Case Report

Pancreatic and Gastric Heterotopia in the Gallbladder: A Rare Incidental Finding

Abstract

Heterotopia is the presence of the tissue outside its normal location, without neural, vascular, or anatomic connection with the main organ in which it normally exists. Predominant heterotopias that occur in the gastrointestinal tract are pancreatic and gastric; however, both these types of heterotopia are rarely seen in the gallbladder. Here, we are presenting two rare, incidentally detected cases of heterotopia, in a 35-year-old male and a 63-year-old female, diagnosed through histopathology and subsequently confirmed by immunohistochemistry. Familiarity with such rare entities is of utmost importance for both pathologists and surgeons as these could result in serious complications including ulceration of the gallbladder and possible malignant changes.

Keywords: *Chromogranin, heterotopia, pancreatic tissue*

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Introduction

Heterotopic or ectopic tissue is a congenital anomaly, which is defined as the presence of the tissue outside its normal location, without neural, vascular, or anatomic connection with the main body of an organ in which it normally exists. This tissue is usually discovered incidentally and may be asymptomatic or may present with nonspecific gastrointestinal (GI) symptoms. Pancreatic and gastric heterotopia are the two predominantly occurring heterotopic tissues in the GI tract.[1,2] The prevalence of ectopic pancreatic tissue in the GI tract ranges from 0.6% to 13.7% of autopsy series and it can be present anywhere in the GI tract with the most common localizations being stomach (27.5%), duodenum (25.5%), colon (15.9%), esophagus, and Meckel's diverticulum.[3-5] It is a rare finding in the gallbladder and its prevalence has not been ascertained due to lack of large-scale studies and systematic review of literature. Similarly, heterotopic gastric tissue is common throughout the GI tract from the tongue to the rectum,[6,7] but it is extremely rare in the gallbladder with only around 34 cases reported in literature so far, while other cases of different types of heterotopic tissues in the gallbladder such as liver tissue and others such as adrenal and thyroid tissues have been described.[8] The most common presentation of ectopic tissue in the gallbladder is colicky pain in the epigastrium or right upper quadrant sometimes associated with nausea and vomiting. Here, we are presenting two incidentally detected cases, each of gastric and pancreatic heterotopias in the gallbladder.

Case Reports

Case 1

A 35-year-old male presented with colicky pain in the abdomen. On ultrasonography, multiple stones were detected in the gallbladder with features of cholecystitis. Cholecystectomy was done, and on gross examination, the gallbladder was measured 7.5 cm × 2.5 cm with unremarkable serosal surface. On cutting open, cut surface shows partially velvety and partially hemorrhagic mucosa with multiple crushed sediments of yellow stones present in the lumen. No growth or polypoidal lesion was noted.

Microscopy revealed partially denuded and atrophic mucosa with wall which showed numerous benign looking pancreatic acini forming lobular architecture exhibiting both exocrine and endocrine components. Endocrine component was confirmed with the help of chromogranin-A immunohistochemistry and showed focal positivity [Figure 1]. The subepithelium

How to cite this article: Pendharkar D, Khetrapal S, Jairajpuri ZS, Rana S, Jetley S. Pancreatic and gastric heterotopia in the gallbladder: A rare incidental finding. Int J App Basic Med Res 2019;9:115-7.

Received: 28 March, 2018.
Accepted: 11 February, 2019.

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Access this article online

Website: www.ijabmr.org

DOI: 10.4103/ijabmr.IJABMR_109_18

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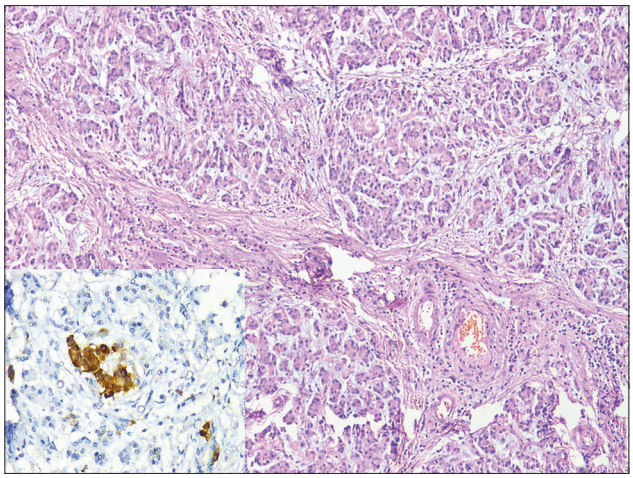

Figure 1: Heterotopic pancreatic tissue in the wall of the gallbladder (H and E, ×10). Inset showing few islet cells in heterotopic pancreatic tissue showing immunoreactivity to chromogranin-A (×40)

showed acute on chronic inflammatory and muscular hypertrophy.

Case 2

A 63-year-old female presented with symptoms of cholelithiasis. Cholecystectomy was done, and the sample was sent for histopathological analysis. On gross examination, the gallbladder was measured 10 cm × 2 cm with unremarkable external surface. Cut surface showed focally velvety mucosa and focal tiny sessile polypoidal areas measuring around 0.2–0.3 cm. Many small yellow stones were present in the lumen.

Microscopy revealed lining epithelium with few Rokitansky–Aschoff sinuses. The subepithelial tissue shows foci of unremarkable gastric fundic glands with surrounding tissue showing mild acute on chronic inflammation.

Discussion

Heterotopia is the presence of normal tissue in an abnormal location. Heterotopic pancreatic tissue is presumed to result from an error during embryological development. The etiology of pancreatic heterotopia is not yet clear, but three theories have been proposed for the mechanism, namely (1) the separation of heterotopic pancreatic tissue from primitive pancreas during embryonic rotation; (2) pancreatic tissue is abnormally transported by the longitudinal growth of the intestine from lateral budding of the rudimentary pancreatic tissue while penetrating the intestinal wall,[9,10] and this is the most accepted theory; and (3) another theory based on abnormalities in the Notch signaling system that leads to changes in differentiation in the developing foregut endoderm.[11]

Heterotopic pancreas is usually found incidentally during surgery or during microscopy. It is usually clinically silent and benign. In 1909, Heinrich *et al*. classified heterotopic pancreas into three types: Type I – with ducts, acini, and endocrine islets similar to those seen in normal pancreatic tissues; Type II – with a large number of acini, a few ducts, and no islets; and Type III – with numerous ducts, a few acini, and no islets. It was observed that 50% of ectopic tissues do not contain islet cells.[12]

Active pancreatic enzymes secreted into the gallbladder and biliary tract may lead to chronic inflammation, hyperplasia, and dysplasia of the gallbladder mucosa and even to carcinoma of the gallbladder.[13,14] Qizilbash[15] reported a case in which the cause of acute symptoms was the inflammation of the heterotopic pancreatic tissue, resembling acute pancreatitis. It has been suggested that pancreatic heterotopia may also be the underlying cause of other cancer, for example, intraductal papillary mucinous neoplasm in the jejunum.[16] Malignant transformation of heterotopic pancreatic tissue is extremely rare. Goodarzi *et al*.[17] reviewed 31 documented cases of carcinoma arising in a heterotopic pancreas and mostly in the stomach and adenocarcinomas histologically. So far, neither ultrasound nor CT and magnetic resonance imaging can confirm the diagnosis of ectopic pancreas or gastric tissue preoperatively. Radical excision is the treatment of choice in pancreatic heterotopia and is aimed at avoiding potential complication.

The first case of heterotopic gastric mucosa was reported by Egyedi.[18] There are three hypotheses present regarding the etiology of heterotopic gastric mucosa:

1. Developmental anomaly
2. Heterotopic differentiation
3. Metaplastic differentiation (23 hgb5).

The incidence in men was slightly higher around 20% higher than women. The age at discovery was ranging from 3 to 78 years with average age being 34 years. The finding of heterotopic gastric mucosa in the biliary tract is usually incidental, and sometimes, patients may present with right upper quadrant pain, abdominal discomfort, nausea, vomiting, and symptoms with biliary obstruction and jaundice. Under the age of 25 years, the presentation of heterotropic gastric mucosa in gall bladder is usually acute and for short duration, however, in older patients it can be associated with cholelithiasis and cholecystitis.[19] The gallbladder may be normal or may show sessile which is more common or pedunculated polypoidal lesion protruding into the lumen or may be localized thickening of the gallbladder wall. Carcinoma must be ruled out in polypoidal lesions of the gallbladder >1.0 cm. The incidence of gallbladder carcinoma is particularly high in sessile polypoidal lesion.[20] In the case presented above, the sessile polypoidal lesion present on the gallbladder mucosa was < 1cm in size which on microscopy revealed heterotopic gastric mucosa along with features of chronic cholecystitis without any features of gallbladder carcinoma.

It is necessary for a pathologist to be aware of these entities; heterotopic gastric mucosa in the biliary tract and

some substantially important complications must also be considered when we deal with heterotopic gastric mucosa in the gallbladder, including ulceration of the gallbladder and possible malignant changes. Ishii *et al*.[21] suggested that heterotopic gastric mucosa may have the potential for carcinogenesis, but so far, no case of malignant transformation has been reported. Dysplasia in heterotopic gastric mucosa in the gallbladder has been reported.

In conclusion, surgeons must be aware of heterotopic gastric mucosa of the gallbladder, especially in young patients with cholecystitis and cholelithiasis with abdominal pain as a main complaint. As heterotopic tissue may promote carcinogenesis of the gallbladder, so close attention should be paid to any such lesions in this region.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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