion of the clinical presentation, imaging findings, and cytological results, the consensus was that surgical resection was indicated given: Size of the lesion (>3 cm), presence of atypical cells on cytology, strong family history of gastrointestinal malignancies, patient's young age and good performance status, Risk of malignant transformation.

Preoperative Preparation

Preoperative evaluation included cardiac assessment with electrocardiogram and echocardiogram, which were normal. Pulmonary function tests were performed and showed no abnormalities. The patient's hypertension was optimized with adjustment of antihypertensive medications. Given the planned splenectomy, the patient received appropriate vaccinations including pneumococcal, meningococcal, and Haemophilus influenzae type b vaccines at least 2 weeks prior to surgery. Detailed informed consent was obtained, discussing the risks and benefits of the procedure, including potential complications such as pancreatic fistula, bleeding, infection, and the long-term implications of splenectomy.

Surgical Procedure

Laparoscopic Distal Pancreatectomy with Splenectomy The patient underwent laparoscopic distal pancreatectomy with splenectomy under general anesthesia. The procedure was performed using a five-port laparoscopic approach with the patient positioned in a modified right lateral decubitus position. Operative Technique- Initial Exploration: After establishing pneumoperitoneum, laparoscopic exploration revealed a large cystic lesion in the pancreatic body-tail region without evidence of local invasion or peritoneal metastases. Mobilization: The gastrocolic ligament was divided to enter the lesser sac, providing excellent visualization of the pancreatic lesion. The short gastric vessels were divided using an energy device. Vascular Control: The splenic artery was identified at the superior border of the pancreas and divided between clips after ensuring adequate collateral circulation.

The splenic vein was similarly identified and divided. Pancreatic Division: The pancreas was divided at the neck using a linear stapler with appropriate staple height for pancreatic tissue. The staple line was reinforced with non-absorbable sutures. Specimen Removal: The specimen, including the distal pancreas, spleen, and cystic lesion, was placed in an extraction bag and removed through a small Pfannenstiel incision. Final Assessment: Hemostasis was ensured, and the pancreatic staple line was inspected for integrity. A closed-suction drain was placed near the pancreatic staple line.

Immediate Postoperative Course

Postoperative recovery was uncomplicated with the following course: Day 1-2: Patient maintained on clear liquids with gradual advancement of diet as tolerated. Pain was well-controlled with patient-controlled analgesia. Drain output was monitored for volume and amylase content. Day 3-4: Diet was advanced to regular solids. Drain amylase levels remained low (<50 U/L), indicating no evidence of pancreatic fistula. Ambulation was encouraged, and respiratory physiotherapy was continued. Day 5-6: Patient demonstrated excellent recovery with normal bowel function, adequate oral intake, and minimal drain output. Laboratory values showed normalization of pancreatic enzymes and no signs of postoperative complications. The patient was discharged home on postoperative day 6 with appropriate discharge instructions, including drain care, dietary recommendations, and signs/symptoms warranting immediate medical attention.

Histopathological Analysis

Gross Examination- The surgical specimen consisted of the distal pancreas measuring $8.5 \times 6.2 \times 4.1$ cm along with the spleen. The cystic lesion measured $6.5 \times 5.8 \times 5.2$ cm and was well-demarcated from the surrounding pancreatic parenchyma. The cyst contained multiple locules filled with clear to slightly turbid fluid. The cyst wall varied in thickness from 1-3 mm, and multiple septations were present throughout the lesion. Microscopic Examination Histopathological examination revealed a complex cystic lesion with features consistent with mixed serous-mucinous cystic neoplasm: Serous Component: Areas of the cyst wall were lined by cuboidal epithelium with clear cytoplasm, characteristic of serous cystadenoma. These cells showed uniform nuclei without significant atypia and demonstrated positive staining for periodic acid-Schiff (PAS). Mucinous Component: Other areas showed columnar epithelium with abundant intracytoplasmic mucin, typical of mucinous cystic neoplasm. These areas demonstrated mild to moderate epithelial dysplasia with nuclear enlargement, hyperchromasia, and loss of polarity. Dysplastic Foci: Several areas within the mucinous component showed high-grade dysplasia characterized by significant nuclear atypia, increased mitotic activity, and architectural complexity. However, no evidence of invasive carcinoma was identified.

Immunohistochemical Studies

Immunohistochemical staining was performed to further characterize the lesion: CK7: Positive in both serous and mucinous components CK20: Focally positive in mucinous areas MUC1: Positive in serous

component MUC2: Positive in mucinous component Ki-67: Elevated (15-20%) in dysplastic areas p53: Focal nuclear accumulation in dysplastic foci

Lymph Node Analysis

Twelve lymph nodes were identified in the surgical specimen, all of which were negative for malignancy on routine histopathological examination. Final Pathological Diagnosis Mixed serous-mucinous cystic neoplasm with high-grade dysplasia, completely excised with negative surgical margins (R0 resection).

Follow-up and Outcomes

Short-term Follow-up (3 months): The patient was evaluated 3 months postoperatively and reported complete resolution of his preoperative symptoms. He had regained 4 kg of his lost weight and demonstrated excellent functional recovery. Physical examination was unremarkable, and laboratory studies showed: Normal pancreatic enzymes (amylase: 45 U/L, lipase: 62 U/L) CA 19-9 normalized to 18 U/mL Complete blood count within normal limits Normal liver function tests Contrast-enhanced CT scan showed no evidence of local recurrence, and the pancreatic remnant appeared normal without ductal dilatation. Medium-term Follow-up (6 months): At 6-month follow-up, the patient remained asymptomatic with continued weight gain and normal activity levels. Surveillance imaging with contrast-enhanced CT demonstrated no evidence of recurrence or metastatic disease. The pancreatic remnant showed no signs of atrophy or ductal abnormalities. Laboratory studies remained stable with normal tumor markers and pancreatic function tests. However, oral glucose tolerance testing revealed mild glucose intolerance, likely related to the reduction in pancreatic parenchyma. This was managed effectively with dietary modifications and lifestyle counseling. Long-term Follow-up (12 months): One-year postoperative evaluation showed excellent long-term outcomes. The patient had returned to full functional status and maintained stable weight. Surveillance CT imaging continued to show no evidence of disease recurrence. Endocrine function remained stable with mild glucose intolerance well-controlled through dietary management. The patient did not require insulin or oral hypoglycemic agents. Exocrine pancreatic function remained adequate without need for enzyme supplementation.

Conclusion

Mixed serous-mucinous cystic neoplasms of the pancreas represent a rare but clinically significant entity that requires a multidisciplinary approach for optimal management. This case demonstrates the importance of comprehensive preoperative evaluation, appropriate surgical intervention, and long-term surveillance in patients with these complex lesions. The successful outcome in this patient underscores the effectiveness of laparoscopic distal pancreatectomy as a treatment modality for appropriately selected cases. The presence of dysplastic foci in the final histopathology validates the decision for surgical resection and highlights the malignant potential of these lesions.

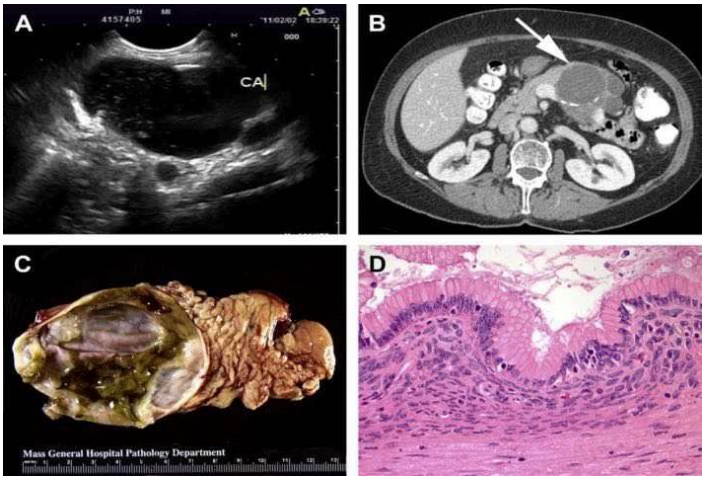

Fig.1

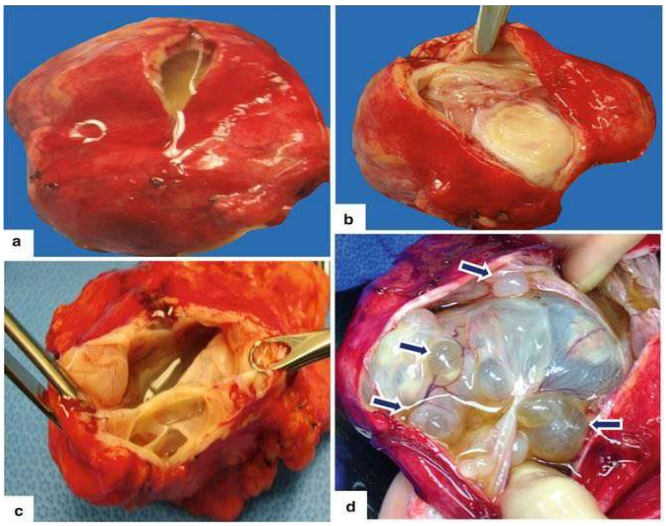

Fig.2

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პანკრეასის შერეული სეროზულ-მუცინური ცისტური ნეოპლაზია

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[1]მედიცინის ფაკულტეტი, თბილისის ივანე ჯავახიშვილის სახელობის სახელმწიფო უნივერსიტეტი

აბსტრაქტი

47 წლის მამაკაცმა მომართა კლინიკას ზოგადი სისუსტის, მადის დაქვეითების და მუცლის ზედა მარჯვენა კვადრანტში არასპეციფიკური ტკივილის ჩივილით, რომელიც გრძელდებოდა ბოლო 3 თვის განმავლობაში. პაციენტმა წონაში დაიკლო დაახლოებით 7 კგ. ჩივილები პროგრესირებადი ხასიათის იყო.

პრეისტორია -პაციენტს ანამნეზში აღენიშნებოდა ჰიპერტენზია, რომელიც კონტროლდებოდა მედიკამენტოზურად. გადატანილი ჰქონდა ქოლეცისტექტომია 8 წლის წინ ქოლელითიაზის გამო. ოჯახურ ანამნეზში აღინიშნებოდა კუჭ-ნაწლავის ტრაქტის ავთვისებიანი სიმსივნეები (მამას - კუჭის კიბო, დედას - პანკრეასის კიბო). პაციენტი არ ეწეოდა და ალკოჰოლს მოიხმარდა ზომიერად.

ფიზიკალური გასინჯვისას აღინიშნებოდა უმნიშვნელო მტკივნეულობა მუცლის ზედა მარჯვენა კვადრანტში, პალპირებადი წარმონაქმნის გარეშე. ლაბორატორიული კვლევებით

გამოვლინდა ამილაზას და ლიპაზას მცირედი მომატება, ღვიძლის ფუნქციური სინჯები ნორმის ფარგლებში იყო. CA 19-9 მარკერი უმნიშვნელოდ მომატებული. კონტრასტული კომპიუტერული ტომოგრაფიით გამოვლინდა 6.5 სმ-ის დიამეტრის კისტური წარმონაქმნი პანკრეასის სხეულისა და კუდის საზღვარზე, შერეული სიმკვრივით. მაგნიტურ-რეზონანსული ქოლანგიოპანკრეატოგრაფიით (MRCP) დადასტურდა კისტური წარმონაქმნი, რომელიც არ უკავშირდებოდა პანკრეასის სადინრებს. ენდოსკოპიურმა ულტრაბგერითმა კვლევამ თხელი ნემსით ასპირაციით (EUS-FNA) გამოავლინა მაღალი სიბლანტის სითხე მუცინის შემცველობით და ატიპიური უჯრედებით. დიფერენციალური დიაგნოსტიკა გატარდა შემდეგ პათოლოგიებთან: 1. შერეული სეროზულ-მუცინოზური კისტური ნეოპლაზია 2. ინტრადუქტალური პაპილური მუცინოზური ნეოპლაზია (IPMN) 3. მუცინოზური კისტური ნეოპლაზია (MCN) 4. ფსევდოპაპილური სოლიდური ნეოპლაზია 5. პანკრეასის ფსევდოკისტა. ციტოლოგიური კვლევის შედეგები, რადიოლოგიური სურათი და კლინიკური მახასიათებლები მიუთითებდა შერეული სეროზულ-მუცინოზური კისტური ნეოპლაზიის დიაგნოზზე მალიგნიზაციის პოტენციალით. მკურნალობა დაიგეგმა და განხორციელდა ლაპაროსკოპიული დისტალური პანკრეატექტომია სპლენექტომიით. ოპერაციის მსვლელობისას გამოვლინდა, რომ კისტური წარმონაქმნი ინვაზირებული არ იყო მიმდებარე ქსოვილებში. ჩატარდა წარმონაქმნის სრული რეზექცია. ჰისტოპათოლოგიურმა კვლევამ დაადასტურა შერეული სეროზულ-მუცინოზური კისტური ნეოპლაზია ინვაზიის ნიშნების გარეშე, თუმცა გამოვლინდა დისპლაზიის კერები, რაც მიუთითებდა მალიგნიზაციის პოტენციალზე. პაციენტის მდგომარეობა შეფასდა ოპერაციიდან 3, 6 და 12 თვის შემდეგ. CT კვლევით 6 და 12 თვის შემდეგ არ გამოვლინდა რეციდივის ან მეტასტაზირების ნიშნები. გლუკოზის ტოლერანტობის ტესტით გამოვლინდა მსუბუქი გლუკოზის მეტაბოლიზმის დარღვევა, რომელიც კონტროლდებოდა დიეტით. პაციენტი რჩება დაკვირვების ქვეშ, რეკომენდებულია ყოველწლიური CT კვლევა და სიმსივნის მარკერების მონიტორინგი მომდევნო 5 წლის განმავლობაში.

საკვანძო სიტყვები: შერეული სეროზულ-მუცინური ცისტური ნეოპლაზია, პანკრეატექტომია, სპლენექტომია, ლაპარასკოპია.