Case Reports and Reviews

Case Report

Pancreatic Intraepithelial Neoplasia in Jejunal Ectopic Pancreas: A Rare Case

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Abstract

Background: *Heterotopic pancreas, also referred to as ectopic pancreas, is a rare congenital anomaly defined by the presence of pancreatic tissue outside its normal anatomical location without ductal or vascular continuity with the orthotopic pancreas. Although frequently asymptomatic and discovered incidentally, heterotopic pancreas is capable of undergoing the same pathological processes as native pancreatic tissue, including premalignant and malignant transformation. Pancreatic intraepithelial neoplasia (PanIN) arising in heterotopic pancreatic tissue is uncommon, particularly within the jejunum.*

Case Presentation: *A 65-year-old woman presented with a six-month history of intermittent upper abdominal pain. Cross-sectional imaging demonstrated a well-circumscribed submucosal mass in the distal jejunum with nonspecific radiologic features, raising concern for neoplasia. Segmental jejunal resection was performed. Histopathologic examination revealed heterotopic pancreas, Heinrich type I, composed of pancreatic acini, ducts, and islets within the jejunal submucosa and muscularis propria. Focal low-grade pancreatic intraepithelial neoplasia (PanIN-1) involving ductal structures was identified. No high-grade dysplasia or invasive carcinoma was present, and surgical margins were negative.*

Conclusion: *This case highlights the diagnostic challenges associated with jejunal heterotopic pancreas and demonstrates that ectopic pancreatic tissue can harbor premalignant ductal lesions analogous to those seen in the orthotopic pancreas. Recognition of this rare entity is important, as definitive diagnosis relies on histopathologic evaluation, and complete surgical excision is curative for low-grade lesions in the absence of invasive malignancy.*

Introduction

Often described as a congenital anomaly, heterotopic - or ectopic- pancreas consists of pancreatic elements situated extrinsically to the primary gland, lacking any structural or circulatory connection to the orthotopic organ [1]. The reported incidence ranges from approximately 0.5% to 13.7% in autopsy series, though most cases are incidentally discovered [1]. Heterotopic pancreas is most commonly found in the stomach, duodenum, and proximal jejunum, with less frequent sites including the ileum, Meckel's diverticulum, biliary tree, and esophagus [2,3]. Although often clinically silent, heterotopic pancreas may become symptomatic due to inflammation, enzyme secretion, bleeding, obstruction, or intussusception [2,3]. The clinical significance of heterotopic pancreas arises from its potential to undergo the same pathological processes as orthotopic pancreatic tissue, including inflammation, cyst formation, and neoplastic transformation [2].

Pancreatic intraepithelial neoplasia (PanIN) represents a spectrum of microscopic, noninvasive ductal epithelial proliferations that are regarded as the most common precursor lesions to pancreatic ductal adenocarcinoma (PDAC) [4,5]. PanINs are defined histologically by architecturally flat or papillary ductal lesions measuring <5 mm and are graded based on increasing degrees of cytologic and architectural atypia into low-grade (PanIN-1 and PanIN-2) and high-grade (PanIN-3) lesions [4,6]. The current two-tiered grading system for PanIN recently replaced the former three-tiered grading scheme (PanIN-1, PanIN-2, PanIN-3) and neoplasms belonging to the former PanIN-1 and PanIN-2 categories are now categorized as low-grade PanIN, and those belonging to the former PanIN-3 category are now categorized as high-grade PanIN [4]. Low-grade PanINs are characterized by mucinous columnar epithelium with basally oriented nuclei, minimal nuclear atypia, and preserved polarity, whereas high-grade PanINs demonstrate nuclear crowding, loss of

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polarity, prominent nucleoli, mitotic activity, and cribriform or micropapillary architecture [4,6].

PanINs are common incidental findings in the pancreas of older adults and increase in frequency with age and in association with chronic pancreatitis, advanced age, obesity, pancreatic fatty infiltration, and diabetes mellitus [4-6]. Molecular studies have demonstrated that PanIN progression is driven by a well-characterized sequence of genetic alterations, including early activating mutations in *KRAS*, followed by inactivation of tumor suppressor genes such as *CDKN2A/p16*, *TP53*, and *SMAD4* in higher-grade lesions [4-6]. These findings support a stepwise model of pancreatic carcinogenesis.

Although PanINs are most frequently identified in the orthotopic pancreas, they have also been described, albeit rarely, in heterotopic pancreatic tissue [6,7]. The presence of PanIN within ectopic pancreas underscores that heterotopic pancreatic tissue retains the full biological potential of normal pancreatic tissue, including susceptibility to premalignant and malignant transformation. Symptomatic cases of jejunal heterotopic pancreas are rare, as most lesions are small (<3 cm) and asymptomatic, and are often discovered incidentally during surgery, endoscopy, or imaging [3].

Here, we present a case of jejunal heterotopic pancreas with associated PanIN-1, highlighting diagnostic challenges and review of relevant literature.

Case Report

A 65-year-old woman presented with intermittent upper abdominal pain of six months' duration, described as dull and cramping. She denied nausea, vomiting, gastrointestinal bleeding, weight loss, changes in bowel habits, or constitutional symptoms. Her past medical history included hypertension, type II diabetes mellitus, and gastroesophageal reflux disease managed with proton pump inhibitors. There was no family history of gastrointestinal malignancy.

On examination, vital signs were stable, and abdominal examination revealed no palpable masses or tenderness. Laboratory investigations including complete blood count, liver function tests, serum amylase, and lipase were within normal limits. Serum tumor markers carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) were not elevated.

Contrast-enhanced computed tomography (CT) of the abdomen demonstrated a well-defined 1.5 cm submucosal mass in the distal jejunum with heterogeneous enhancement, without evidence of obstruction or perforation. Mild upstream small-bowel dilatation raised concern for partial luminal compromise. Imaging differential diagnosis included gastrointestinal stromal tumor (GIST), neuroendocrine tumor (NET), adenocarcinoma, and metastatic disease.

Given persistent symptoms and concern for neoplasm, the patient underwent segmental jejunal resection. Gross examination revealed a well-circumscribed, tan-yellow submucosal nodule measuring 1.8 × 1.0 × 1.0 cm with a lobulated cut surface. The overlying mucosa was intact.

Microscopically, pancreatic acini, ducts, and scattered islets of Langerhans were observed within the submucosa and muscularis propria of the jejunum (see Figure 1 and Figure 2) consistent with heterotopic pancreas (Heinrich type I). Several ductal structures showed low-grade epithelial changes consistent with PanIN-1, characterized by mucinous epithelium with minimal cytologic atypia and preserved nuclear polarity (see Figure 3 and Figure 4). No higher-grade PanIN or invasive carcinoma was identified (see Figure 5). Surgical margins were negative.

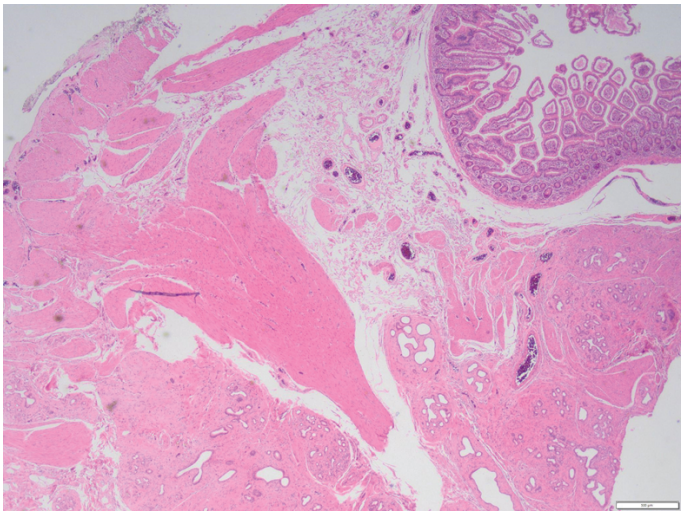

Figure 1. *Routine hematoxylin & Eosin stain, x40 showing pancreatic acini, ducts, and scattered islets of Langerhans within the submucosa and muscularis propria of the jejunum.*

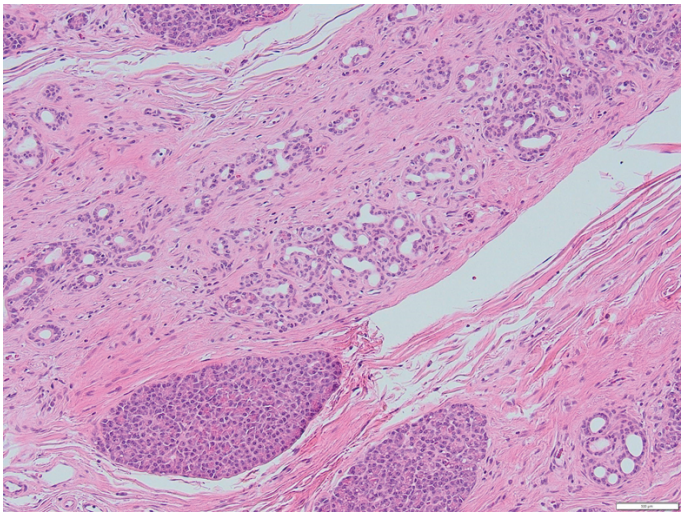

Figure 2. *Routine hematoxylin & Eosin stain, x100 showing higher magnification of pancreatic acini, ducts, and scattered islets of Langerhans within the submucosa and muscularis propria of the jejunum.*

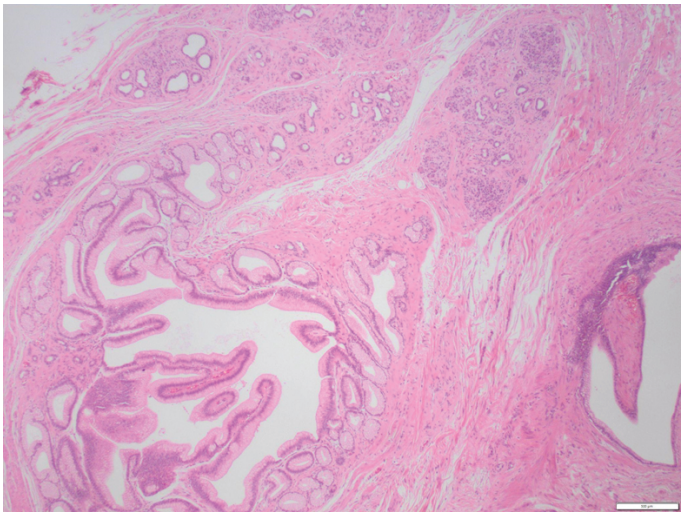

Figure 3. *Routine hematoxylin & Eosin stain, x100 showing pancreatic duct forming papillae and micropapillae to the left and pancreatic duct with normal histology to the right.*

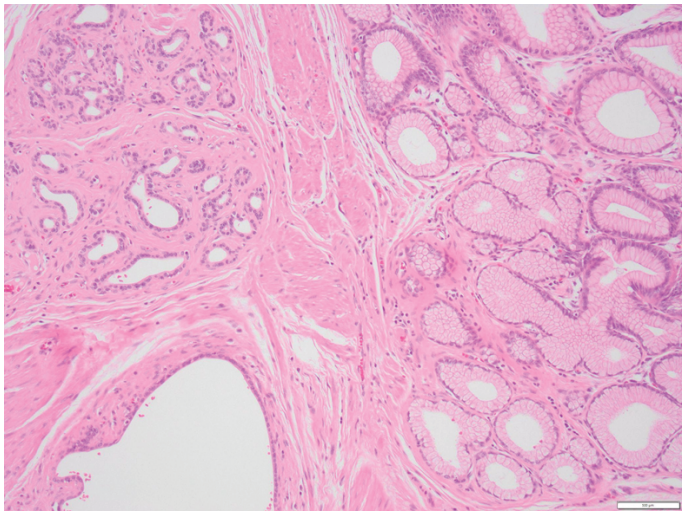

Figure 4. *Routine hematoxylin & Eosin stain, power x100 showing small ductules lined by tall, columnar mucinous epithelial cells without loss of polarization or nuclear atypia.*

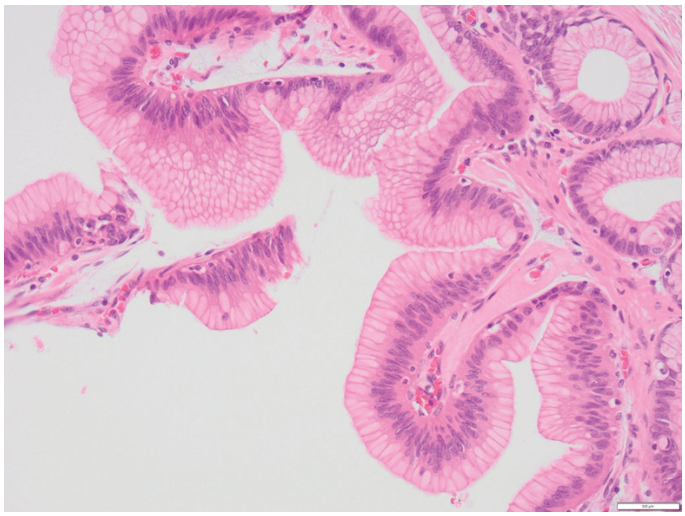

Figure 5. *Routine hematoxylin & Eosin stain, x200 showing the PanIN at a higher magnification exhibiting no loss of polarization or nuclear atypia.*

Discussion

Heterotopic pancreas arises from aberrant migration of pancreatic tissue during embryogenesis and thought to result from the displacement of pancreatic primordia during early forgut development [1,3]. Most lesions are asymptomatic, but clinical manifestations occur when the ectopic tissue produces pancreatic enzymes or when the lesion is large enough to cause obstruction, intussusception, bleeding, or perforation [2,8,9]. Case reports describe jejunal heterotopic pancreas presenting as intussusception or small-bowel obstruction, emphasizing the diagnostic challenge [8,9]. Literature reviews indicate that most lesions are small, asymptomatic, and discovered incidentally [3]. This is in contrast to our index case who had a small heterotopic pancreas but presented with persistent abdominal pains. Notably, she had no clinico-radiological evidence of obstruction, intussusception, bleeding, or perforation and pancreatic enzymes were within normal limits. However, pancreatic intraepithelial neoplasia (PanIN) lesions are more frequently observed in older individuals and have been associated with diabetes mellitus (DM), consistent with the findings in our case.

PanIN lesions identified within heterotopic pancreas are uncommon but increasingly recognized due to improved histopathologic awareness and reporting. Similar to PanINs arising in the orthotopic pancreas, these lesions are most often low-grade and incidentally detected [6,7]. From a histopathologic standpoint, PanIN must be distinguished from reactive ductal changes, which lack true epithelial dysplasia and preserved mucinous differentiation [6]. The identification of PanIN requires careful evaluation of cytologic atypia, nuclear polarity, and architectural complexity.

Importantly, the biological significance of PanIN in heterotopic pancreas mirrors that of orthotopic pancreatic tissue. Molecular and morphologic data suggest that ectopic pancreatic ducts can undergo the same neoplastic progression sequence as native pancreas, including accumulation of *KRAS* mutations in early lesions [6,10,11]. While the majority of reported cases involve PanIN-1, rare instances of high-grade PanIN and invasive adenocarcinoma arising in heterotopic pancreas have been documented, reinforcing the concept that ectopic pancreatic tissue is not biologically inert [6,10,11].

Radiologic diagnosis is challenging because imaging features overlap with other submucosal lesions [11]. CT or MRI may show a small, well-defined intramural mass with microlobulated margins and enhancement patterns correlating with histology, such as acinar-dominant or duct-dominant tissue [2,11,12]. Occasionally, a central umbilication may represent an ectopic ductal opening [2,11,12]. Despite these features, preoperative diagnosis is uncommon without histologic confirmation.

From a clinical management perspective, low-grade PanIN (PanIN-1) does not warrant additional treatment beyond complete excision of the lesion when identified incidentally, provided surgical margins are negative and no invasive carcinoma is present as documented in our case [4,6]. However, recognition and documentation of PanIN are important for accurate pathologic classification and for contributing to the growing body of literature on neoplastic transformation in heterotopic pancreas.

Conclusion

We report a rare case of jejunal heterotopic pancreas with associated PanIN-1 presenting as a submucosal mass with chronic abdominal pain. This case underscores the diagnostic challenge in distinguishing heterotopic pancreatic tissue from other small-bowel neoplasms on imaging and highlights that ectopic pancreatic tissue can undergo premalignant changes similar to the orthotopic pancreas. Histopathologic evaluation is required for definitive diagnosis, and complete resection with negative margins is curative for low-grade lesions without invasive carcinoma.

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