

Heterotopic pancreatic tissue in the gallbladder. Two case reports and brief review of the literature

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SUMMARY: Heterotopic pancreatic tissue in the gallbladder. Two case reports and brief review of the literature.

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Heterotopic pancreas tissue in the gallbladder is a rare benign condition with no clinical relevance and found incidentally in most cases. Only 28 cases of heterotopic pancreas are reported until 2007 in the worldwide literature. The preoperative diagnosis is very hard, so that it could be considered in differential diagnosis with other benign and malignant disease of gallbladder and biliary tree. The surgical approach for the excision of a undefined lesion and the histological identification is a correct procedure in suspect case. We report 2 cases of heterotopic pancreatic tissue of the gallbladder.

RIASSUNTO: Eterotopia pancreatica della colecisti. Due casi clinici ed una breve revisione della letteratura.

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La localizzazione ectopica pancreatica nella colecisti è una condizione rara e benigna, senza rilevanza clinica e spesso di rilievo occasionale dopo intervento di colecistectomia. Nella letteratura internazionale sono riportati solo 28 casi fino al 2007. La diagnosi preoperatoria è difficile per cui, di fatto, tale patologia entra in diagnosi differenziale con altre patologie benigne e maligne della colecisti e dell'albero biliare. Nei casi sospetti l'approccio chirurgico con escissione della colecisti ed esame istologico rappresenta una corretta procedura. Riportiamo due casi clinici operati nel nostro Dipartimento.

KEY WORDS: Heterotopic pancreas - Gallbladder.
Eterotopia pancreatica - Colecisti.

Introduction

Heterotopic pancreas is defined as the presence of pancreatic tissue, histologically identified, without any anatomic connection or vascular continuity with the main body of the gland. The most frequent heterotopic pancreas location are: gastric wall (25-60%), duodenum (25-35%), and upper jejunum, ileum, ampulla of Vater, Meckel's diverticulum and spleenⁱ, with higher incidence in male (sex ratio 3:1)ⁱⁱ. Aberrant pancreatic tissue in the gallbladder wall is a very rare case. Heterotopic pancreas of the gallbladder has no clinical relevance, because it is

absolutely a benign condition, so it is found incidentally in most cases.

Only 28 cases of heterotopic pancreas are reported until 2007 in the worldwide literature (1). We report two cases of heterotopic pancreas located at gallbladder.

Case reports

Case 1

A 53 year-old woman was referred to our department of general surgery, complaining of chronic epigastric and left upper quadrant pain and dyspepsia. No pancreatitis episodes were reported in the clinic history of the patient. On physical examination, the right upper abdomen was tender with a slight positive Murphy's sign. Usual preoperative assessment was performed with chest x-ray, electric cardiograms and blood tests. The laboratory tests revealed normal levels of bilirubin, transaminases SGOT and SGPT, and abnormal sieri values of Alkaline Phosphatase = 253 U/l, Amylase = 145 U/l, Lipase = 111 U/l, Cholesterol = 242 mg/dl. An upper abdominal ultrasound revealed a 6 mm "adenomioma" at posterior wall of gallbladder fundus without any stones. Based on the diagnosis of chronic cholecystitis and for the suspicious nature of the polyp at gallbladder fun-

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dus, a laparoscopic cholecystectomy was performed. The examination showed macroscopically a gallbladder, 7 cm length, with quite thickened wall and green coloured mucosa; Microscopic examination revealed chronic cholecystitis with exudative area, and heterotopic pancreatic tissue at gallbladder fundus. The heterotopic pancreas showed both the exocrine components, ducts and acini, but no signs of endocrine elements (Figs.1 a,b,c). Patient was discharged 2 days after the operation without any complication. The final diagnosis was thereby established as chronic cholecystitis with heterotopic pancreas tissue.

Case 2

A 51 years old female, presented to the general surgery department with abdominal pain localized at bright upper quadrant and radiated to her back and right scapula. The patient suffered of frequent episodes of slight abdominal pain and dyspepsia since 2 years ago. The patient was obese (BMI 31,7 Kg/m²), with a positive Murphy's sign and negative Bloomberg's sign, and with fever (37,8 °C). The laboratory tests showed abnormal levels of SGOT 61 U/L, SGPT 115 U/L, cholesterol 271 mg/dl. At transabdominal ultrasound examination of liver and biliary tree the images were unhelpful due to the obesity and to the considerable intestinal gas. As a diagnose

of acute cholecystitis was made, the patient was operated on with laparoscopic approach and colecistectomy was performed. The patient was discharged home 2 days after. The final diagnosis was established by histological examination (Fig. 1d). At macroscopic examination the gallbladder had a length of 5 cm with fairly thickened wall and green coloured mucosa. The microscopic observation showed heterotopic pancreatic tissue characterized by pancreatic acini without ducts or Langerhans islets.

Discussion

The heterotopic pancreas is the second pancreas abnormality for frequency after the "pancreas divisum" (1), but the gallbladder localization is extremely rare. In fact, in a study by Mayo clinic the heterotopic pancreas located in the gallbladder wall was found in one out of 212 heterotopic pancreas cases(1, 3, 4). The frequency of heterotopic pancreas ranges from 0,55 to 13,7% in the autopsies, but clinically (1, 5) heterotopic tissue has been di-

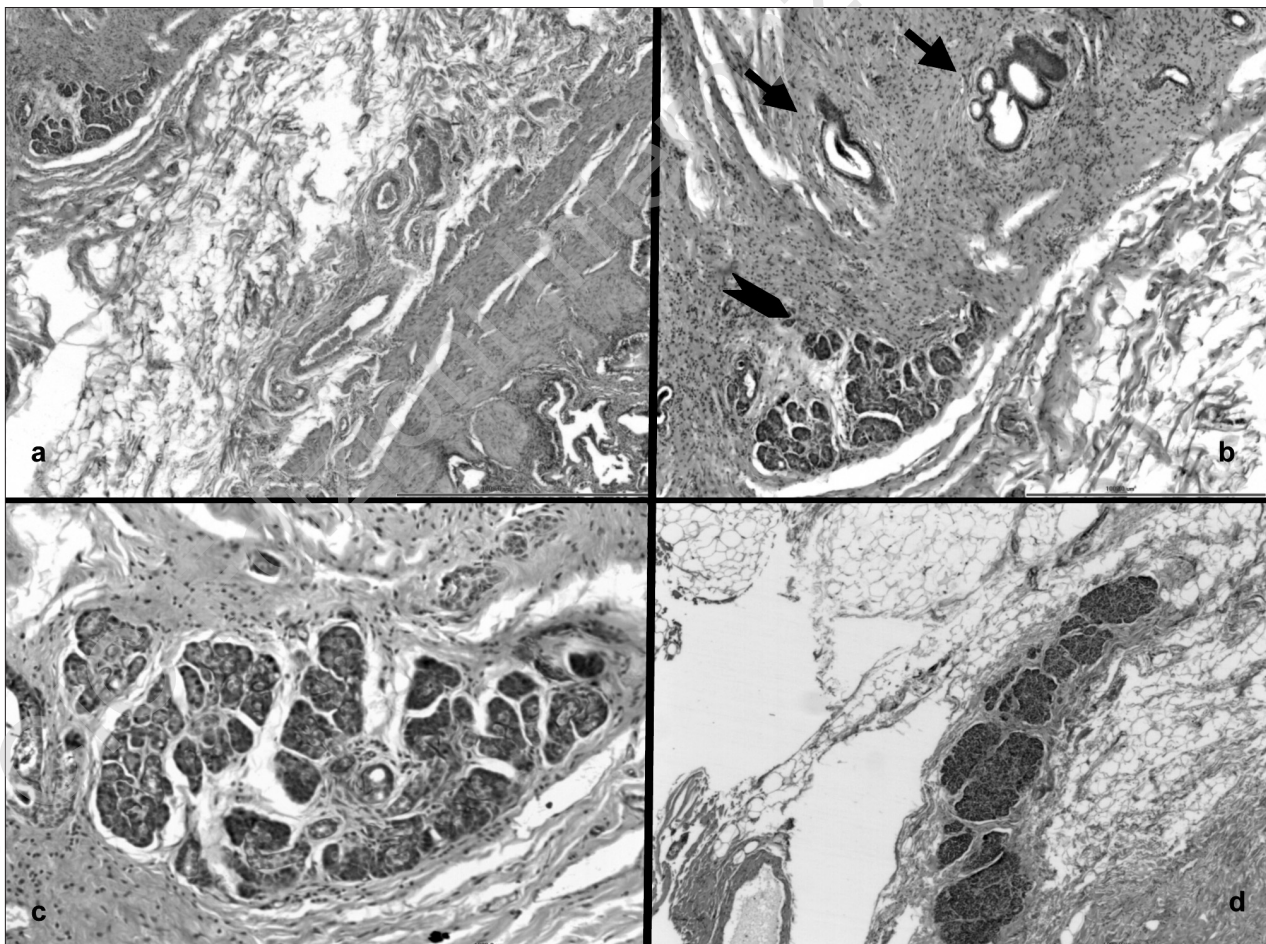


Fig. 1 - Case 1 - a) lobules of pancreatic tissue are localized in the perimuscular connective tissue; b) arrow head indicates acinar component while arrows indicate ductal components. No islets of Langerhans are evident (Haematoxylin and Eosin, 2,5x); c) PAS stain (Periodic Acid-Schiff) highlights the zymogen granules of the acinar component, 10x.
Case 2 - d) pancreatic acini are evident in the perimuscular connective tissue. Neither ductal component nor islets of Langerhans are present (haematoxylin and eosin, 2,5x).

discovered in 0,2% patients undergone surgical operation. In particular, the heterotopic pancreatic tissue located in the gallbladder wall is discovered only in 1% of patient with generic heterotopic pancreatic tissue (6).

Histology shows various degrees of excretory ducts, exocrine glands and islets of Langerhans within the heterotopic tissue, and as the main pancreas it could be affected by pathologic manifestation such as acute pancreatitis, cyst and abscess formation, pancreatic cancer, and islet cell tumor (1, 7, 8). The heterotopic pancreatic tissue has an unknown origin, but there are some hypothesis about its genesis. The first one suggests the separation between the future heterotopic tissue from the primitive pancreas during the embryonic rotation phase; the second one suggests an abnormal transportation of the pancreatic tissue by the longitudinal growth of the small bowel during the growth of the ventral pancreatic bud. More considerations and a lot of studies should be needed for the determination of the extracellular signaling and intracellular transcriptional factor networks that allow the development, the growth, and the persistence of heterotopic pancreatic tissue in the gallbladder (7, 9).

The first case of heterotopic pancreatic tissue was described by Schultz in 1727, while in 1859 Klob defined the morphologic histology (1). The first case of heterotopic pancreas in the gallbladder was described by Poppi in 1916, and until 2007 only 28 cases are reported in the literature (1,9). The higher incidence of heterotopic pancreas located in the gallbladder is in female sex, with age between fourth to fifth decade of life (5). In half of the reported cases worldwide, the location of the ectopic pancreas is close to the neck of the gallbladder (5), while in our patient the pancreatic tissue was located in the fundus region.

The pancreatic tissue in the gallbladder is very rarely symptomatic. In most reported cases, it is an incidental pathological findings, but few symptomatic gallbladder diseases due to heterotopic pancreas have been reported (5,8,10). The clinical findings in most cases suggest cholecystopathy, gallstones-associated disease, but the biochemistry is usually negative for pancreatitis. Anyway, in the first case we found abnormal value of lipase and amylase sieric levels, as it is probably the result of heterotopic pancreatic tissue inflammation. The heterotopic pancreas in the gallbladder is a benign condition but sometimes it could be a cause of some pathological findings, such as cholecystopathy, or perforation of gallbladder wall and peritonitis, or chronic pancreatitis of the ectopic tissue, or haemorrhage. The ectopic pancreas located in the cystic duct or in the neck region could promote hydrops of the gallbladder or obstruction of bile ducts.

There are no laboratory test or instrumental examination, with enough specificity and sensibility for this rare condition. The diagnosis is very hard, and also with the ultrasonography a differential diagnosis with gallstones,

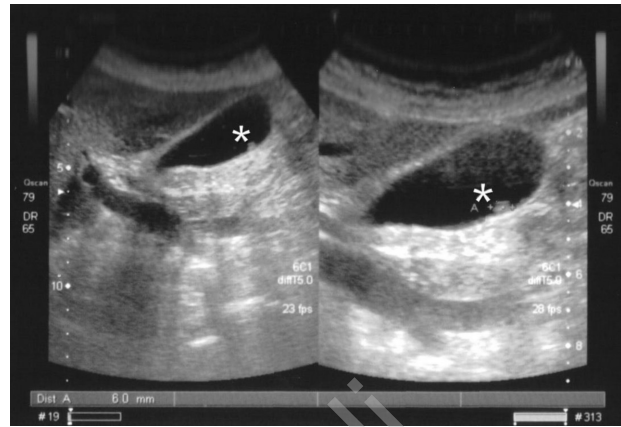


Fig. 2 - Abdominal ultrasonography shows a hypoechoic tissue (6 mm) in the gallbladder fundus with diagnostic suspicious of adenomyoma.

cholelithiasis, cholecystitis, adenomyoma, carcinoma, cholesterol polyps and other lesions, is very difficult. The ultrasounds (US), also with high resolution, cannot help differential diagnosis (1,2,5,6), as well as endoscopic ultrasound, CT, magnetic resonance (10), and MRCP (11). The main presentation of heterotopic pancreatic tissue in the gallbladder is a lesion with the same echogenicity of the pancreas, not producing any shadow, and not mobile. The dimension can be variable since some millimetres to centimetres (1,10). In our first case the ultrasonography images were confused with an adenomyoma located at gallbladder fundus. Gallstones can be frequently associated to heterotopic pancreatic tissue in the gallbladder and their presence represents a very hard condition for differential diagnosis at the ultrasound examination especially.

Only histology of the specimen can confirm the diagnosis and the therapy of election for the symptomatic heterotopic pancreas is the surgical excision (1). As in our patients-every case described worldwide with heterotopic pancreas in the gallbladder was symptomatic (acute cholecystitis) and patient they became asymptomatic after surgical excision. Some studies and reviews (12) of the literature reveal adenocarcinomas arising from heterotopic pancreas located in the gastrointestinal tract. However, these patients have a slightly better prognosis than patient with the common adenocarcinoma of the pancreas and no case of metastatic diffusion is reported yet.

In conclusion, heterotopic pancreas in the gallbladder is a benign condition, but the possible complications need attention. The preoperative diagnosis is very hard, so it could be considered in differential diagnosis with other benign and malignant disease of gallbladder and biliary tree. The surgical approach for the excision of a undefined lesion and the histological identification is a correct procedure in suspect case. More studies are required for a better knowledge of this extremely rare condition.

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