CASE REPORT

Acute pancreatitis: pancreas divisum with ventral duct intraductal papillary mucinous neoplasms

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SUMMARY

Acute recurrent pancreatitis occurs rarely in individuals with pancreas divisum. A 39-year-old woman with no significant history presented with pancreatitis. CT scan and MRI suggested acute on chronic pancreatitis with calcifications and pancreatic divisum. An endoscopic ultrasound demonstrated complete pancreas divisum. A large calcification measuring 12 mm × 6 mm was seen in the head of the pancreas with associated dilation of the ventral pancreatic duct. Fine-needle aspiration of the dilated ventral pancreatic duct showed an amylase level of 36 923 U/L and a carcinoembryonic antigen of 194. A ventral duct intraductal papillary mucinous neoplasm was suspected and a pancreaticoduodenectomy procedure was recommended. After the procedure, pathology demonstrated an intraductal papillary lesion in the main duct with moderate dysplasia. A pancreatic intraepithelial neoplasia, grade 2 was also present. Margins of resection were clear. This case represents the importance of assessing for secondary causes of pancreatitis in pancreas divisum.

BACKGROUND

Recurrent pancreatitis usually accounts for 10% of all hospital admissions for pancreatitis.¹ There are numerous causes of recurrent pancreatitis, but the primary causes include microlithiasis, sphincter of Oddi dysfunction, tumours and intraductal papillary mucinous neoplasm (IPMN). Rarely, pancreas divisum, which occurs in approximately 10% of the population, can also be the source of recurrent pancreatitis.² Even more uncommon is the occurrence of pancreas divisum and IPMN together as a cause of recurrent pancreatitis.

Pancreas divisum is a developmental anomaly where the dorsal duct (ie, minor or accessory duct) and ventral duct (ie, main duct) of the pancreas fuse incompletely or not at all.³ Thus, the majority of pancreatic juices drain from the minor instead of the major duct. It is theorised that the pancreatic juices drain poorly through the minor duct resulting in build up and potentially causing pancreatitis.¹ However, it is still strongly debated if this condition causes significant pancreatitis. In fact, the majority of patients with pancreas divisum are asymptomatic without episodes of acute recurrent pancreatitis.

It is well known that pancreatic cysts are associated with recurrent pancreatitis.⁴ The incidence of IPMN has increased 14-fold since it was initially identified, mainly as a result of increases in cross sectional imaging modalities.⁵ It is quite rare to

find IPMN in conjunction with pancreas divisum. However, when there are cases of IPMN in pancreas divisum, they usually affect the dorsal duct.⁶ We report only the second case of IPMN with pancreas divisum in the ventral duct and the first case with calcification and stones mimicking chronic pancreatitis.

CASE PRESENTATION

A 39-year-old Caucasian woman presented to an outside hospital with significant abdominal pain in the epigastric area. She had no history of smoking, consumed small amounts of alcohol occasionally, and did not take any medications or herbal products. Laboratory work-up was significant for increased levels of amylase of 2774 U/L (normal range 30–110 U/L) and a lipase of 17 863 U/L (normal range 7–60 U/L). Bilirubin and liver enzymes were within normal limits. An abdominal ultrasound showed no gallstones or any other abnormalities. A CT scan, performed for further evaluation of pain, demonstrated calcification of the uncinate process and dilation of the ventral duct to 1.2 cm (figure 1). Further evaluation with MRI showed not only the calcification but also pancreas divisum (figures 2 and 3). The patient was treated with supportive care and was discharged after 3 days.

The patient then presented to our practice 2 weeks later with recurrent abdominal pain that would resolve by itself. The pain episodes were sharp, located in the epigastrium and associated with nausea; they were self-limited and there were no exacerbating or relieving factors.

Figure 1 CT of the abdomen: acute on chronic pancreatitis with calcification of uncinate process.

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Figure 2 MRI: pancreas divisum with calcifications in ventral pancreatic duct.

INVESTIGATIONS

Further laboratory testing revealed normal antinuclear antibodies and immunoglobulin G subtype 4 (IgG4) levels. Pancreas gene testing for serine protease inhibitor Kazal-type (SPINK 1), cationic trypsinogen gene (CTG) and cystic fibrosis transmembrane conductance regulator (CFTR) were negative. Due to her history of pancreatitis and abnormal imaging, the patient underwent an endoscopic ultrasound (EUS).

EUS confirmed the previous CT findings, revealing a large calcification seen in the head of the pancreas with associated cyst or dilation of the ventral pancreatic duct to 1.2 cm (figure 4). A stone measuring 12 mm × 6 mm was also noted proximal to the enlarged pancreatic duct. Additional calcification was present in the uncinate pancreas measuring 5 mm. The ventral pancreatic duct could not be followed completely to the dorsal duct, thus suggesting complete pancreas divisum. Under Doppler guidance, fine-needle aspiration of the ventral duct was performed. The aspirated fluid demonstrated a carcinoembryonic antigen of 194 ng/mL and amylase level of 36 923 U/L. The fluid type was highly viscous. Cytological evaluation demonstrated rare mildly atypical ductal cells combined with benign-appearing ductal cells, histocytes and mucin. Genetic testing of the fluid revealed

Figure 3 MRI, coronal section: demonstrating pancreatic divisum.

Kirsten Rat sarcoma viral oncogene homologue (KRAS) and guanine nucleotide binding protein, α stimulating (GNAS) point mutations. These findings suggested main duct IPMN of the ventral pancreas duct.

DIFFERENTIAL DIAGNOSIS

Acute pancreatitis in a woman in her late 30s is most likely from gallstones or alcohol. Since both of these were not significant from history, other differentials including hypertriglyceridemia, hypercalcemia, pancreas divisum, autoimmune, IPMN and medications were investigated. Teasing out the causes of pancreatitis is very important to prevent recurrence or further complications or morbidity. In this case CT scan and MRI were performed and the diagnosis of pancreas divisum was made. Such findings warrant additional investigation as occult tumours may mimic pancreas divisum on imaging by obstructing a segment of the ventral duct. By performing the EUS we were able to discern that the pancreatitis was a combination of IPMN and pancreas divisum. By careful examination IPMN was diagnosed and subsequently appropriate steps of management were performed.

TREATMENT

With the suspicion of a ventral duct IPMN, the patient underwent a pancreaticoduodenectomy. The final pathology was consistent with a main duct IPMN of intestinal type with moderate dysplasia (figures 5 and 6), and presence of pancreatic intraepithelial neoplasia (highest grade 2). The background pancreas had chronic obstructive pancreatitis with glandular atrophy. The surgical specimen had benign resection margins and lymph nodes.

OUTCOME AND FOLLOW-UP

Six months postsurgery the patient had no recurrence of abdominal pain. She has no complications and is able to perform daily activities of living without restrictions.

DISCUSSION

IPMN has been diagnosed more frequently over the past few decades due to advances in imaging.⁵ Approximately 19% to 23% of patients with acute recurrent pancreatitis have an underlying cystic neoplasm of the pancreas.⁴ IPMN is classified into three different categories including main duct, branch duct and combined or mixed IPMN.⁷ Main duct IPMNs have a 70% increased likelihood of becoming malignant as compared with branch duct IPMN, and thus are treated more aggressively.^{8 9}

IPMN has been associated with 12–67% of acute pancreatitis cases.⁴ The pathogenesis of acute pancreatitis with IPMN is theoretically an obstructive phenomenon due to excessive mucin production, which in turn elevates the ductal pressure and prematurely activates pancreatic enzymes.¹⁰ There is no significant correlation that explains whether malignant or benign IPMN is causing the acute pancreatitis.⁴ Further, the risk of acute pancreatitis is similar between main duct IPMN and branch duct IPMN.^{7 11} CT, MRI and EUS can help diagnose IPMN and therefore should be utilised in cases of recurrent acute pancreatitis or suspected ductal pathology.^{11 12}

In pancreas divisum, there is significant controversy whether it is an actual cause of pancreatitis or an incidental finding. Initial studies by Cotton *et al* demonstrated a correlation between the two, but other studies have contradicted this finding and suggested that the results by them were consistent with a referral bias.^{13 14} A theory relating to increased minor papilla spasm or narrowing has been implicated as the cause of pancreatitis in pancreas divisum.¹⁵ Takuma *et al*¹⁶ investigated

Figure 4 Large calcification observed in the head of the pancreas with associated cyst versus dilation of the ventral pancreatic duct. Cyst/dilation measured 12 mm.

Figure 5 Intraductal papillary mucinous neoplasm with intermediate grade dysplasia at $\times 20$ and $\times 40$ magnification.

Figure 6 Intraductal papillary mucinous neoplasm at low resolution $\times 2$ and $\times 4$.

this question by reviewing pancreatogram films and found that the incidence of complete and incomplete pancreas divisum was 1.6% and 1.4%, respectively. He later looked at the relationship of acute and chronic pancreatitis in association with alcohol and found that the majority of complete pancreas divisum patients ingested only a mild amount of alcohol and had more acute pancreatitis episodes as compared with controls. Additionally, pancreas divisum patients had an increased chance of having chronic pancreatitis in association with low to no alcohol consumption compared with controls. This suggests at least a reduced threshold for the development of pancreatitis when pancreas divisum is present. Unfortunately, imaging modality

using EUS and MRI fail to predict which cases of pancreas divisum will progress to pancreatitis.^{3 17 18} In situations with recurrent pancreatitis from pancreas divisum, minor papilla sphincterotomy has been shown to be helpful.¹⁹

This case is particularly distinct because there is a main duct IPMN in the ventral duct of pancreas divisum, as opposed to previous cases, which have demonstrated IPMNs in the dorsal duct.^{20–23} This is the second case of IPMN affecting only the ventral duct of pancreas divisum and the first to present with signs of chronic pancreatitis.^{6 24} Another unique aspect of the present case is the presence of pancreatic lithiasis. Most cases of IPMN have no signs of calcification. The possible explanations

for stone formation in IPMN are twofold. One explanation could be the increased mucin production, which in turn causes microlithiasis. Another explanation could be recurrent low-grade pancreatitis causing chronic pancreatitis and stone formation.²⁵

Multiple studies have investigated the association between pancreas divisum and malignancy. Some studies found a higher incidence of pancreatic adenocarcinoma in association with pancreas divisum.^{6 16} Takuma *et al*¹⁶ actually demonstrated that 9% of patients with pancreas divisum have pancreatic cancer, much higher than the normal population. All of the cancers in this study involved the dorsal duct. It is postulated that chronic obstruction of the pancreatic duct with recurrent inflammation can possibly promote oncogenesis.^{16 26}

In summary, pancreatic stones can occasionally be seen in pancreas divisum or IPMN and, therefore, further investigation is warranted. These should not be disregarded as chronic pancreatitis. It is also crucial to investigate the ventral duct in pancreas divisum as IPMNs and malignancy can still arise from this area. Studies have shown a predilection for pancreatic cancer in pancreas divisum and, therefore, it is extremely important to carefully assess the pancreas for secondary causes of recurrent pancreatitis. Detailed ductal and parenchymal evaluation of patients is necessary for early diagnosis and treatment so as to avoid progression to unresectable disease.

Learning points

- ▶ Pancreatic stones can occasionally be seen in intraductal papillary mucinous neoplasm and pancreas divisum.
- ▶ It is important to fully evaluate ventral duct of pancreas divisum to rule out other pathologies.
- ▶ It is crucial to fully investigate the causes of pancreatitis in patients who lack any risk factors for pancreatitis.
- ▶ There is a predilection for increased pancreatic malignancies associated with pancreas divisum than previously thought.

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REFERENCES

- 1 Guda NM, Romagnuolo J, Freeman ML. Recurrent and relapsing pancreatitis. *Curr Gastroenterol Rep* 2011;13:140–9.
- 2 Levy MJ, Geenen JE. Idiopathic acute recurrent pancreatitis. *Am J Gastroenterol* 2001;96:2540–55.
- 3 Kanth R, Samji NS, Inaganti A, *et al*. Endotherapy in symptomatic pancreas divisum: a systematic review. *Pancreatol* 2014;14:244–50.
- 4 Venkatesh PG, Navaneethan U, Vege SS. Intraductal papillary mucinous neoplasm and acute pancreatitis. *J Clin Gastroenterol* 2011;45:755–8.
- 5 Klibansky DA, Reid-Lombardo KM, Gordon SR, *et al*. The clinical relevance of the increasing incidence of intraductal papillary mucinous neoplasm. *Clin Gastroenterol Hepatol* 2012;10:555–8.
- 6 Sakate Y, Ohira M, Maeda K, *et al*. Intraductal papillary-mucinous adenoma developed in the ventral pancreas in a patient with pancreas divisum. *J Hepatobiliary Pancreat Surg* 2004;11:366–70.
- 7 Kobari M, Egawa S, Shibuya K, *et al*. Intraductal papillary mucinous tumors of the pancreas comprise 2 clinical subtypes: differences in clinical characteristics and surgical management. *Arch Surg* 1999;134:1131–6.
- 8 Serikawa M, Sasaki T, Fujimoto Y, *et al*. Management of intraductal papillary-mucinous neoplasm of the pancreas: treatment strategy based on morphologic classification. *J Clin Gastroenterol* 2006;40:856–62.
- 9 Tanaka M, Chari S, Adsay V, *et al*. International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. *Pancreatol* 2006;6:17–32.
- 10 Tanaka M, Kobayashi K, Mizumoto K, *et al*. Clinical aspects of intraductal papillary mucinous neoplasm of the pancreas. *J Gastroenterol* 2005;40:669–75.
- 11 Ringold DA, Shroff P, Sikka SK, *et al*. Pancreatitis is frequent among patients with side-branch intraductal papillary mucinous neoplasia diagnosed by EUS. *Gastrointest Endosc* 2009;70:488–94.
- 12 Taouli B, Vilgrain V, Vullierme MP, *et al*. Intraductal papillary mucinous tumors of the pancreas: helical CT with histopathologic correlation. *Radiology* 2000;217:757–64.
- 13 Burtin P, Person B, Charneau J, *et al*. Pancreas divisum and pancreatitis: a coincidental association? *Endoscopy* 1991;23:55–8.
- 14 Cotton PB. Congenital anomaly of pancreas divisum as cause of obstructive pain and pancreatitis. *Gut* 1980;21:105–14.
- 15 Satterfield ST, McCarthy JH, Geenen JE, *et al*. Clinical experience in 82 patients with pancreas divisum: preliminary results of manometry and endoscopic therapy. *Pancreas* 1988;3:248–53.
- 16 Takuma K, Kamisawa T, Tabata T, *et al*. Pancreatic diseases associated with pancreas divisum. *Dig Surg* 2010;27:144–8.
- 17 Catalano MF, Lahoti S, Alcocer E, *et al*. Dynamic imaging of the pancreas using real-time endoscopic ultrasonography with secretin stimulation. *Gastrointest Endosc* 1998;48:580–7.
- 18 Khalid A, Peterson M, Slivka A. Secretin-stimulated magnetic resonance pancreaticogram to assess pancreatic duct outflow obstruction in evaluation of idiopathic acute recurrent pancreatitis: a pilot study. *Dig Dis Sci* 2003;48:1475–81.
- 19 Rustagi T, Golio M. Diagnosis and therapy of pancreas divisum by ERCP: a single center experience. *J Dig Dis* 2013;14:93–9.
- 20 Akizuki E, Kimura Y, Mukaiya M, *et al*. A case of intraductal papillary mucinous tumor associated with pancreas divisum. *Pancreas* 2006;32:117–18.
- 21 Kamisawa T, Yoshiike M, Egawa N, *et al*. Pancreatic tumor associated with pancreas divisum. *J Gastroenterol Hepatol* 2005;20:915–18.
- 22 Yarze JC, Chase MP, Herlihy KJ, *et al*. Pancreas divisum and intraductal papillary mucinous tumor occurring simultaneously in a patient presenting with recurrent acute pancreatitis. *Dig Dis Sci* 2003;48:915.
- 23 Sakurai Y, Matsubara T, Imazu H, *et al*. Intraductal papillary-mucinous tumor of the pancreas head with complete absence of the ventral pancreatic duct of Wirsung. *J Hepatobiliary Pancreat Surg* 2004;11:293–8.
- 24 Santi L, Renzulli M, Patti C, *et al*. First case of 2 intraductal papillary mucinous tumors of both ventral and dorsal ducts in pancreas divisum. *Pancreas* 2010;39:110–11.
- 25 Kimura W. Pancreatic lithiasis and intraductal papillary-mucinous neoplasm with special reference to the pathogenesis of lithiasis. *J Hepatobiliary Pancreat Sci* 2010;17:776–81.
- 26 Traverso LW, Kozarek RA, Simpson T, *et al*. Pancreatic duct obstruction as a potential etiology of pancreatic adenocarcinoma: a clue from pancreas divisum. *Am J Gastroenterol* 1993;88:117–19.

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