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## Case Series

# Ectopic Pancreatic Tissue Adherent to the External Gallbladder Wall

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## Keywords

Gallbladder · Ectopic pancreatic tissue

## Abstract

Heterotopic pancreatic tissue can be found in the gastrointestinal tract, with the stomach and small bowel being the most common sites of localization. The gallbladder is seldom affected. Here, we report 2 cases of ectopic pancreas within the fatty tissue adherent to the organ wall. Both cases concerned young women (31 and 36 years old) who were treated with a laparoscopic cholecystectomy due to persistent abdominal symptoms thought to be related to chronic cholecystitis. Pathological examination revealed the presence of ectopic pancreatic tissue type 1.

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## Introduction

The presence of ectopic pancreatic tissue in an anatomic place other than the main pancreas is an embryologic abnormality. Such an ectopic tissue can most often be found in the

stomach and small and large bowel, while, less commonly, it has been reported in Meckel's diverticulum and in the esophagus, spleen, liver, and lung [1]. Although the first report in PubMed goes back to 1946 [2], heterotopic pancreas was first described in 1727 by Jean Schultz, while von Heinrich [3] provided the first classification of the lesion in 1909.

The gallbladder is a rare anatomic site of ectopic pancreatic tissue development, as till 2009, less than 35 cases had been reported in the literature [4]. Another 3 cases have been more recently reported [5–7].

Here, we report 2 cases of ectopic pancreatic tissue that was identified within the fatty tissue surrounding the gallbladder of young women who underwent cholecystectomy for gallbladder-related symptomatology.

### Case 1

A 31-year-old woman presented with epigastric and back pain, accompanied with nausea after meals. These symptoms persisted for a year and a half before her admission to our hospital. Physical examination showed a slight sensitivity of the upper right quadrant of the abdomen during palpation. Laboratory tests showed normal values of white blood cells, hemoglobin, platelet counts, serum and urine amylase, as well as of coagulation-related parameters. Liver biochemistry revealed normal SGOT/SGPT and ALP but abnormally high levels of direct bilirubin (0.3 mg/dL) and of  $\gamma$ -GT (6 U/L). Tumor epithelial markers (CEA, Ca125, Ca15-3, and Ca19-9) and  $\alpha$ -fetoprotein were normal. Although abdominal ultrasonography revealed that the gallbladder was normal in size (5 × 2 cm), a small nodule (0.5 cm in diameter) was evident on its wall. Laparoscopic cholecystectomy was performed.

Macroscopic assessment of the specimen showed a gallbladder with the dimensions of 5 × 2 cm, with 1 white lesion of 0.4 cm. Microscopical examination revealed findings compatible with chronic cholecystitis and Rokitsansky-Aschoff sinuses. Regarding the nodule described above, histology confirmed the presence of ectopic pancreatic tissue (Fig. 1a, b). It consisted of acini, ducts and Langerhans islets and was located in the fatty tissue surrounding the gallbladder. The lesion was adherent to the external organ wall.

Immunohistochemical examination of the ectopic tissue showed CK19 (Fig. 1c), CK7, and Ca19-9 positivity of the ducts. Acinic cells were positive for chymotrypsin and trypsin. Synaptophysin, chromogranin, and somatostatin were expressed by Langerhans islets (Fig. 1d). CEA and Ca125 were not expressed. Details on the antibodies and dilutions are reported in Table 1.

### Case 2

A 36-year-old obese (140 kg) woman, with a history of diabetes mellitus, was admitted to our hospital due to nonspecific abdominal pain after fatty meals. Physical examination showed a slight sensitivity of the upper right quadrant of the abdomen during palpation. All hematological and biochemical laboratory tests and tumor markers were within the normal limits. Ultrasound examination of the upper abdomen showed a slight enlargement of the

gallbladder (8 × 3 cm) with presence of stones. Laparoscopic cholecystectomy was performed, and the patient left the hospital without any postoperative complications.

Macroscopic inspection showed an enlarged gallbladder (8 × 3 cm), while microscopic examination revealed chronic cholecystitis and Rokitansky-Aschoff sinuses. Moreover, ectopic pancreatic tissue (0.9 cm in diameter) was detected in the fatty tissue surrounding the gallbladder. Again, the lesion was adherent to the external gallbladder wall. Histopathological appearance and immunohistochemical features were identical to the ones reported for case 1.

## Discussion

Heterotopic pancreas is a rare entity. Most frequently, it appears in the gastrointestinal tract, with the stomach and small bowel/duodenum being the most frequent sites [1, 8]. The actual incidence of ectopic pancreatic tissue in the gallbladder is unknown, as a lack of clinical symptoms may prevent the diagnosis. In a recent study from China by Zhang et al. [9], examining 184 cases of ectopic pancreas, only 1 case was described in the gallbladder (0.5%). In a study from the Mayo Clinic on 212 cases of ectopic pancreatic tissue, only 1 case concerned the gallbladder and 1 the common bile duct [10]. It is unclear, however, taking into account the description available from the reported papers, whether the fatty tissue around the gallbladder was affected in any of the described cases.

Most patients with ectopic pancreatic tissue have nonspecific symptoms. These include pain in the upper abdomen, anorexia, vomiting after meals, and weight loss. Anemia or melena has been also reported. Nevertheless, such symptoms are, presumably, a result of a coexisting lithiasic cholecystitis. In both our cases, we histopathologically confirmed the presence of chronic cholecystitis. As gallbladder stones were found only in one of our cases, inflammation due to exocrine activity of the ectopic tissue could underlie the symptomatology. Indeed, Sato et al. [11] reported increased amylase and lipase levels in the bile of such patients. Regarding the reported association of ectopic pancreatic tissue with the development of dysplasia or cancer [12], none of our 2 patients showed any evidence of cellular atypia.

Concerning the classification of ectopic pancreatic tissue, the initial classification by von Heinrich [3] was subsequently modified by Gaspar Fuentes et al. [13] in 1973. It describes 4 different types of pancreatic heterotopia, as follows:

- 1 Type 1: presence of acini, ducts, and islet-like pancreatic gland.
- 2 Type 2: canalicular variant with pancreatic ducts.
- 3 Type 3: exocrine pancreas with acinar tissue.
- 4 Type 4: endocrine pancreas with cellular islets.

Both our patients were diagnosed with type 1, with evidence of all components of the pancreas.

Usually, the ectopic tissue is small, but it can reach up to 3 cm in dimension [14]. Our 2 cases showed dimensions of 0.4 and 0.9 cm. As far as the location is concerned, it is usually found in the submucosa and by imaging techniques is difficult to differentiate radiologically from gastrointestinal stromal tumor [15]. In both our cases, however, ectopic tissue was

located in the fatty tissue around the gallbladder, adherent to its wall, which is an unusual location.

It can be concluded that, although ectopic pancreatic tissue can be found in the gallbladder wall, the adjacent fatty tissue is also a possible location. Radiological imaging of the lesion cannot provide a diagnosis, as it can easily be interpreted as a tissue of neoplastic origin. Removal of the gallbladder should be performed to confirm the diagnosis and to eliminate the symptomatology related to cholecystitis.

### Statement of Ethics

Written informed consent was obtained from the patients to use surgical materials for research and educational purposes.

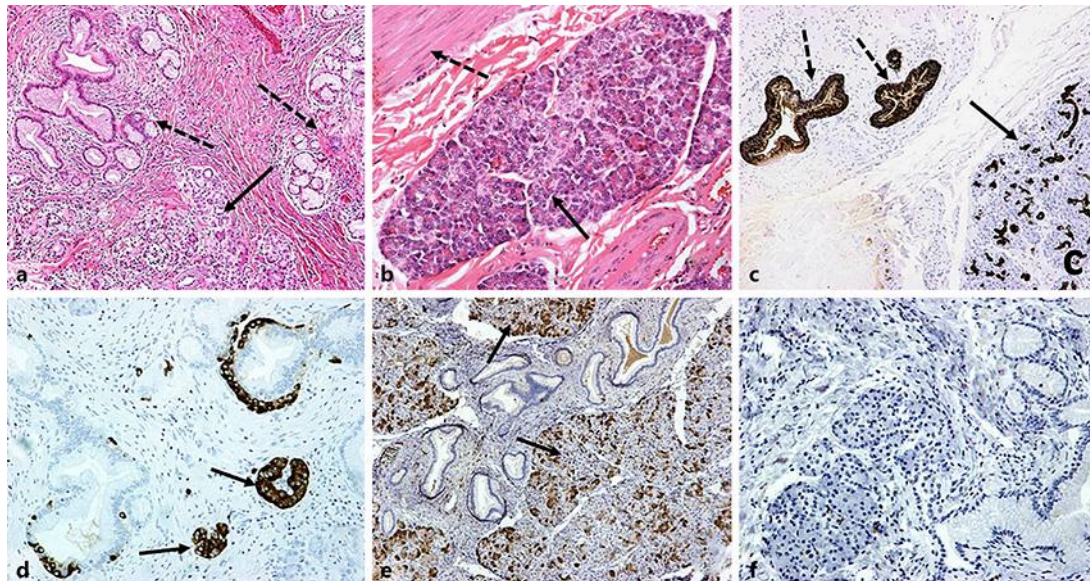
### Disclosure Statement

The authors have no conflicts of interest to declare.

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**Fig. 1.** **a** HE staining showing the gallbladder glands (dashed arrows) and the ectopic pancreatic tissue (black arrow); magnification  $\times 10$ . **b** HE staining showing the gallbladder muscularis layer (dashed arrow) and the ectopic pancreatic tissue (black arrow); magnification  $\times 20$ . **c** Immunohistochemical staining for cytokeratin 19 showing reactivity of the gallbladder glands (dashed arrows) and of the ectopic pancreatic tissue ducts (black arrow); magnification  $\times 20$ . **d** Immunohistochemical staining for chromogranin showing reactivity of the Langerhans islets in the ectopic pancreas; magnification  $\times 20$ . **e** Immunohistochemical staining for chymotrypsin showing reactivity of the acinar cells (arrows) in the ectopic pancreas; magnification  $\times 10$ . **f** Immunohistochemical staining for CEA showing lack of reactivity; magnification  $\times 20$ .

**Table 1.** Antibodies and dilutions used for immunohistochemistry

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CK7 (mouse monoclonal, Menarini, clone CV-TL 12/30, dilution 1/200)
CK19 (mouse monoclonal, BioGenex, clone RCK108, dilution 1/100)
Ca19-9 (mouse monoclonal, Dako, clone 1116-NS-19-9, dilution 1/50)
Ca125 (mouse monoclonal, Dako, clone M11, dilution 1/20)
CEA (mouse monoclonal, Menarini, clone 12-140-10, dilution 1/50)
CD56 (rabbit monoclonal, Menarini, clone MRQ42, dilution 1/200)
Chromogranin (mouse monoclonal, Thermo Fisher Scientific, clone LK2H10, dilution 1/800)
Synaptophysin (rabbit monoclonal, Menarini, clone MRQ40, dilution 1/300)
Somatostatin (rabbit polyclonal, Dako, clone A0566, dilution 1/200)
$\alpha_1$ -Antitrypsin (polyclonal rabbit, Dako, dilution 1/6,000)
$\alpha_1$ -Antichymotrypsin (polyclonal rabbit, Dako, dilution 1/100)

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