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Heterotopic pancreatic tissue in gallbladder

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ABSTRACT

The heterotopic pancreas (PH) is the atypical presence of pancreatic tissue without any anatomic or vascular continuity with the pancreas. PH is a rare condition that can be observed at any level of the gastrointestinal tract and even in other organs. Histopathological characterization of PH allows surgeons to distinguish it from other lesions. Although it is usually a benign and asymptomatic disease, it can occasionally cause complications (obstruction, hemorrhage, inflammation, or malignant transformation). In conclusion, localization in the gallbladder in the few cases of PH is very rare. We present two cases in which, after cholecystectomy indicated by other causes, in the pathological study of the surgical specimen, type 2 pancreatic tissue was found according to the Heinrich classification.

Key words: *Gallbladder, pancreatic heterotopia, heterotopic pancreatic tissue, heterotopic pancreas, ectopic pancreas, pancreatic choristoma*

Introduction

Pancreatic heterotopia (PH), also called ectopic pancreas or pancreatic choristoma, is defined as the existence of pancreatic tissue in an abnormal location, without vascular or neuronal anatomical continuity with the pancreas [1].

A PubMed literature search was performed up until February 1, 2015 with the following search strategy: (gallbladder) AND ((heterotopic pancreas) OR (choristoma pancreas) OR (pancreatic heterotopia) OR (heterotopic pancreatic tissue) OR (ectopic pancreas)); the search located 64 relevant papers. References of these papers were also investigated.

Below, we describe two cases of PH in gallbladder, diagnosed incidentally during histological examination after cholecystectomy for other indications. We discuss the characteristics of this entity with regard to etiology and treatment.

Case Presentation

Case 1

The subject was a 21-year-old female, without relevant medical history, who reported repeated episodes of epigastric abdominal pain. Abdominal palpation was normal. The analytical study did not reveal abnormalities; liver function was normal, and abdominal ultrasound identified stones in the gallbladder, but no other alterations. Due to episodes of biliary colic and the presence of cholelithiasis, we scheduled a laparoscopic

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cholecystectomy that revealed a distended gallbladder with no other pathological intraoperative findings. There were no postoperative complications.

Gross pathologic examination revealed a gallbladder measuring 9.5 x 3 cm, with congestive surface and lumen occupied by dense yellowish bile and multiple stones.

Microscopic findings were: at the gallbladder neck measuring 1 inch and located in the subserosa, we observed well-defined pancreatic cells with typical histological features corresponding to Heinrich's classification type 2 (Figure 1).

Case 2

The subject was a 43-year-old female with previous medical history of hyperthyroidism who consulted the Emergency Department for epigastric pain and vomiting. Physical examination revealed abdominal pain localized in the right upper quadrant. The analytical studies showed: leukocytes 11.33x1000 µl, normal hepatic profile, and C reactive protein 25 mg/dl. Abdominal ultrasound showed thickened gallbladder wall, biliary sludge, and a small amount of free perivesicular fluid. Sonography Murphy sign was positive. With the diagnosis of acute cholecystitis, emergency surgery was performed. A large amount of bile was found in the abdominal cavity (microbiology: sterile fluid), and the gallbladder was distended, with very thick walls. Cholecystectomy was performed, and the postoperative course was uneventful.

Macroscopic pathologic examination revealed a gallbladder measuring 10 x 5 x 3 cm with a smooth inner surface. The content was hemorrhagic with some biliary sludge, and an edematous thick wall of variable size (5-15 mm) with transmural necrosis was observed. Pancreatic acinar tissue and ducts were attached to the gallbladder wall at the vesicular neck level. The patient was defined as type 2 according to Heinrich's classification (Figure 2).

Discussion

PH is a rare entity that may be observed at any level of the gastrointestinal tract, and even outside it. It is usually discovered incidentally [2]. PH can be distinguished from other entities by histopathological characterization. It is usually benign and asymptomatic, but occasionally leads to obstruction, hemorrhage, inflammation, or neoplasm [3].

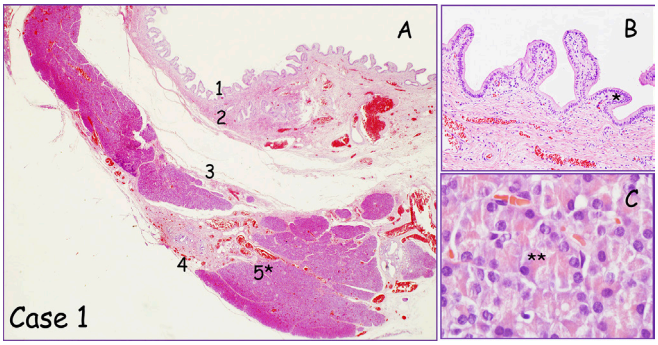

Figure 1. Heterotopic pancreatic tissue in the gallbladder (Hematoxylin eosin staining).
A. Panoramic view showing the normal layers of the gallbladder including the mucosa (1), (surface epithelium and lamina propria) smooth muscle (2), subserosa connective tissue (3), and serosa (4). The heterotopic pancreatic tissue was found at the subserosa level (5) as lobules of normal-appearing pancreatic acinar structures.
B. High magnification of normal gallbladder surface mucosa lined by columnar cells*.
C. Acinar cells are spherically arranged and contain abundant granular eosinophilic cytoplasm.**

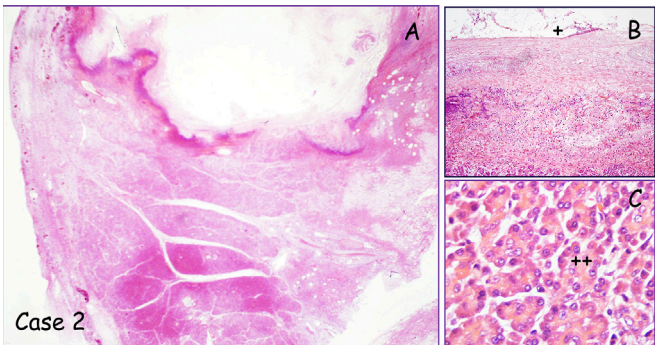

Figure 2. Heterotopic pancreatic tissue in the gallbladder with acute cholecystitis (Hematoxylin eosin staining).
A. Panoramic view showing the necrotic gallbladder wall with the heterotopic pancreatic tissue at the subserosa level
B. In this case, the epithelium in the damaged gallbladder was lost (+) with acute inflammation in the lamina propria.
C. Acinar cells with abundant granular eosinophilic cytoplasm arranged in small nests.(++)

PH is identified in the gastrointestinal tract in between 0.5 and 13.7% of autopsy series and in 0.2% of laparotomies [3]. The most common sites are the stomach (25-60%), duodenum (25-30%), jejunum, and Meckel's diverticulum; it is rarely found in the ileum, gallbladder, bile ducts, splenic hilum, or liver [4].

PH is the second most common anomaly of the pancreas after pancreas divisum [2]. The first author to describe heterotopic pancreatic tissue was Jean Schultz in 1727; the first histological confirmation was performed by Klob in 1859. In 1916, Otschkin reported the first case of heterotopic pancreas in the gallbladder [5].

PH can occur at any age, although 50% of cases are found between the fourth and sixth decades of life [6]. Men are affected between 2-5 times more frequently

than women. However, the incidental pathological diagnosis in the gallbladder is higher in female patients, probably due to the greater frequency of gallstones in women [1].

The etiology of PH is not clearly established, but there are three hypotheses. The first is that it occurs during the embryonic stage, since part of the pancreatic tissue becomes separated during rotation: the pancreas develops during the fifth week of endodermal budding [1]. Another widely accepted hypothesis is that part of the pancreatic tissue is transported by a rotation of the rudimentary pancreatic duct, penetrates the intestinal wall, and is carried by the longitudinal growth of the intestines. The third theory is based on anomalies in the Notch signaling system, which is responsible for the differentiation in the development of the foregut endoderm [7].

Most cases are asymptomatic. However, 30-40% may have nonspecific gastrointestinal symptoms: abdominal pain, gastrointestinal bleeding, and intestinal occlusion, among others [1]. PH may also present similar complications to those that occur in the normal pancreas, including acute or chronic pancreatitis, calcifications, abscess, neuroendocrine tumors (insulinomas or gastrinomas), cystic degeneration, and, on rare occasions, malignant transformation. [4]

Macroscopically, PH in the gallbladder can range in size from millimeters to centimeters [1]. Fifty per cent are located in the neck [4], as in our first case. Microscopically, PH in the gallbladder is intramural. Fifty per cent of PH contain endocrine or exocrine tissue that is confirmed by immunohistochemical staining [6]. Heinrich classified PH into three groups according to the presence or absence of exocrine and endocrine tissue (Table 1) [8-10]. Type 1 contains acini, islets, and ducts; type 2, acini and ducts; and type 3, channels. Both cases reported here are classified as type 2.

Our diagnosis was the result of the post-operatory histological study. Preoperative diagnosis of PH is rare. Imaging methods such as computed tomography, MRI, or ultrasound cannot confirm diagnosis. Only endoscopic ultrasound appears to be useful in the assessment of submucosal lesions of the digestive tract [1]. The definitive diagnosis is histological and is usually made in the postoperative period [4]. When PH is located in the gallbladder, the treatment of choice is cholecystectomy in order to avoid complications.

Table 1. Classification of ectopic pancreas (Von Heinrich) [10,16].

Type 1	Ectopic tissue with acini, ducts, and islets of Langerhans (exocrine and endocrine tissue).
Type 2	Ectopic tissue with incomplete or lobular (select multiple acini and ducts) elements. Endocrine elements are absent.
Type 3	Proliferating ducts ectopic tissue (called adenomyoma). Missing both exocrine and endocrine elements.

In conclusion, PH is a rare entity, and its location in the gallbladder is even rarer. We present two cases in which, during histological study of the surgical specimen after cholecystectomy for other causes, Heinrich's classification type 2 (acini and ducts) was assessed. PH was diagnosed as an incidental finding on pathology.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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