Small Pancreatic Cancer with Pancreas Divisum Preoperatively Diagnosed by Pancreatic Juice Cytology

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Abstract

We present a case of small pancreatic head cancer with pancreas divisum preoperatively diagnosed by pancreatic juice cytology. A 60-year-old woman was referred to our hospital for evaluation of a dilated main pancreatic duct (MPD). A small and poorly reproducible low-echoic lesion in the pancreas was suspected by ultrasonography (US) and endoscopic ultrasonography (EUS). Magnetic resonance cholangiopancreatography (MRCP) failed to visualize the ventral pancreatic duct, and the upstream dorsal pancreatic duct was dilated. Endoscopic retrograde cholangiopancreatography (ERCP) was indicative of pancreas divisum, and complete obstruction of the MPD in the pancreatic head was seen. Cytology of pancreatic juice obtained from the dorsal pancreas after minor papilla sphincterotomy revealed the presence of adenocarcinoma cells. Pancreatoduodenectomy was performed under the diagnosis of pancreatic head cancer with pancreas divisum. Histological examination revealed moderately-differentiated tubular adenocarcinoma 20 mm in diameter, located in the pancreatic head. Dilatation of the dorsal pancreatic duct is sometimes observed in cases with pancreas divisum without the presence of tumors. When pancreatic duct stenosis also exists in such cases, even if a tumor is not clearly visualized by diagnostic imaging, vigorous examinations such as pancreatic juice cytology are recommended to establish an accurate diagnosis.

Key words: pancreatic cancer, pancreas divisum, minor papilla sphincterotomy, pancreatic juice cytology

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Introduction

Pancreas divisum is a common anomaly of the pancreas. In patients with pancreas divisum, pancreatic juice is drained mainly through the minor papilla, which may result in inadequate drainage of the dorsal pancreas, leading to dilatation of the dorsal pancreatic duct or even pancreatitis. On the other hand, the relationship between pancreas divisum and pancreatic malignancy is controversial. We present a case of small pancreatic head cancer with pancreas divisum preoperatively diagnosed by endoscopic retrograde cholangiopancreatography (ERCP) and pancreatic juice cytology.

Case Report

A 60-year-old woman with hypertension, who had a family history of pancreatic cancer, was examined by her family physician. Although she did not complain of any abdominal symptoms, her periodical blood tests showed transient elevation of serum amylase and elastase-I levels. Endoscopic ultrasonography (EUS) and multidetector-row CT (MDCT) showed a slightly dilated main pancreatic duct (MPD), but no mass lesion in the pancreas. For the purpose of repeated evaluation of the pancreas, she underwent abdominal ultrasonography (US), MDCT scan, and magnetic resonance cholangiopancreatography (MRCP) thirteen months later on an outpatient basis. US showed the MPD to be 5 mm in maximal diameter, and a small low-echoic lesion was suspected.

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in the pancreatic head (Fig. 1), although the finding was not unequivocal. MDCT revealed that dilation of the MPD was greater than in the previous year, but no apparent mass lesion was identified (Fig. 2a, b). MRCP revealed a short stenosis of the dorsal pancreatic duct in the pancreatic head with moderate dilatation of the upstream duct (Fig. 3). Although she was still asymptomatic, she was referred to our hospital for further evaluation.

Her physical examination on admission was unremarkable. She was anicteric, and neither lymph node swelling nor abdominal masses were detectable. Laboratory data on admission were nearly normal (including amylase, elastase-I, CEA, and CA19-9). The oral glucose tolerance test showed a diabetic pattern. EUS detected a small low-echoic lesion in the pancreatic head, but it was ill-defined (Fig. 4). Endoscopic retrograde pancreatography (ERP) through the major papilla revealed a short arborizing ventral pancreatic duct without connection to the dorsal pancreatic duct. ERP via the accessory papilla showed obstruction of the dorsal pancreatic duct in the pancreatic head without opacification of the upstream duct (Fig. 5). The diagnosis of pancreas divisum was made based on the ERP and MRCP findings. Because co-existent pancreatic cancer was suspected from the ERP findings, transpapillary biopsy and pancreatic juice cytology were performed after minor papilla sphincterotomy (Fig. 6a, b). The biopsy specimen showed atypical epithelial cells (Fig. 7a). Cytologic examination verified adenocarcinoma cells (Fig. 7b). Based on these results, a preoperative diagnosis of pancreatic head cancer originating from the dorsal pancreas with pancreas divisum was made, and pancreateoduodenectomy was performed.

Resected specimen and histological mapping are shown in Fig. 8a. Pancreatography of the resected specimen from the minor papilla showed a short stenosis, and extravasation of contrast medium (Fig. 8b). Macroscopically, a whitish, irregular-shaped tumor was recognized in the pancreatic head along with the presence of possible pancreas divisum.
ERP via the major papilla opacified a short, arborizing ventral pancreatic duct without connection to the dorsal duct.

ERP via the minor papilla opacified a dorsal pancreatic duct, showing obstruction at the pancreatic head.

Minor papilla sphincterotomy with a wire-guided sphincterotome was performed to facilitate diagnostic procedures.

Transpapillary biopsy and pancreatic juice cytology were performed through a 7Fr sheath catheter.

Histology of the specimen taken by transpapillary biopsy showed atypical epithelial cells (Hematoxylin and Eosin staining, ×100).

Cytology of the collected pure pancreatic juice showed a cluster of adenocarcinoma cells (Papanicolaou stain, ×100).

head (Fig. 9a). Microscopically, a moderately differentiated tubular adenocarcinoma with focal invasion to the retropitoneal fatty tissue was confirmed (Fig. 9b). Although adenocarcinoma was identified in sections I-L (pathological tumor size, 20x11x6 mm), the tumor size was small in each section and carcinoma cells infiltrated into the pancreatic parenchyma sporadically, forming only small clusters except in section J. Findings of chronic pancreatitis concordant with secondary pancreatitis caused by the pancreatic cancer were seen in sections H-L.

On the other hand, the pancreatic tissue was almost normal in the downstream of the stenosis. Atypical epithelial
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Figure 8a. Resected specimen and histological mapping (arrow: the minor papilla, arrowhead: histologically confirmed Wirsung’s duct, circle: Santorini’s duct, red line: the presence of cancer, white line: the presence of chronic pancreatitis). Pathologically, adenocarcinoma cells were proven in sections I-L.

Figure 8b. Resected specimen and histological mapping (arrow: the minor papilla, arrowhead: histologically confirmed Wirsung’s duct, circle: Santorini’s duct, red line: the presence of cancer, white line: the presence of chronic pancreatitis). Pathologically, adenocarcinoma cells were proven in sections I-L.

Figure 9a. Pancreatography of the resected specimen through the minor papilla showed a short stenosis of the dorsal pancreatic duct, and extravasation of contrast medium (at risk).

Figure 9b. Microscopic view of the tumor. Arrowhead shows retropitoneal invasion (Hematoxylin and Eosin staining, ×2.5).

cells were seen in the MPD and branch ducts. According to the UICC criteria (TNM Classification of Malignant Tumors, Sixth Edition), the pathological classification was pT3N0M0, G2, Stage IIA (T3: retropitoneal invasion). According to Classification of Pancreatic Carcinoma (2nd English edition (1)) by the Japan Pancreas Society, the pathological stage was pStage III (pT3N0M0). Her postoperative course was uneventful. Since being discharged, she has been followed up at an outpatient clinic without any apparent signs of recurrence for 3 years.

Discussion

The frequency of pancreas divisum in ERCP series is reported to be 1.3-6.7% (2) in the English literature and 0.7-3.0% in the Japanese literature. The relationship between pancreas divisum and dorsal pancreatitis, especially idiopathic acute pancreatitis of a recurrent or relapsing nature has been discussed (2-5). It is speculated that the disproportion between the small minor papilla as an outlet and a large volume of pancreatic juice secreted from the dorsal pancreas (‘relative stenosis’) plays a predisposing role for pancreatitis. In patients with pancreas divisum, dilatation of the dorsal pancreatic duct is occasionally observed. According to Kamisawa et al (6), the maximal diameter of the dorsal pancreatic duct exceeded 4 mm in 11 out of 32 cases (34%) with complete pancreas divisum. Dilatation of the dorsal pancreatic duct associated with pancreas divisum may be difficult to differentiate from the dilatation caused by pancreatic cancer in some cases. According to Hayakawa et al (3), the incidence of pancreatic cancer in patients with pancreas divisum was 6% in English series and 2% in Japanese series. Similar to the present case, pancreatic cancers associated with pancreas divisum in past reports mostly developed from the dorsal pancreas. As far as we could determine from our review of the literature using Japan Centra Revuo Medicina and PubMed with the key words pancreatic cancer and pancreas divisum during the period from 1983 to 2007, a total of 41 cases of pancreatic cancer associated with pancreas divisum were reported in the Japanese literature. The average age was 64.0 (38-80), with man predominance (31:10). The tumor location was the pancreatic head in 17 cases, the body and/or tail in 17 cases, and the entire pancreas in 4 cases (tumor locations were not mentioned in 3 cases). In all but one case, the tumor developed from the dorsal pancreas. In the English literature, seven cases of pancreatic cancer with pancreas divisum have been reported (6-10). Cancer
developed from the dorsal pancreas in all cases.

One may speculate that the short Wirsung’s duct in this particular case resulted from cancer invasion. The distance from the major papilla to the ventral duct measured less than 10 mm on the pancreatogram as well as in histological examination, while in the histological examination, the distance from the major papilla to the stenosis was 37 mm, and the branches of Santorini’s duct were visualized in most parts of the pancreatic head. Therefore, it is quite reasonable to regard the present case as having unfused pancreatic ducts, i.e., pancreas divisum, with hypoplasia of the ventral pancreas.

The relationship between pancreas divisum and pancreatic cancer has not been well established. Nishino et al (12) reported on their analysis of 118 cases of complete pancreas divisum and 7,850 cases of fused pancreas identified among the 8,537 cases in their consecutive ERCP series. The prevalence of pancreatic cancer was significantly higher in patients with pancreas divisum than in those with a fused pancreas (10% vs. 4.8%). However, Delhaye et al (2) described that the frequency of pancreatic cancer was not significantly higher in patients with pancreas divisum than in patients with a fused pancreas (5.3% vs. 5.4%).

With regard to the possible relationship between pancreas divisum and pancreatic cancer, Traverso et al (10) speculated in a case study that chronic dorsal pancreatitis should be performed when pancreatic duct stenosis is also present, regardless of identification of any tumorous lesion by diagnostic imaging.

References


The detection rate of small pancreatic cancer by EUS is reportedly 74-94% (13, 14), which is higher than the rates by other imaging modalities. In the present case, preoperative diagnosis was difficult because the tumor was not reproducibly visualized by imaging modalities, including EUS. In addition to the small tumor size and co-existent secondary chronic pancreatitis, the mode of tumor invasion and tumor location (pancreatic neck portion) may be possible explanations for the diagnostic difficulty. Transpapillary biopsy and pancreatic juice cytology after minor papilla sphincterotomy provided important information for the establishment of the preoperative diagnosis.

The sensitivity and specificity of pancreatic juice cytology (15-19) are reportedly 30-79% and 94-100%, respectively. Nakaizumi et al (17) reported a high accuracy of pancreatic juice cytology (100%) for small pancreatic cancers (TS1; macroscopic tumor size of 2 cm or less). Takasawa et al (19) also reported the sensitivity of transpapillary pancreatic juice cytology in pTS1 (pathologically proven tumor size of 2 cm or less) cases to be 70%. Therefore, pancreatic juice cytology should be considered, especially when the tumor is small or equivocal.

In this particular case, although the tumor size was small (2 cm in maximal diameter), retroperitoneal invasion was histologically proven. The rate of retroperitoneal invasion and 4-year survival rates in pTS1 cases are reported to be 45.2% and 54.5%, respectively (13). We have to recognize that even pTS1 cancer is not an early cancer. Development of new diagnostic methods is mandatory for the improvement of the prognosis.

In conclusion, although dilatation of the dorsal pancreatic duct is often observed in cases with pancreas divisum, vigorous examinations including pancreatic juice cytology should be performed when pancreatic duct stenosis is also present, regardless of identification of any tumorous lesion by diagnostic imaging.