

Heterotopic Pancreas in Gastric Antrum: A Report of Two Cases

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Abstract

Pancreatic glandular tissue situated outside the normal anatomical site of the human body is called heterotopic pancreas. The incidence is very low as mostly it remains asymptomatic. It is usually found in association with stomach and duodenum, but it may be found in relation with any organ and even outside the abdominal cavity. When symptomatic, it may present as pain in the abdomen, pancreatitis, gastrointestinal tract bleed, abscesses, cysts, or malignancy of the concerned organ. Gastric ectopic pancreas is diagnosed by ultrasonic endoscopy and tissue biopsy. Conservative treatment gives a temporary relief. Local wedge resection of this non-malignant lesion is the ultimate treatment of choice. In the present study, we report cases of ectopic gastric antral pancreas in two young males aging 20 and 16 years who happened to be cousins. They presented with vague symptoms of epigastric pain, nausea, vomiting, etc. One of the patients had h/o melena. The diagnosis was made by endoscopic ultrasonography and confirmed by endoscopic biopsy. This study further supports the genetic theory of ectopic pancreas as there could be a common type of abnormal genetic signaling pathway leading to trans-commitment of non-pancreatic tissue progenitors to pancreatic lineage in both patients leading to a common type of ectopic pancreatic pathology.

Key words: Abnormal organogenesis, Endoscopic ultrasonography, Gastric antrum, Heterotopic pancreas

INTRODUCTION

Heterotopic or ectopic pancreas is defined as the presence of abnormally located pancreatic glandular tissue with no structural and vascular connection with main pancreas. Most of the heterotopic pancreatic lesions are asymptomatic and are found incidentally along gastrointestinal tract (GIT) during endoscopic examinations, laparotomies, and autopsies. However, this anomalous pancreatic tissue may present as various types of acute or chronic gastrointestinal manifestations. Eventually, many serious complications may develop including upper GI bleeding, gastric ulcers, pyloric obstruction, pancreatitis, pseudocysts, abscesses, or even malignant degenerations.¹ The incidence of ectopic pancreas seen at autopsies ranges between 5% and 13.7%. It is more common in the age group of 30-50 years, having

male predominance, with male to female ratio as 3:1.² The most recognized locations of ectopic pancreatic tissue includes: (1) Proximal duodenum (17-36%), (2) gastric antrum including gastric duplication cysts - 25-38%, (3) jejunum - 15-21%, (4) Meckel's diverticulum 5.3%, and (5) ileum 5.8%. Less common regions involved are esophagus, gallbladder, common bile duct, spleen, mesentery, mediastinum, perampullary site of duodenum, and fallopian tube 7%;^{1,2} least common sites being tongue, submandibular salivary gland, and lymph node.³

Most of the time, the heterotopic pancreas is located in the stomach where it is maximally seen in the antrum; either on the posterior wall or anterior wall, being more common along the greater curvature. The involvement of submucosal layer, muscularis, and subserosal layer is 73%, 17%, and 10%, respectively. The macroscopic appearance is that of a benign firm submucosal mass on a broad base, sharply circumscribed from the surrounding tissue. The diagnostic tools include contrast radiography, computerized tomography (CT) scan, and endoscopic ultrasonography (EUS).¹ Findings of endoscopy of upper GIT: The typical endoscopic finding is a firm round or oval subepithelial lesion with a central umbilication or depression, which

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corresponds to the opening of a duct. This central dimpling or umbilication implies a presumptive diagnosis of ectopic pancreas during preoperative endoscopy.⁴ The findings may sometimes be also that of polypoid mass (submucosal or muscularis growth) with central umbilication. The tissue area appears as discrete, yellowish gray nodules with well-defined lobules of acinar tissues that may be replete with islets of Langerhans as well as exocrine glands. The nodules are small (1-3 cm) in diameter though lesions in the stomach are usually larger than other sites averaging 2.4 cm.⁵ However, these findings are not present in all the patients. In these patients, EUS would be helpful for predicting ectopic pancreas.⁴ The characteristic EUS features of ectopic pancreas reported are as: (1) Indistinct borders, (2) heterogeneous echogenicity, (3) the presence of an anechoic area, and its location within the second, third, fourth, or fifth layers of the stomach.⁴

Classification of Heterotopic Pancreas

Based on the sonographic appearance of the layer of origin, ectopic pancreas is classified into two types:

1. Superficial type (s-type)
2. Deep type (d-type).⁴

Histological classification⁵

Heinrich classified heterotopic pancreas histologically into three types: Type 1 - Showing all the components of pancreas such as ducts, acini, and endocrine islets, Type 2 - Showing ducts type with acini, Type 3 - Showing ducts with only a few acini or dilated ducts only, the so called adenomyoma.

Etiology

Two important factors are recognized; they are:

Embryological factors

- a. Buds of embryonic tissue penetrate into the wall of rapidly growing intestine with a consequent of separation from the main pancreas and subsequent autonomous growth¹
- b. An inappropriate expression of pluripotent embryonic mesenchymal tissue of the gastrointestinal tract with subsequent development of pancreatic tissue^{1,3}
- c. According to Derbyshire RC, prior to the fusion of the ventral and dorsal pancreatic buds, small branches from them may become attached to the gut wall at various locations. These branches remain anchored to the gut wall and as the pancreatic gland pulls away from the gut, these remain grafted in its new location on the gut wall and develop as heterotrophic pancreatic tissue.³

Genetic factors

1. Hes-1 - Main effectors of Notch signaling pathway regulates fate and differentiation of many cell types during the development including region - appropriate specification of pancreas in the foregut endoderm

through the regulation of expression of Ptf1a (a transcription factor). Any deviation and abnormality in this pathway is considered to be responsible for the pathogenesis of ectopic pancreas⁶

2. Pancreatic and duodenal homeobox gene-1 (Pdx1) is region - specific transcriptional regulators playing a pivotal role in pancreas organogenesis. Pdx1 - Null mutants have an early block in pancreas formation⁶
3. Transforming growth factor-B, (TGF-B), fibroblast growth factor (fgf), notch and hedgehog signaling pathways regulate and interact with each other to govern pancreas development; anything going wrong with their interactive activity leads to anomalies⁷
4. Inhibition of sonic hedgehog (shh) leads to ectopic development of pancreatic tissue⁶
5. Trans-commitment of non-pancreatic tissue progenitors to pancreatic lineage.⁶

CASE REPORTS

We present the case reports of two patients who are Afghani nationals and happen to be distant cousins.

Case I (Figures 1-3)

A 21-year-old male from Afghanistan visited the Department of Gastroenterology of a private super specialty hospital at New Delhi, with H/O vague pain in the upper abdomen and chronic dyspepsia for a period of 1-year. There was no H/o weight loss, malena, haemetamesis, drug intake for any chronic disease, etc.

General physical examination

All parameters were within normal limits. Abdominal examination revealed tenderness in epigastric and umbilical region on deep palpation. Routine blood, urine, stool, and all biochemical tests were within the normal range. The

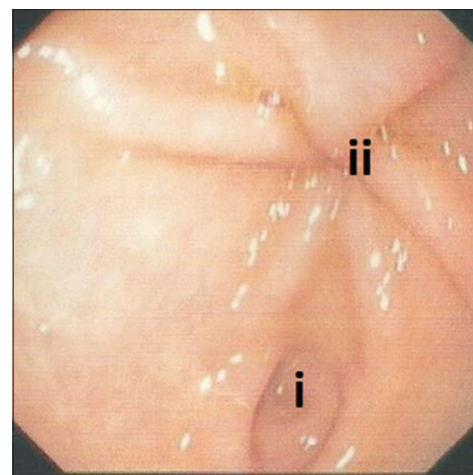


Figure 1: Plain endoscopic images of the stomach (Case I). Gastric antrum showing, (i) A simple umbilicated lesion, (ii) closed pyloric end of the stomach

patient was advised for plain endoscopy followed by EUS of upper gastrointestinal organs.

Endoscopic report

A small umbilicated lesion of the size of 5 mm was noted in the antrum of the stomach. The surface of the lesion appeared smooth without any features of ulceration. Small erosion at the incisura of lesser curvature and the features of gastritis in the mucosa of antrum were noted. Rest of the stomach and duodenal mucosa looked normal. This was followed by EUS of stomach and duodenum.

EUS report

The mucosal umbilicated lesion seen in plain endoscopy was assessed and found to be 2 mm × 4 mm in size. It arose

from 3rd and 4th gastric layer, the lesion was heterogeneous with hypo echogenic patchy echostucture; no distinct ductal component was noted; the outer serosal layer was intact, with no adjacent lymphadenopathy noted. All these features were suggestive of the aberrant gastric antral pancreas. For confirmation of diagnosis, an EUS-guided TRU- Cut biopsy was performed and sent for evaluation. The patient was put on conservative treatment and referred to the surgical unit for further treatment and course of action.

Case II (Figures 4-6)

A young, 16-year-old boy, was admitted to the causality department of the same hospital (as mentioned above) with H/O acute pain epigastric region and vomiting. On enquiring, he gave past H/O recurrent attacks of pain in upper abdomen, nausea, vomiting, and generalized weakness for the last 3 months, with a past H/O of malena once. There was no H/O drug intake, hematemesis, jaundice, etc.

General physical examination

There was mild anemia; rest all of the parameters were within the normal limits. Routine blood, urine, stool, and biochemical tests were normal except for hemoglobin level, which was 9 g%.

Endoscopic report

A 2 cm raised subepithelial lesion with a dimpled surface in the antral region was visualized. On the surface of the lesion and extending to the adjacent gastric antral mucosa, there was 1 cm clean based ulcer. The whole of the antral mucosa was hyperemic showing features of severe gastritis. Rest of the gastric and duodenal mucosa was looking normal.

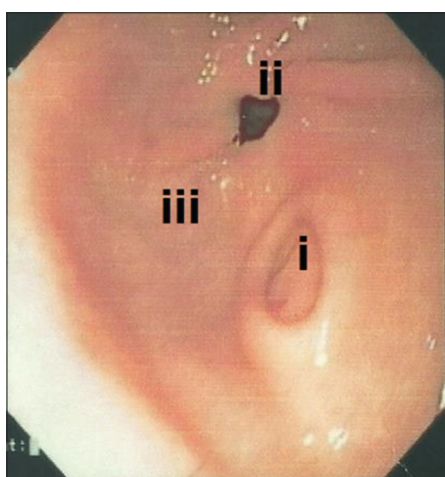


Figure 2: Plain endoscopic images of the stomach (Case I).
(i) Gastric antrum showing the same simple umbilicated lesion suspicious of ectopic pancreas, (ii) pyloric end open, (iii) features of acute gastritis in the antral mucosa

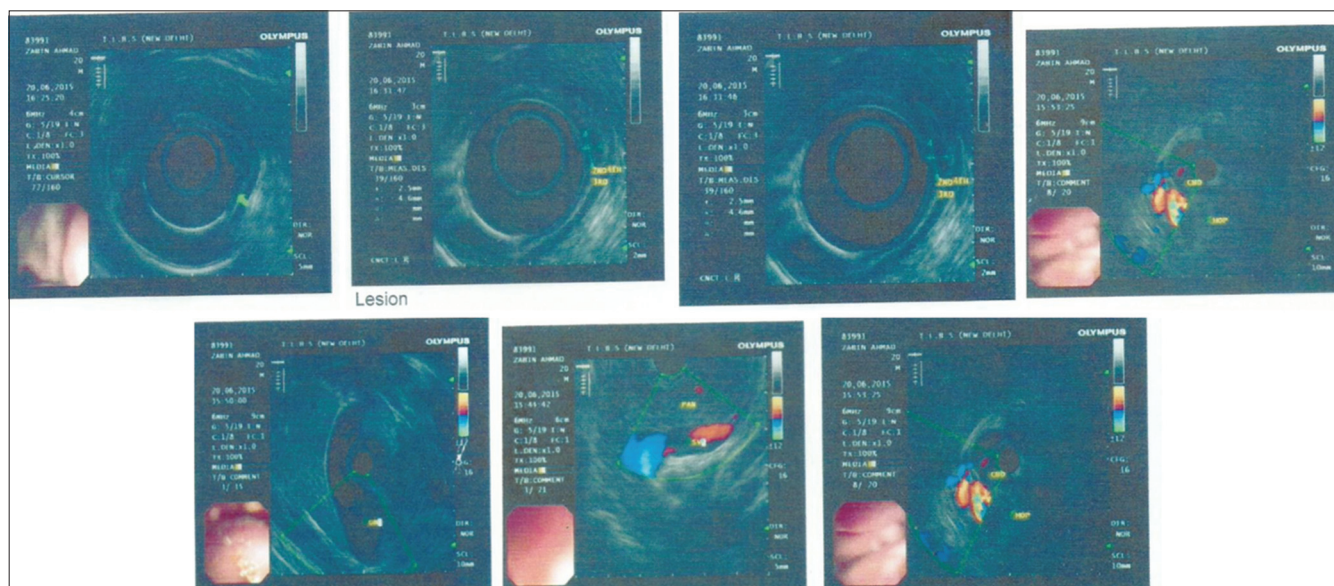


Figure 3: Ultrasonographic endoscopic images of the gastric antrum. Various images of the interior of gastric antrum showing the umbilicated lesion arising from 3rd and 4th layers, is heterogeneous in nature with hypo echogenic patchy echostucture

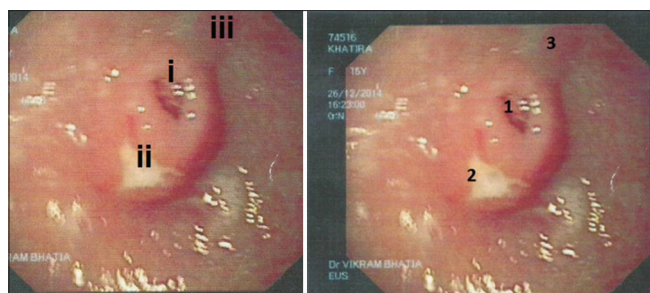


Figure 4: Plain endoscopic images of gastric antrum (Case II).
(i) A raised subepithelial lesion with a dimpled surface seen in the gastric antrum, (ii) a clear-based ulcer on the surface of the lesion, (iii) hyperemic antral mucosa

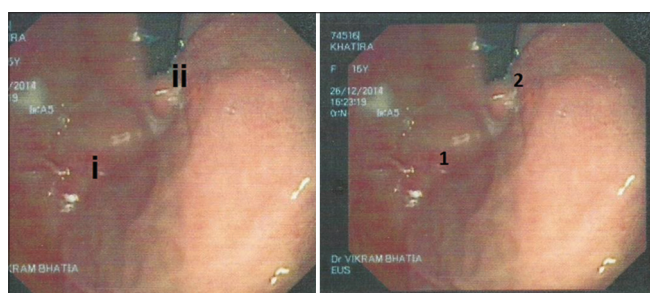


Figure 5: Plain endoscopic images of gastric antrum (Case II).
(i) Hyperemic antral mucosa, (ii) pyloric end open

EUS report

There was a 16 mm × 8 mm mural lesion in the antrum of the stomach. The location of the lesion was in the deep mucosal and submucosal layers, with extension into the muscularis propria layer. There was no extension through and beyond the muscularis propria. The margins of the lesion were ill-defined. The internal echotexture was heterogeneous, with hypo echogenic pathy/lobular echo structure. Besides, anechoic irregular tubular structures were present in the lesion. No enlarged perigastric lymph nodes were seen. A EUS guided Tru-Cut biopsy was also performed for the confirmation of diagnosis.

Plain endoscopy and EUS findings were suggestive of pancreatic rest/ectopic pancreatic tissue with an antral benign clean-based ulcer. This patient was also treated conservatively and was then referred to the surgical unit for simple resection or endoscopic mucosal resection.

DISCUSSION

The pathological condition - Ectopic pancreas has been found to be associated with various organs of the body, mostly upper GIT. Hence, its presentation is also varied. The condition was diagnosed very early in the 18th century. Schultz, in 1727, was the first to report the incidence of heterotopic pancreas¹ which was found in upper GIT in an ileal diverticulum during the autopsy of a new born.³

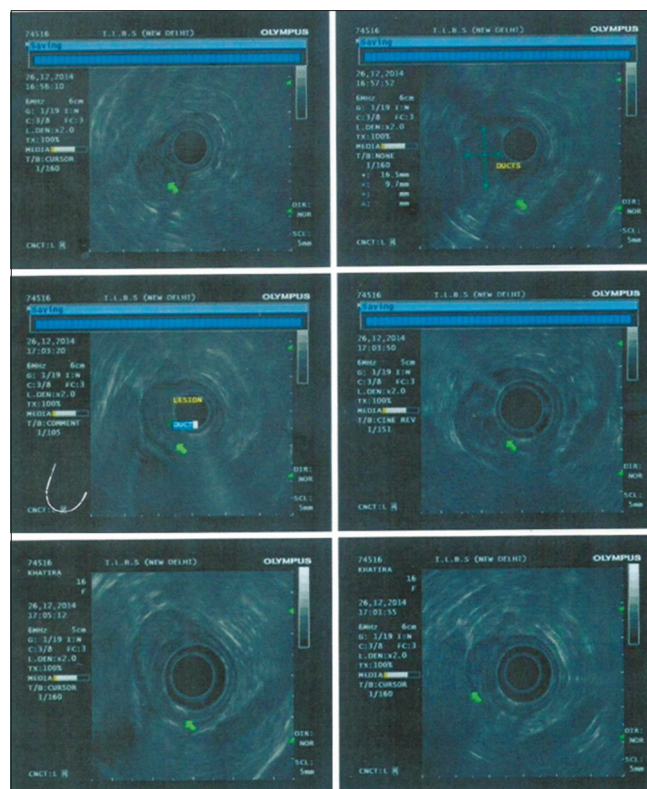


Figure 6: Endoscopic ultrasonography images of gastric antrum. Hyperemic antral mucosa suggestive of severe gastritis and pyloric end open. Various images of the interior of gastric antrum showing a big mural lesion lying in the deep mucosal and submucosal layers with extension into muscularis externa. The interior echo texture is heterogeneous, with hypo echogenic lobular echo texture. An echogenic, irregular tubular structures presence in the lesion

Klob published his first microscopic list of observations of ectopic pancreas in 1859.^{1,3} Later on after a gap of more than one century, a large series of about 212 cases of heterotrophic pancreas were published by Dolan *et al.*¹ A 60-year-old patient with hiatus hernia had ectopic pancreatic tissue at the esophago-gastric junction, which was presented as ductal adenocarcinoma. Malignant changes at such gastric sites are rare.⁸ Hlavaty *et al.*, in 2002, identified an 8 mm gastric hemispherical polyp as a case of heterotopic pancreas in a 60-year-old woman.¹

Out of 105 gastrostomies performed in the past 5 years, ectopic pancreas was found only in one case, i.e. 0.9% by Christodoulidis *et al.*, in their study. They reported a case of ectopic pancreas in gastric antrum, measuring 5 cm × 3 cm × 4 cm extending into the submucosa and partially into muscularis externa.²

Basilius Papaziogas *et al.* confirmed ectopic pancreas with endoepithelial carcinoma of gastric antrum in a female of 56 years of age.⁵ A 25-year-old lady was diagnosed as a case of ectopic pancreas in the gastric fundus at gastroesophageal junction. The histological findings of the biopsy specimen

of the same patient were reported as gastric heterotopic pancreas with pancreatic intraepithelial neoplasm-2 which is believed to represent a precursor lesion for the development of ductal adenocarcinoma.⁹ Various sites other than the stomach, where ectopic pancreas was diagnosed by various researchers are: A 5-year-old child with a diagnosis of Meckel's diverticulum was found to have heterotopic pancreatic tissues in the various parts of the gastrointestinal tract by Baysoy *et al.*¹⁰ An isolated heterotopic pancreas, at the terminal ileum of a 47-year-old male, was found to be the cause of ileo-ileal intussusception by Ahmed Monier *et al.*¹¹ Heterotopic pancreas in the spleen with malignant degeneration to mucinous cyst adenocarcinoma was reported by Nisar *et al.*¹²

A case of heterotopic pancreas adjacent to ampulla of Vater mimicking cholangiocarcinoma was reported by Atindriya Biswas *et al.* in UK.³ Goodarzi *et al.* reported a case of pancreatic heterotopia in the rectum of a 42-year-old female in whom it had turned into ductal adenocarcinoma.¹³ An 18-year-old post-pubertal girl having an H/O cholecystitis was diagnosed as a case of heterotopic pancreas in the gallbladder, the ectopic pancreas being responsible for cholecystitis.¹⁴ A 45-year-old healthy lady who went for a routine medical check-up was found to have soft tissue mass in the left lobe of liver on CT scan. Left hepatic lobectomy was performed and subsequent histopathological study of the mass removed revealed the presence of ectopic pancreatic tissue present in the liver. This intrahepatic pancreatic tissue had changed into adenocarcinoma.¹⁵ Lizhi-Zhang *et al.* reported two very rare cases of ectopic pancreatic mass in anterior mediastinum of thoracic cavity in two young females who were 15 and 16 years old respectively.¹⁶

CONCLUSION

Although pancreatic heterotopia is a rare entity, yet it should always be considered in the differential diagnosis of extra mucosal gastric lesion/GI stromal tumor and any undiagnosed abdominal ailment. The quick and easy diagnostic tool is to do EUS and a simultaneous biopsy.

Such diagnostic procedures are all the most important in the cases where pancreatic heterotopia presents primarily as pancreatitis, hyperinsulinism, Zollinger Ellison syndrome, common bile duct obstruction, etc. It is often impossible to distinguish gastric pancreatic heterogenic tissue from primary or metastatic cancer on endoscopy because endoscopic biopsies are sometimes unremarkable. Hence, a frozen section should be taken at the time of surgery to confirm

the diagnosis. Surgical excision provides symptomatic relief and treatment also. Surgery is recommended, especially if the diagnosis is uncertain. Our case study of two patients revealed that ectopic pancreas can also be present at a young age as described by a few authors rather than conventionally declared in the third or fourth decade of life. Our patients had the same diagnosis and were also related to each other. This fact further enlightens the role of genetic theory in the pathogenesis of ectopic pancreas. It is presumed that both of them had some common genetic pattern and abnormal genetic signaling pathway which predisposed to the formation of ectopic pancreas in both individuals, that too involving antrum of the stomach in both cases.

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