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High-grade pancreatic intraepithelial neoplasia diagnosed with the change of findings in magnetic resonance cholangiopancreatography: A case report

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Abstract

BACKGROUND

High-grade pancreatic intraepithelial neoplasia (PanIN) exhibits no mass and is not detected by any examination modalities. However, it can be diagnosed by pancreatic juice cytology from indirect findings. Most previous cases were diagnosed based on findings of a focal stricture of the main pancreatic duct (MPD) and caudal MPD dilatation and subsequent pancreatic juice cytology using endoscopic retrograde cholangiopancreatography (ERCP). We experienced a case of high-grade PanIN with unclear MPD at 20 mm, but without caudal MPD dilatation in magnetic resonance cholangiopancreatography (MRCP).

CASE SUMMARY

A 60-year-old female patient underwent computed tomography for a follow-up of uterine cancer post-excision, which revealed pancreatic cysts. MRCP revealed unclear MPD of the pancreatic body at a 20-mm length without caudal MPD dilatation. Thus, course observation was performed. After 24 months, MRCP revealed an increased

caudal MPD caliber and a larger pancreatic cyst. We performed ERCP and detected atypical cells suspected of adenocarcinoma by serial pancreatic juice aspiration cytology examination. We performed a distal pancreatectomy and obtained a histopathological diagnosis of high-grade PanINs. Pancreatic parenchyma invasion was not observed, and curative resection was achieved.

CONCLUSION

High-grade Pan-IN may cause MPD narrowing in the long length without caudal MPD dilatation.

Key Words: Pancreatic cancer; Pancreatic intraepithelial neoplasm; High-grade pancreatic intraepithelial neoplasm ; Magnetic resonance cholangiopancreatography; Carcinoma *in situ*; Case report

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Core Tip: High-grade pancreatic intraepithelial neoplasia (PanIN) is diagnosed using pancreatic juice cytology. Most reasons for performing endoscopic retrograde cholangiopancreatography (ERCP) are focal main pancreatic duct (MPD) stenosis and/or caudal MPD dilatation. Poor MPD depiction without caudal MPD dilatation in MRCP sometimes occurs in normal individuals. Thus, we hesitate to send these patients to ERCP. As such, course observation is necessary to confirm whether or not caudal MPD dilatation and/or cyst formation develops. Accordingly, it is better to send the patient to ERCP to detect high-grade PanIN if caudal MPD dilatation and/or cyst formation occurs.

INTRODUCTION

High-grade pancreatic intraepithelial neoplasia (PanIN) grows in the pancreatic duct with flat or low-papillary progression and is included in pancreatic cancer (PC) stage 0. Thus, high-grade PanIN is considered a curative PC, and attention has been paid to diagnosing them. Unfortunately, PanIN does not form a mass and can only be diagnosed by pancreatic juice cytology from indirect findings (e.g., main pancreatic duct (MPD) stricture and dilatation, pancreatic cyst, pancreatic atrophy, *etc.*). Most cases were characterized by limited MPD stenosis following caudal MPD dilatation. Herein, we experienced a case of high-grade PanIN that demonstrated a poor description of the MPD in a rather long range, with no caudal MPD dilatation.

CASE PRESENTATION

Chief complaints

None

History of present illness

A 60-year-old female patient underwent a computed tomography for a follow-up of uterine cancer post-excision, which revealed pancreatic cysts.

History of past illness

The patient had diabetes mellitus and did not smoke or drink alcohol.

Personal and family history

She had no family history of PC or chronic pancreatitis.

Physical examination

Physical examination on admission indicated a height of 156 cm, weight of 68.5 kg, and body mass index of 27.4 kg/mm^2. Her abdomen was soft and flat with no palpable mass.

Laboratory examinations

Her relevant laboratory data included hemoglobin A1c of 11.8% and CA19-9 of 57U/mL.

Imaging examinations

Contrast-enhanced computed tomography (CE-CT) revealed a round 5-mm cyst in the pancreatic tail but with no solid mass, atrophy, or fatty change in the pancreas (Figure 1A and 1B). Further, endoscopic ultrasonography (EUS) revealed a diffuse high echoic spot in the whole pancreas (Figure 2A and 2B), indicating early chronic pancreatitis and a small round cyst in the pancreatic tail (Figure 2C) and there was no caudal MPD dilatation (Figure 2D). A solid mass, hypoechoic area around the MPD, and caudal MPD dilation were not detected. Magnetic resonance cholangiopancreatography (MRCP) poorly described the MPD at the 20-mm length of the pancreatic body/tail (Figure 3A), with no caudal MPD dilation. This finding appeared like irregular MPD narrowing in other MRCP sequences (Figure 3B). Imaging examination for pancreatic cysts was followed up twice a year. MPD findings indicated no changes after 6 months (Figure 4A and 4B). The range of MPD narrowing did not change over 24 months, but caudal MPD dilatation was slightly detected and the cyst size had increased (Figure 4C and 4D).

FURTHER DIAGNOSTIC WORKUP

We performed a further examination considering the induction of high-grade PanIN. CE-CT revealed no solid space-occupying lesion, including a delayed enhanced area, but the pancreatic tail cyst grew to 10 mm, and the caudal MPD was slightly dilated (Figures 5A–5F). In EUS, the cyst was described as like a solid mass (Figure 6A), but

contrast-enhanced EUS using Sonazoid showed the mass as a round cystic lesion (Figure 6B). In CT, MRCP, and EUS, we could not find a connection between MPD and the cyst. Endoscopic retrograde cholangiopancreatography (ERCP) revealed that the MPD in the pancreatic tail was irregularly narrowing at 20 mm and caudal MPD was slightly dilated (Figure 7A). Serial pancreatic juice aspiration cytology examination (SPACE) revealed adenocarcinomas in 3 out of 4 samples (Figure 7B). Whole body CE-CT, positron emission tomography, and magnetic resonance imaging with gadoxetate sodium revealed no PC metastasis.

FINAL DIAGNOSIS

We diagnosed the patient with PC, and suspicion of high-grade PanIN.

TREATMENT

We performed a distal pancreatectomy.

OUTCOME AND FOLLOW-UP

Surgical results included a 10-mm round cyst located in the pancreatic tail and a low-papillary adenocarcinoma cell (Figure 8A and 8B) that spread in the cyst wall. Cancer cells had spread to the MPD and branch duct, at 20 mm toward the pancreatic body (Figure 8C). Pancreatic parenchyma invasion was not observed, and the final diagnosis of her tumor was high-grade PanIN. The samples demonstrated some low-grade PanINs in the pancreas, with few fibrotic areas around the MPD with high-grade PanIN. Figure 8D shows the distribution of PanIN. The patient is alive without relapse 17 months postoperatively.

DISCUSSION

We experienced a case of high-grade PanIN, which was effectively diagnosed by course observation with MRCP. Cyst growth and caudal MPD dilatation enabled the SPACE. PC has high malignancy and is frequently detected in progressive situations. Thus, PC

is the worst prognostic cancer, with a 5-year survival rate of approximately 7.1% and 10% in Japan and the United States, respectively [1,2]. PanIN is a tumor that develops in a flat or low papillary shape within the pancreatic duct, of which highly atypical ones are classified as high-grade PanIN and included in PC Stage 0. Thus, many physicians have been exerting an effort to detect stage 0 PCs. However, the corresponding proportion of stages 0 and 1A cases accounted for only 1.7% and 4.1%, respectively [3,4]. High-grade PanIN does not form a mass, and imaging modalities cannot identify the carcinoma; therefore, recently, stage 0 has been diagnosed using pancreatic juice cytology [5,6], focusing on indirect findings, including MPD dilatation and/or stenosis, cyst formation, and focal atrophy of the pancreas [4,7-9]. Fibrosis around the MPD from obstructive pancreatitis by high-grade PanIN or immunological reaction for PanIN was believed to induce MPD stenosis [10].

Clear pancreatic duct stenosis or caudal MPD dilatation in any imaging modalities warrants readily recommending a trial of ERP cytology to the patient. However, the poor delineation of the MPD at relatively long distances by MRCP is a finding observed in normal cases. Pancreatic duct stenosis is frequently detected using MRCP, but which finding should be used to perform ERCP seems to be a problem, which is fraught with the risk of acute pancreatitis.

In recent years, Hanada *et al* [11] classified high-grade PanINs based on histopathological features. It is categorized into a flat type, in which mainly the flat tumor cells are limited to the branch duct (BD), and a low papillary type, in which the low papillary tumor cells spread over a long distance from the BD to the MPD. Thus, the reason for MPD stenosis in the flat type is frequently induced by fibrosis around the tumor, the short length of stenosis, and strong caudal MPD dilatation. In comparison to the flat type, the low papillary type induces MPD stenosis by both tumor progression in the MPD and fibrosis around the tumor. Thus, the length of stenosis can be longer than a flat type due to tumor progression in the MPD. Additionally, the stenosis might be milder in the low papillary type than in the flat type if the low papillary type demonstrates little fibrosis around the tumor. In our case, low papillary progression

and little fibrosis around the MPD might have reduced MPD stenosis and caudal MPD dilatation in the first visit.

We collected and reviewed previous reports. We searched PubMed and Ichushi-web (Japanese) from 2012 to 2022 for cases of high-grade PanIN with detailed information on MRCP and histopathological findings (Table 1). We found 27 cases [12-35], including 9 head lesions, 10 body lesions, and 8 tail lesions. Compared to the usual PC, body and tail tended to be more frequent. Of the 27 cases, MPD stenosis was observed in 24 cases. Further, all MPD stenosis, caudal MPD dilatation, and caudal cyst findings were present in 13 cases. Notably, not only the caliber of the MPD, but also the caudal cyst, which is a dilated BD, is an important finding in the search for high-grade PanIN. Based on histopathological findings, in 24 cases we found that the causes of MPD stenosis were fibrosis around the MPD. Fibrosis around the stricture and carcinoma *in situ* proliferation contributed to pancreatic duct stricture in 15 cases, and in four cases was due to fibrosis alone. Five cases demonstrated almost no fibrosis, and the stenosis may have been caused by the tumor tissue itself. Fibrosis around the pancreatic duct was considered a major factor in stenosis. Among the 21 patients with low papillary type, 13 demonstrated both fibrosis and carcinoma *in situ* proliferation in the stenosis area, and four cases exhibited only fibrosis, indicating the frequent involvement of stenosis. Only three cases were caused by the growth of carcinoma *in situ*.

In this case, the cyst expansion over time and the caudal MPD dilatation triggered the discovery of PanIN. Further, the MPD stenosis was thought to be caused by the progression of tumor cells because the tumor tissue was low-papillary and almost no fibrosis was observed in the stenotic part. Papillary hyperplasia may have progressed along the pancreatic duct wall, causing a long and irregular MPD narrowing, which may have taken a long time for the caudal MPD dilation to become clear. Poor MPD visualization by MRCP, as in this case, is a finding that can be observed even in a normal pancreas. However, in this case, PanIN seems to have already existed two years ago. We believe that early diagnosis and treatment will be possible, considering that PanIN caused long and irregular strictures and cases with caudal cysts were numerous.

In this case, there was a challenge to our diagnostic strategy. Recently, fine needle aspiration using EUS (EUS-FNA) has been shown to improve diagnostic accuracy in pancreatic cystic neoplasm (PCN) when differentiating mucinous *vs* non-mucinous PCN, and malignant *vs* benign PCN, in cases where CT or MRI are unclear [36]. We performed ERP, but not EUS-FNA for the cyst due to concerns of needle tract seeding and peritoneal dissemination by aspiration for a pancreatic tail lesion. In Japan, aspiration for suspicion of cystic neoplasm is typically performed only as clinical research. As such, we need to pay attention to the development and progression of a diagnostic strategy for PCN.

CONCLUSION

Here, we report a case of high-grade PanIN, which was diagnosed by continuous cytology of pancreatic juice based on changes in MRCP findings over time. This case was considered as very suggestive when considering an early diagnosis system for PC.

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