

A Case of Paraduodenal Pancreatitis and Immunohistochemical Analysis

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Paraduodenal pancreatitis (PP) is a rare, distinct form of chronic pancreatitis, and it is related to alcohol abuse in middle-aged men. A 36-year-old man with a history of chronic recurrent pancreatitis for 4 years and alcohol abuse for 15 years presented with abdominal pain. Computed tomography revealed a multilocular cystic mass 3.2 × 3 × 3 cm in size and it was located within the muscular layer of the duodenal wall. The cysts were lined by a single layer of eosinophilic cuboidal epithelial cells that stained positively for mucin (MUC)1, MUC6, cytokeratin (CK)7 and CK19 and they stained negatively for MUC2, MUC5AC and CK5/6. Mild, chronic inflammatory reaction around the cystic wall, Brunner's gland hyperplasia and several clusters of heterotopic pancreatic tissue were noted. We report here on a case of PP and we demonstrated that the pancreatitis was of pancreatic ductal cell origin according to the MUC and CK expression patterns we observed on the immunohistochemical analysis.

Key Words : Pancreatitis, chronic; Pancreatic ducts; Cysts

Paraduodenal pancreatitis (PP) is a rare and distinct form of chronic pancreatitis, and PP has been reported under various names such as cystic dystrophy of a heterotopic pancreas, pancreatic hamartoma of the duodenum, para-ampullary duodenal wall cyst, myoadenomatosis and groove pancreatitis.¹ This illness has relatively specific characteristics for the clinical history and pathologic findings. Men in their 30s or 40s with a history of alcohol abuse are predominantly affected, and severe upper abdominal pain is the main presenting symptom.¹ The "groove area", which lies between the common bile duct, pancreas and duodenum, is usually involved.² The characteristic pathologic findings include dilated ducts or pseudocystic change in the duodenal wall, adjacent stromal reaction, Brunner's gland hyperplasia, myoid stromal proliferation and spillover of fibrosis into the groove area.¹

"Paraduodenal pancreatitis" has been suggested as unifying terminology by Adsay and Zamboni¹ because this is a distinct clinicopathologic entity. Two cases of "groove pancreatitis" have currently been reported in the Korean literature.^{3,4} All cases involved alcohol abuse, chronic pancreatitis and duodenal stenosis. Although only 1 case was pathologically proven,⁴

none of them demonstrated the origin of the PP. The present report suggests a pancreatic ductal epithelial origin of PP according to the immunohistochemical analysis.

CASE REPORT

A 36-year-old man presented with abruptly aggravated abdominal pain in the right upper quadrant and persistent nausea. He had a history of alcohol abuse for the previous 15 years. He had been followed-up as a chronic pancreatitis patient for the previous 4 years. The computed tomography (CT) findings obtained 2 years ago suggested a pancreatic pseudocyst or cystic neoplasm in the groove region between the duodenum and the pancreas. The abdominal pain was recently aggravated and the cystic lesion was enlarged on the follow-up CT (Fig. 1A). Laboratory analyses revealed a normal serum amylase level of 149 IU/L (normal range, 25 to 150 IU/L) and an increased serum lipase level of 83 U/L (normal range, 13 to 60 U/L). The man's condition was intractable with the administered medical therapy. The patient insisted on surgical resec-

tion for his persistent abdominal pain. Pylorus-preserving pancreaticoduodenectomy was performed under the impression of a mucinous cystadenoma or pseudocyst complicated by chronic pancreatitis. Cholecystectomy was also performed owing to the cholecystitis with gallstones. Gross examination revealed that

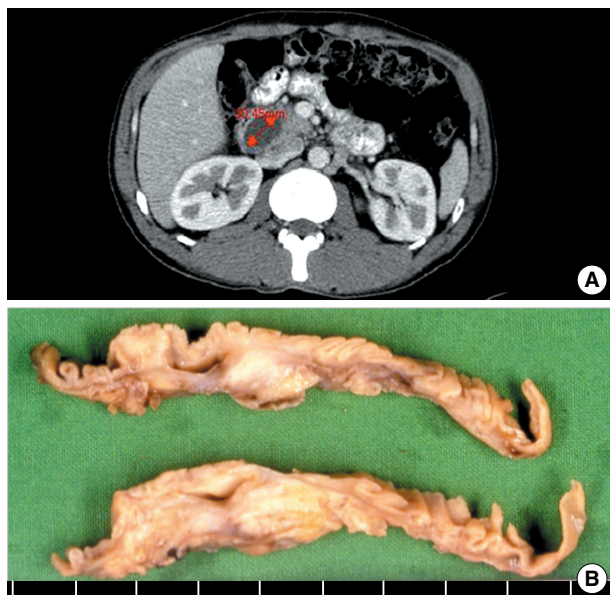


Fig. 1. (A) The abdomen computed tomogram shows a cystic mass 30 mm in size in the duodenal wall in the “groove area”, which lies between the pancreas and the duodenum. (B) A multilocular cyst is present in the muscular layer of the duodenal wall.

the pancreas was neither enlarged nor shrunken. The pancreas was attached to the duodenal wall with a broad base. The duodenal mucosa was edematous and inflamed, but there was no stricture. Serial sectioning revealed 3 cysts within the duodenal wall in the region of the minor papilla (Fig. 1B). The multilocular cyst was composed of 3 cysts with the smallest cyst measuring 1.5×1.0 cm and the largest measuring 3.2×3.0 cm. The largest cyst extended to the adjacent pancreas. The cystic lesions were clearly demarcated, and the inner surface of the cysts was smooth and grayish. The pancreatic duct was dilated. Micrograph revealed that the cysts were located within the duodenal muscle layer. The 2 cystic masses were lined by low cuboidal to columnar epithelium surrounded by muscle bundles (Fig. 2A). The cytoplasm of the epithelial cells lining the cysts was clear to eosinophilic, and it mimicked that of the pancreatic duct epithelial cells. One cyst showed pseudocystic change without an epithelial lining. The Brunner’s glands were hyperplastic in the duodenal submucosa. Mild, chronic inflammatory reaction was noted in the periphery of the cystic wall without severe fibrosis. The pancreas itself and the heterotopic pancreatic tissue containing acini and Langerhans islets in the duodenal muscle layer showed mild, chronic inflammation with interlobular fibrosis (Fig. 2B). The apical portion of the lining epithelium of the cystic lesion stained positive for periodic acid stain (PAS), PAS after diastase digestion (D-PAS), mucin (MUC)1, MUC6, cytokeratin (CK)7 and CK19, while

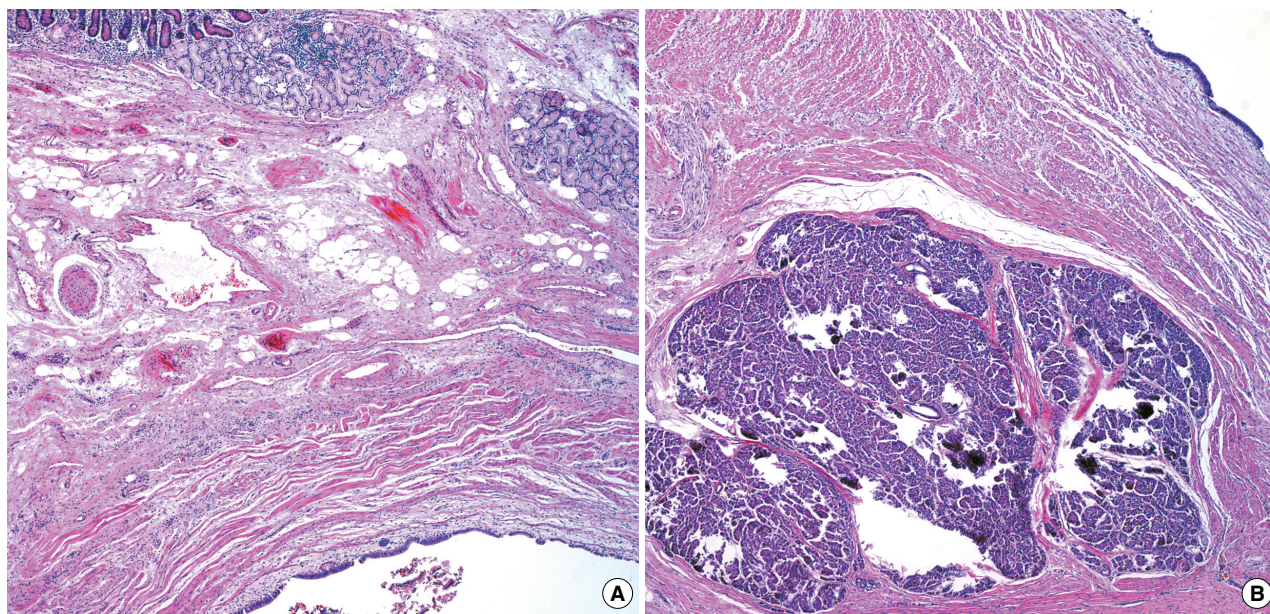


Fig. 2. (A) The single-layered cuboidal epithelial cyst is located in the muscular layer of the duodenal wall. (B) Heterotopic pancreatic tissue is present around the cyst.

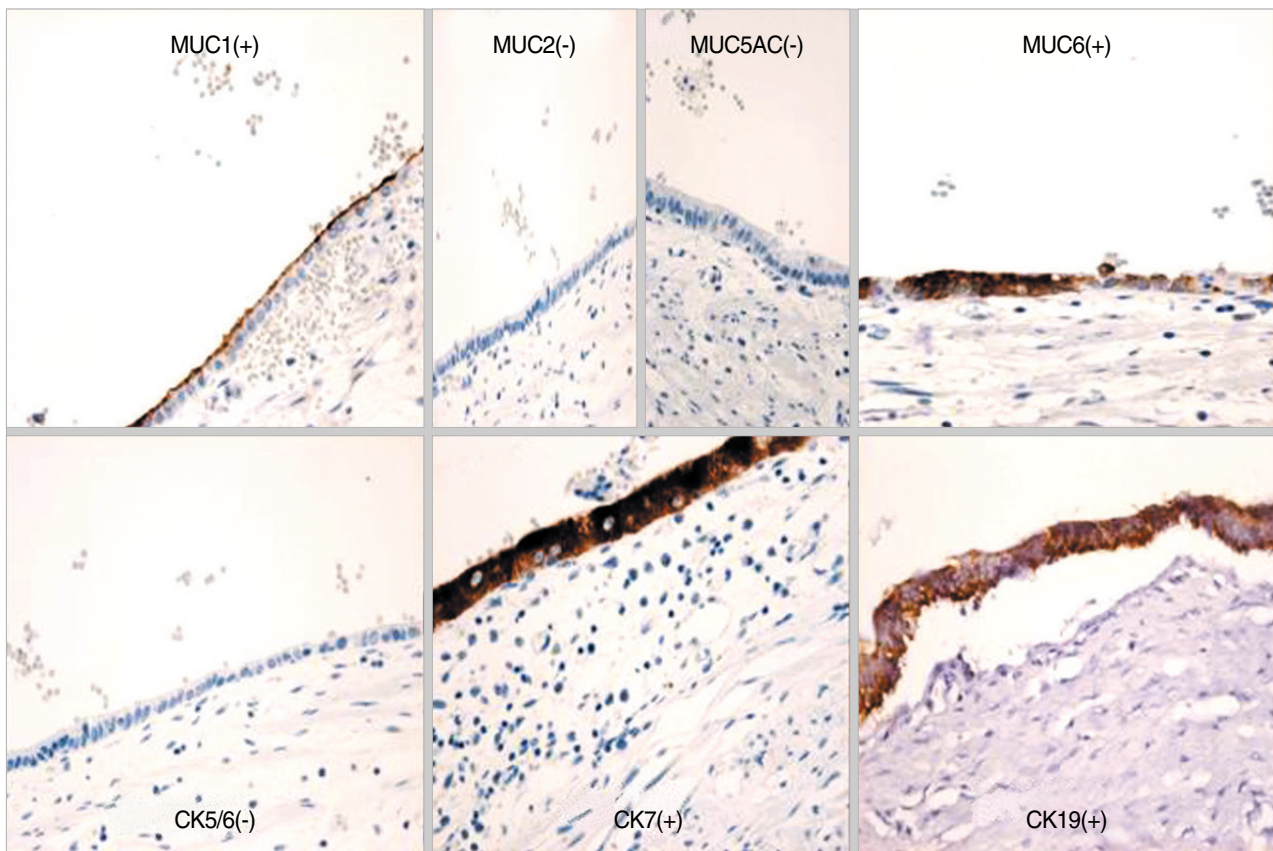


Fig. 3. Immunohistochemical analysis yields positive results for mucin (MUC)1, MUC6, cytokeratin (CK)7 and CK19 and negative results for MUC2, MUC5AC and CK5/6.

it stained negative for MUC2, MUC5AC and CK5/6 (Fig. 3).

DISCUSSION

PP is considered to involve a retention cyst of the cystically dilated duct segments of heterotopic pancreatic tissue.² In our case, the epithelial cells lining the cystic lesion were positive for MUC1, MUC6, CK7 and CK19 and they were negative for MUC2, MUC5AC and CK5/6. MUC1 is expressed in the cell apices of the centroacinar cells, the intercalated ducts and intralobular ducts, and MUC1 is focally expressed in the interlobular ducts, but not in the main pancreatic ducts, acini or islets.⁵ A MUC6 expression is observed in the periductal glands and the normal ductal epithelium in 67% of cases.⁶ MUC2 and MUC5AC are never expressed in normal pancreatic tissue.⁵ With regard to the cytokeratin pattern of the normal pancreas, the acinar cells express CK8 and CK18, whereas the ductal cells express CK7, CK8 and CK19.⁶ Accordingly, our immunohistochemical results clearly demonstrated that the PP origi-

nated from the pancreatic ductal epithelium. To the best of our knowledge, this is the first case of PP that was evaluated by immunohistochemical staining and reported in the English medical literature.

The pathogenesis of PP is unclear, but a strong possibility exists that repeated chronic inflammation may be the stimuli that resulted in an intense fibrotic reaction in the area between the duodenum and pancreas.^{1,2} The most common location where PP occurs is the region of the minor papilla, which is the drainage region for the accessory duct of the pancreas.¹ The minor papilla can contain a small cluster of pancreatic elements, including ducts, acini and islets at an incidence of 1-14%, in the submucosal layer.^{1,7} Alcohol can easily result in injury to the anatomic variations of the pancreas.¹ It is one of the most common causes of chronic pancreatitis, with up to 40-70% of all cases of chronic pancreatitis being due to alcohol;⁸ alcohol is probably also toxic to the acinar cells in heterotopic pancreatic tissue and it leads to fatty degeneration and necrosis of the acinar cells, as is seen in chronic pancreatitis.⁹

Although 4 cases of PP are known to have been published

Table 1. Review of the reported cases of paraduodenal pancreatitis in the Korean literature

	Case	Park <i>et al.</i> ⁴	Hwang <i>et al.</i> ³
Gender/age (yr)	M/36	M/43	M/46
Complaint	Abd pain, vomiting	Postprandial abd pain	Postprandial abd pain
Alcohol abuse Hx	+	+	+
Accompanying symptom	Cholecystitis with GB stone	-	Weight loss, watery diarrhea
Cyst (cm)	+ (3.2×3)	+ (small size)	+ (3.2)
Duodenal mucosa	Unremarkable	Redness, edema	Inflammation
Duodenal wall thickening	+	+	+
Duodenal stenosis	-	+	+
Serum amylase	Normal range	↑	Normal range
Serum lipase	↑	↑	↑

M, male; abd, abdominal; Hx, history; GB, gallbladder.

in the Korean literature, we could only find 2 cases. As in the present case, the patients of the other cases were middle-aged (range, 36 to 46 years; mean, 41 years) men with a history of alcohol abuse, and each complained of abdominal pain. Weight loss was observed in 1 case, and the present case was only accompanied with cholecystitis with gallbladder stone. The average size of the cyst in the previous 2 cases was 3.2 cm, and an edematous change and redness in the duodenal mucosa was found in the previous cases, except for the present one. Although a thickened duodenal wall was observed in all the cases, the previous cases were accompanied with duodenal stenosis. The serum lipase levels were increased in all the cases, while the serum amylase levels were within the normal range or they were increased (Table 1).

The clinical differential diagnoses of PP include periampullary or pancreatic cancer, neoplastic cyst, pseudocyst and intestinal duplication. PP is most commonly accompanied with duodenal stenosis (91%) and less commonly, with cystic mass lesion (54%).⁹ The former finding is easily misdiagnosed as pancreatic or periampullary cancer because of observing severe fibrosis and an ill-defined border on radiologic examination. Cystic mass lesion must be distinguished from neoplastic cysts such as mucinous or serous cystadenomas or a pseudocyst complicated by chronic pancreatitis. Duodenal stenosis was observed in all of the previously reported cases in Korea, and the main differential diagnosis was pancreatic or periampullary cancer. On the other hand, our case presented as a cystic mass, and the main differential diagnosis was a neoplastic cyst in the pancreatic head.

The histological differential diagnosis of neoplastic cysts is important when a cystic mass is manifested because of its malig-

nant potential. In our case, the cystic wall was lined by a single layer of eosinophilic, cuboidal to columnar epithelial cells, and the cysts were located within the muscle layer of the duodenal wall. A cystic mass accompanied with PP is prominently distinguished from a pseudocyst by the pseudocyst having a fibrous cystic wall that is devoid of an epithelial cell lining, and it distinguished from an intestinal duplication by an intestinal-type mucosa with goblet cells in the cystic wall.² Serous oligocystic adenomas are rare, but they usually occur in the pancreatic head and body portions. They are lined by a single layer of low cuboidal to flattened epithelial cells. The cytoplasm of the epithelial cells is clear and rarely eosinophilic and granular. Owing to the presence of abundant intracytoplasmic glycogen, the cells of serous oligocystic adenomas are positive for PAS and negative for D-PAS. As for PP, the lining cells are more columnar-like ductular cells and they are positive for both PAS and D-PAS. Mucinous cystadenomas predominantly occur in women, and they are composed of a columnar mucinous epithelial layer and a densely cellular ovarian-type stromal layer.² The present case was devoid of ovarian stroma.

We report here on the third Korean case of cystic PP, and we demonstrated the MUC and CK expression patterns, which suggest its pancreatic ductal epithelial origin.

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