

CASE REPORT

Heterotopic Pancreas of the Gallbladder Associated with Chronic Cholecystitis and High Levels of Amylasuria

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ABSTRACT

Context Heterotopic pancreas of the gallbladder is an extremely rare entity, especially when pancreatic tissue appears histologically with an exclusively exocrine structure. **Case report** We report the case of a 35-year-old man who presented with symptoms of acalculous gallbladder disease with high levels of amylasuria. Immunohistochemical analysis of the surgical specimen of the cholecystectomy revealed pancreatic tissue at the gallbladder wall. **Conclusions** Heterotopic pancreatic tissue is a rare pathological finding in the gallbladder. It requires consideration and sensitization in the differential diagnosis of acalculous gallbladder disease, which can explain hyperamylasuria in cases of unknown origin.

INTRODUCTION

Heterotopic pancreas is defined as the presence of pancreatic tissue which lacks anatomic and vascular continuity with the main pancreas [1]. In 90% of reported cases, heterotopic pancreas has been found in the upper gastrointestinal tract [2, 3, 4]. In addition, other locations of aberrant pancreatic tissue have occasionally been detected in the spleen, omentum, mediastinum, lungs, umbilicus, gallbladder and bile ducts [3, 5, 6, 7].

Heterotopic pancreas in the gallbladder is an extremely rare entity. Only thirty-three cases have been reported in the literature [2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16]. In the majority of cases, the heterotopic pancreas was an incidental finding following a cholecystectomy performed for symptomatic gallbladder disease.

We report the case of heterotopic pancreas which presented with clinical symptoms of cholecystitis and high levels of amylasuria.

CASE REPORT

A 35-year-old man was admitted to the hospital complaining of anorexia, nausea and abdominal pain.

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The onset of the pain was insidious, starting 48 hours previously and gradually worsening. On physical examination, the abdominal pain was located in the right upper quadrant. Palpation of the abdomen revealed tenderness and guarding in the right upper quadrant, and the Murphy sign was positive.

Furthermore, examination of the other systems did not disclose pathological findings. The patient's temperature was 37.2°C. Laboratory data other than amylasuria (1,030 IU/L; reference range: 0-500 IU/L) were within the reference limits. The ultrasonographic study showed a small well-defined, non-mobile echogenic structure of 4 mm in diameter attached to the wall of the gallbladder. The features of the echogenic structure were suggestive of a gallbladder polyp (Figure 1) but not of a gallstone. Therefore, the most likely diagnosis was a gallbladder polyp and a laparoscopic cholecystectomy was carried out.



Figure 1. An echogenic non-mobile structure attached to the gallbladder wall: features suggestive of a polyp.

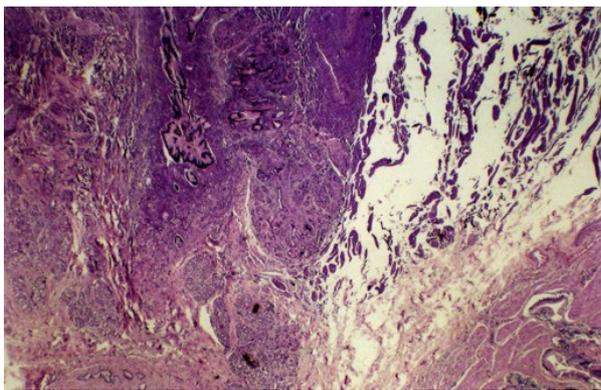


Figure 2. Ectopic pancreas in the gallbladder. Pancreatic ducts, acinar component and gallbladder epithelium (H&E; original magnification x25).

On macroscopic examination, the gallbladder was 70 mm long and 30 mm wide with a mural thickness of 60 μ m. Gallstones were not present in the gallbladder lumen. An 8 mm intramural, yellow nodule was found in the body of the gallbladder. Its consistency was firm and it was protruding under the serosa.

On microscopic examination of the gallbladder, a mixed chronic inflammation in the lamina propria, submucosa and muscular wall was found. The nodule showed ectopic pancreatic tissue, consisting of acini, ducts without any connection to the gallbladder lumen, and no islet cells (Figure 2).

Immunohistochemical analysis was performed using a series of immunologic markers to identify this heterotopia. The ductal epithelium was surrounded by a smooth muscle component and exhibited a typical pancreatic duct-like immunophenotype, characterized by immunoreactivity to cytokeratins 7, 8, 18, 19 and to carbohydrate antigen (CA) 19-9. No reactivity against CEA, vimentin and CK20 was found. The pancreatic acini, composed of polygonal cells arranged in a single layer, with typical exocrine differentiation, were positive for alpha-1-antitrypsin and alpha-1-chymotrypsin (Figure 3). The other immunohistochemical markers, such as somatostatin, insulin and chromogranin A, were negative for endocrine activity.

A subsequent diagnosis of chronic cholecystitis with heterotopic pancreas was reached. The patient's postoperative course was uneventful and he was discharged on the 3rd postoperative day. After a follow-up of three months, the patient was asymptomatic without any discomfort.

DISCUSSION

Heterotopic pancreas is believed to result from early separation of the pancreas during rotation of the gastrointestinal tract in the embryonic stage. There is not a universally accepted theory as to the exact origin of this aberrant tissue [3, 4, 6].

Heterotopic pancreas can be found in all age groups. It is more frequent in men than in women [2, 7]. In one

series of 212 cases of aberrant pancreas, only one case was found to be located in the gallbladder [4].

Heterotopic pancreas in the gallbladder presents as an exophytic growth and may be similar to polypoid lesions or as yellow-colored nodules, varying in dimension from a few millimeters to 4 cm. Fifty percent of heterotopic pancreatic tissue arises in the neck of the gallbladder [2, 3, 7, 8, 9, 14]. In our case, the heterotopic pancreas was subserosal. It is less common and is found in only 10% of cases. The submucosal presentation is most common and is found in 73% of cases [16].

Our histopathological examination revealed a heterotopic pancreas made up of exocrine acinar and ductal components without islet cells, corresponding to incomplete heterotopia. Islets of Langerhans are identified in only one-third of cases [16].

An immunohistochemical study was carried out to identify and characterize the endocrine and exocrine activity in the ectopic pancreas situated in the gallbladder. The literature contains only a few reports concerning the immunohistochemical profile [7, 9]. We used an ample variety of immunologic markers. Vimentin is a marker of pancreatic precursor cells and has been used by Ko *et al.* [17] as expression in proliferative duct cells. However, Beltran and Barria [7], and Pilloni *et al.* [9], reported the negative immunoreactivity in pancreatic duct cells to vimentin as happened in our case. Tubular and epithelial structures were immunoreactive to cytokeratins 7, 8, 18, and 19, and to CA 19-9. Exocrine activity was identified by immunoreactivity to alpha-1-antitrypsin and alpha-1-chymotrypsin but endocrine activity was not.

Most patients with heterotopic pancreas are asymptomatic, and the heterotopic tissue is found incidentally at histological exam following a cholecystectomy. Heterotopic pancreas in the gallbladder is rarely symptomatic. The manifestation of symptoms is largely associated with acute or chronic cholecystopathy, with or without gallstones [5, 6, 7, 13, 14, 16]. Qizilbash [12], reported a case in which the

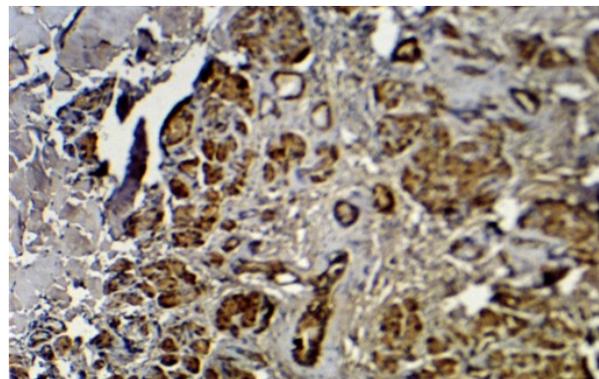


Figure 3. Pancreatic tissue was reactive to alpha-1-chymotrypsin, demonstrating exocrine activity (alpha-1-chymotrypsin; original magnification x100).

cause of acute symptoms was the inflammation of the heterotopic pancreatic tissue, resembling acute pancreatitis.

Inceoglu *et al.* [11] reported a case of heterotopic pancreas in the cystic duct with hydrops of the gallbladder and chronic pancreatitis due to ectopic tissue. In three cases similar to our case, heterotopic pancreas has been found to stimulate cholecystopathy with all symptoms disappearing after a cholecystectomy. Malignant transformation of an ectopic pancreas may occasionally occur [10].

The mechanism whereby this aberrant tissue may produce various symptoms is unclear. Previous studies [18] have suggested that active pancreatic enzymes, such as amylase and trypsin, refluxing into the biliary tract and gallbladder lumen might produce inflammation, spasm and biliary symptoms in patients without gallstones, and acute cholecystitis in patients with gallstones [6, 7, 13, 16, 18].

In our case, we could hypothesize that the cause of gallbladder symptomatology may have been due to the continuous secretion of active pancreatic enzymes, mainly amylase, directly into the gallbladder lumen, causing damage to the epithelium and producing symptoms associated with chronic inflammation.

The preoperative diagnosis of an aberrant pancreas in the gallbladder is impossible using the imaging exams currently available. Ultrasonography and computed tomography cannot distinguish an aberrant pancreas in the gallbladder from other lesions, such as cholesterol polyps, adenoma and carcinoma [14].

However, an ectopic pancreas in the gallbladder, despite its rarity, should be considered in the differential diagnosis of acalculous lesions, such as polypoid formations, isolated parietal thickenings or nodulations, especially when these coexist with hyperamylasuria of unknown origin.

Conflict of interest The authors have no potential conflicts of interest

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