ABSTRACT
Pancreatic heterotopia in the gall bladder is a rare entity, with approximately 31 cases reported in English language literature until 2006; there are no Brazilian studies on the topic. As it is usually asymptomatic, the definitive diagnosis is made by the anatomopathological material excised due to common diseases of the organ, such as lithiasis, inflammatory processes, polyps and tumors. A case is reported of a 40-year-old female patient submitted to surgery with a diagnosis of lithiasic cholecystopathy. Ectopy was evidenced by the histological study, due to the presence of acinar and ductal components of the pancreas and gall bladder corpus. The authors used their own pathological classification for this ectopy, and recommended that this entity be included more frequently in the differential diagnosis of alithiasic cholecystopathy and intramural and exophytic lesions of the gall bladder.

Keywords: Gallbladder; Choristoma; Pancreas/anomalities; Case reports

INTRODUCTION
Aberrant, ectopic, heterotopic pancreas (HP), or pancreatic rest is defined as the presence of pancreatic tissue in an anomalous topographic location, with no anatomic, neural, or vascular connection to the normal pancreas.(1) Despite its congenital origin, the HP is usually diagnosed during adult life, preferentially in the stomach, duodenum, and jejunum, during procedures motivated by other digestive diseases (endoscopy, surgery) (1-2).

The first case of HP on the wall of the gall bladder was reported by Otsckin, in 1916(3). Since then and until 2007, 33 cases were published in English language literature, most of them incidental findings, and in females(4).

The ectopic pancreas is usually asymptomatic, and is only recognized during the anatomopathological study of the gall bladder, removed due to lithiasis, polyps, and inflammatory or neoplastic processes.

The rarity of this anomaly and the absence of Brazilian studies on the topic motivated the publication of this report.

CASE REPORT
A white 40-year-old woman was referred to the Institution presenting colic pain in the right hypochondrium and epigastrium, accompanied by nausea and rare vomiting unrelated to food for five days. Over the previous 48

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hours, she had experienced afternoon fever. One year prior, she had experienced a similar crisis which was ceased with home medication.

Upon physical examination, she had normal colored mucosae, no jaundice, blood pressure (BP) of 125/75 mm/Hg, heart rate (HR) of 96 bpm, and axillary temperature of 37.4 °C. The abdominal examination revealed pain on palpation of the right hypochondrium, at the level of the bladder, radiating to the right flank. The remaining abdominal examination provided nothing noteworthy. Examination of the other body regions proved normal. An ultrasound test of the gall bladder showed thin walls, with hyperechogenic shadows in its interior.

Except for the blood work (hemoglobin (Hb) 14.1 g/l, hematocrit (Ht) 44%, leukocytes 5,000, with 1% band neutrophils, 56% segmented neutrophils, 0% eosinophils and basophils, 40% lymphocytes, and 3% monocytes), the other laboratory tests were normal.

With the diagnosis of lithiasic cholecystopathy, she was taken to surgery. Upon opening of the abdomen, adhesions of the large omentum were noted, which were easily undone. The liver was preserved and the gall bladder was slightly dilated, tense, with congested walls. The gall bladder was punctured and emptied of slightly murky bile; three small stones were palpated. Fundus-cystic cholecystectomy was performed with no complications. Intraoperative cholangiography displayed a normal sized choledocus, with no calculi and normal drainage of its content to the duodenum. There were no complications during the post-operative period, and the patient was released on the third day, in good clinical condition.

The anatomopathology department received the fixed gall bladder, which was 8.5 cm long, with 0.4 cm thick walls, with color varying from greenish to brownish, granulous aspect, containing three calculi in its interior, measuring 0.2 to 0.4 cm along the greatest diameter. Slices of the walls showed a whitish color with fasciculate aspect and firm consistency. The microscopic examination determined the diagnosis of chronic lithiasic cholecystitis. In the vesicular corpus, the presence of pancreatic tissue was noted, occupying areas of the gall bladder itself and containing a few acinar lobules; adjacent, were conglomerates of small pancreatic ducts, slightly dilated (Figures 1 and 2). The acini were composed of pyramidal cells with rounded nuclei arranged primarily at its base, with granular cytoplasm.

**DISCUSSION**

The pancreas is formed from two endodermal buds coming from the primitive ventral and dorsal duodenum, which fuse during the sixth week of gestation during the embryological rotation of the gut. The corpus and tail come from the dorsal bud and the head and unciform process from the ventral bud[2]. Different hypotheses are given to explain the pathogenesis of the ectopic pancreas.

One of the most accepted theories indicates the detachment of the pancreatic tissue from the original buds of the primitive gut towards the neighboring structures during the axial rotation of the normal intestine[2]. There is also the point of view that the permanence of residual embryonic tissue in the primitive gut would be a plausible explanation, since the longitudinal growth of that segment would lead these pancreatic rests to locations above and below that tract[1]. In cases of more distant locations, metaplasia and irregular differentiation of multipotent cells are considered[1]. It is believed that the HP situated in the gall bladder originates from the ventral bud; it was also pointed out that heterotopic associations, such as gastric and pancreatic heterotopias, may coexist in the gall bladder.

**Figure 1.** Ectopic pancreas components in the gall bladder. Pancreatic ducts (left arrow), acinar component (central arrow) and gall bladder epithelium (right arrow) (40 x, HE)

**Figure 2.** Ducts and acini in the gall bladder muscular layer (100 x, HE)
Heterotopic pancreatic tissue is found in greater proportions in the upper gastrointestinal tract, which represents 70 to 90% of the cases studied\(^1,2\). More rarely, the literature records implantations of pancreatic tissue in extraintestinal locations, such as the spleen, omentum, liver, coledocus, mediastinum, lungs, etc. In the largest series reported, the presence of pancreatic rests in the gall bladder was noted in 6 of 471 cases\(^3\), while the other cases refer to the presence of only one to three cases\(^4,3,5,6\). Thus, the statement that until 2006 there were only 31 cases reported in English language literature of confirmed HP in the gall bladder, is not surprising\(^4\).

Heterotopic tissue may display exophytic growth and be similar to polypoid lesions or remain intramural, generally with small dimensions that vary from 0.1 to 1.0 cm, located preferentially in the neck or fundus regions of the gall bladder\(^6-7\). Due to the lack of a submucosal layer, it is usually identified in the midst of the muscular layer of the organ, rarely occupying the vesicular chorion. The intramyenteric location of the present report corroborates these data.

The histological study of the HP should be divided into two parts, as expressed in this study: Type I, also called complete heterotopia, is composed of all the pancreatic cell components (acini, ducts, and islets of Langerhans); Type II, when there are two portions of these components; and Type III, when there is only one component. When the islet components exist isolatedly, heterotopia may also be called endocrine; in the presence only of ducts or acini, it may be called canalicular heterotopia and exocrine heterotopia, respectively. The ectopic pancreas of this study is an example of Type III, which shows acini and ducts. This classification attends to all cases of this anomaly.

Sometimes the ductal structural aspect shows histological similarity with adenomyomas and Rokitansky-Aschoff sinuses, and some scientists believe that these lesions might have a common histogenetic origin\(^8\).

As is true in other locations of this anomaly, in the gall bladder it practically does not cause any symptoms; the presence of symptoms is generally associated with pathological processes of the organ (inflammation, polyps, lithiasis, and neoplasms), reasons for the surgical indication. Therefore, pancreatic tissue is always identified by the anatomopathological examination of the surgical specimen removed\(^5,9\). The patient in this report is included in these statements, whether due to the absence of symptoms and laboratory tests related to pancreatic clinical manifestations or to the absence of any macroscopic finding that might suggest the presence of HP.

Nevertheless, several scientists confirmed that this ectopy is responsible for the clinical picture displayed by some patients. Thus, acute inflammatory crises were reported caused by acute and chronic pancreatitis in the aberrant vesicular tissue; vesicular hydropsy due to the presence of an ectopic nodule obliterating the cystic duct, and perforation and hemorrhage of the gall bladder; cholecystectomy was curative in all of them\(^3,5,7,9\). In reality, the anomalous tissue is subject to the same pathological alterations found in the normal pancreas and can, therefore, originate corresponding symptomatology.

The use of a series of immunohistochemical markers demonstrated that there is a complete endocrine and exocrine activity in the ectopic pancreas situated in the gall bladder\(^4\). Enzymes (trypsin, amylase, phospholipase) activated by bile, may cause inflammatory, hyperplastic, dysplastic, and tumor processes in the gall bladder and biliary tree, as well as the consequent symptoms, such as lesions caused by pancreatic reflux which are well-known\(^4,10\).

The diagnosis of ectopic pancreas in the gall bladder with the current imaging resources has not yet been reported. Echography, computed tomography, and echoendoscopy do not distinguish it from other nodular or polypoid lesions – adenomas, cholesterolosis, malignant or extra-mucosal lesions – and they do not individualize possible parietal thickening caused by the heterotopia. However, echoendoscopy is an investigative procedure capable of furnishing the extension and characteristics of the intraparietal formation, besides differentiating them from extrinsic compressions\(^4,6\).

Considering the current availability of diagnostic resources, ectopic pancreas should be included more often in the differential diagnosis of alithiasic lesions of the gall bladder, especially in the presence of polypoid formations and isolated parietal thickenings or nodulations. We hope that in the future possible markers or indicators of this anomaly may contribute to its earlier diagnosis, thus enabling a more effective therapeutic management.

REFERENCES