



Imaging Features in Pancreatic Neuroendocrine Tumor with Intraductal Growth and Venous Invasion: A Case Report and Literature Review

췌관내 발생 및 정맥 침범을 동반한 췌장 신경내분비
종양의 영상 소견: 증례 보고 및 문헌 고찰

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Pancreatic neuroendocrine tumors (PanNETs) are a rare type of pancreatic neoplasm. PanNETs with intraductal growth are considered extremely rare, and ductal involvement in NETs has been reported to correlate with aggressive clinical behavior. A 67-year-old male was referred to our hospital for further evaluation of a pancreatic tumor. Various imaging modalities, including ultrasonography, contrast-enhanced CT, MRI, and endoscopic ultrasonography (EUS), demonstrated a well-defined pancreatic mass in the head and body, primarily located within the main pancreatic duct with extension to the main portal vein. Histological diagnosis from an EUS-guided biopsy revealed a grade 3 well-differentiated NET. The patient was scheduled for surgery; however, multiple additional bone metastases were identified on ¹⁸F-fluorodeoxyglucose PET/CT. Although the presence of intraductal growth and portal vein invasion is uncommon in PanNETs, aggressive workup and treatment are essential in such cases.

Index terms Pancreatic Neuroendocrine Tumor; Intraductal Tumor; Main Pancreatic Duct; Portal Vein Invasion

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INTRODUCTION

Pancreatic neuroendocrine tumors (PanNETs) are rare pancreatic neoplasms, accounting for 2%–5% of all pancreatic tumors, and are classified as either functioning or non-functioning (1). Non-functioning PanNETs, due to the absence of endocrine symptoms, are typically associated with signs of an expanding mass in the pancreatic parenchyma. PanNETs are often detected at advanced stages, frequently involving invasion of surrounding structures or metastasis to the liver and lymph nodes (2). Pancreatic duct involvement is an uncommon imaging feature of PanNETs, and tumor growth within the main pancreatic duct (MPD) is extremely rare. This unusual neoplasm is linked to multiple unfavorable clinical and pathological features (3). Here, we report on PanNETs with intraductal growth and tumor thrombus in the portal vein, focusing on the imaging features and clinical outcomes.

CASE REPORT

A 67-year-old male was admitted to our institute with a pancreatic mass incidentally detected during routine screening US at a local clinic. The physical examination results were unremarkable. Laboratory data, including serum tumor markers, were also within normal limits: amylase, 78 IU/L (reference range [RR], 30–117 IU/L), lipase, 35 mg/dL (RR, 16–57 mg/dL), alpha-fetoprotein, 8.7 ng/mL (RR <8.78 ng/mL), serum carcinoembryonic antigen, <1.730 ng/mL (RR <5.0 ng/mL), and CA 19-9, 6.41 U/mL (RR <37.0 U/mL).

An initial US performed at the local clinic revealed a well-defined, homogeneous, hypoechoic mass in the pancreatic body (Fig. 1A).

Dynamic contrast-enhanced abdominal CT demonstrated an approximately 6.2 cm homogeneous, enhancing solid mass in the pancreatic head and body with a gradual enhancement pattern (precontrast/arterial/portal-venous/delayed phases, Hounsfield units: 38/77/110/91). The upstream pancreatic parenchyma also exhibited atrophic changes. The mass showed good demarcation, with a mainly smooth, lobulated margin and was confined to the pancreatic parenchyma. However, a small portion of the mass showed direct invasion into the adjacent main portal vein (Fig. 1A). No lymphadenopathy or intra-abdominal metastases were identified.

The patient underwent enhanced magnetic resonance cholangiopancreatography (MRCP) using an extracellular contrast agent (Fig. 1B). The morphology and dynamic enhancement pattern of the pancreatic mass on MRCP were similar to those observed on CT. The mass demonstrated relatively high signal intensity (SI) on T2-weighted images and iso-SI on T1-weighted images, with restricted diffusion. Similar to CT findings, most of the tumor was located within the MPD, with upstream parenchymal atrophy and direct invasion with focal extension into the adjacent main portal vein. Based on the intraductal pancreatic mass with relatively well-defined and homogeneous enhancement, the initial differential diagnoses included intraductal tubular neoplasm, intraductal tubulopapillary neoplasm, and, less commonly, intraductal acinar cell carcinoma. On hospital day 9, an endoscopic ultrasonography-guided biopsy was performed. Histopathological examination of the biopsy specimen revealed a tumor with an organoid growth pattern (Fig. 1C). The tumor consisted of uniform round cells with finely stippled nuclei and inconspicuous nucleoli. Cytological atypia was

Fig. 1. A 67-year-old male with pancreatic neuroendocrine tumor.

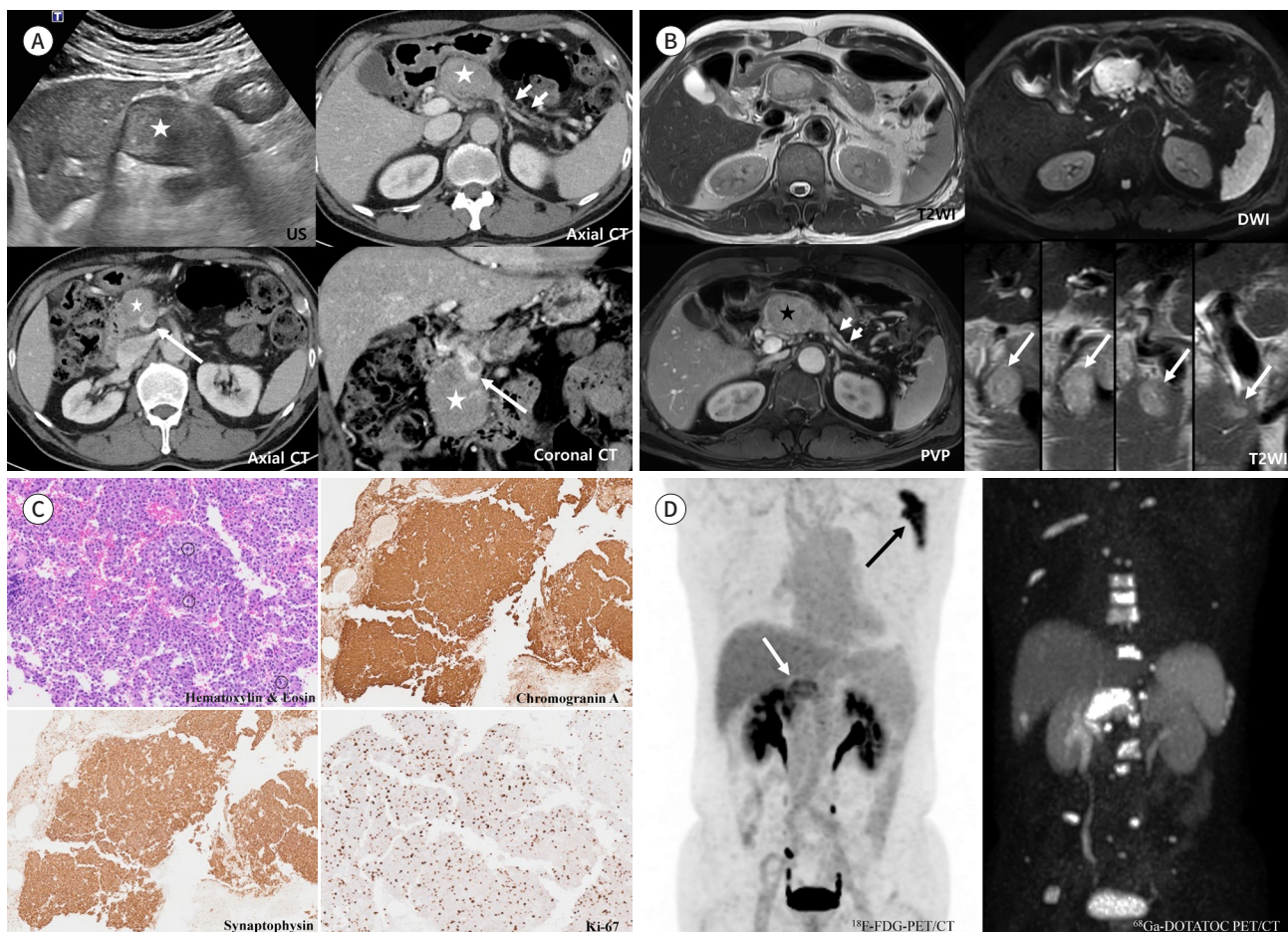
A. Transabdominal ultrasonography and dynamic contrast-enhanced abdominal CT with axial portal venous and coronal images. Ultrasonography shows a well-defined, homogeneous hypoechoic mass in the pancreas body. On CT, a 6.2 cm well-defined, homogeneous enhancing mass (asterisks) is noted in the pancreatic head and body. A small portion of the mass demonstrates direct invasion to the adjacent main portal vein (long arrows), and the upstream pancreatic parenchyma reveals atrophic changes (short arrows).

B. Dynamic enhanced magnetic resonance cholangiopancreatography using an extracellular contrast agent with axial T2WI, DWI, and PVP images. The PVP image shows that most of the tumor (asterisk) is located within the main pancreatic duct, with upstream parenchymal atrophy (short arrows). Coronal T2WIs with serial scans reveal an intraductal pancreatic mass (long arrows).

C. Histopathologic/immunohistochemical images with high-power view ($\times 200$). Hematoxylin and eosin stain shows monotonous tumor cells with minimal atypia and frequent mitoses. Chromogranin A and synaptophysin are positive in tumor cells. Ki-67 immunostaining shows focal nuclear labelling, with a 30% Ki-67 proliferation index.

D. ^{18}F -FDG-PET/CT and ^{68}Ga -DOTATOC PET/CT images. The initial ^{18}F -FDG-PET/CT image shows intense uptake in the primary pancreatic tumor (white arrow) and additional metastasis in the left scapula (black arrow). After 6 months of chemotherapy, the ^{68}Ga -DOTATOC PET/CT image reveals additional multiple metastases in the spine and hepatic tip, showing disease progression.

DWI = diffusion-weighted image, FDG = fluorodeoxyglucose, PVP = portal-venous phase, WI = weighted image



minimal to moderate, and the mitotic rate was 5/10 high-power fields. Immunohistochemical staining showed that the tumor cells expressed neuroendocrine markers, including synaptophysin and chromogranin-A, with a Ki-67 proliferation index of 30%. Consequently, according to the World Health Organization (WHO) 2019 classification, the patient was diagnosed with a grade 3 well-differentiated PanNET.

The patient was scheduled for surgery. However, an ^{18}F -fluorodeoxyglucose PET/CT scan for metastasis workup revealed additional bone metastasis in the left scapula. Despite systemic

chemotherapy for 6 months, ^{68}Ga -DOTATOC PET/CT images revealed multiple additional metastases in the spine and liver, indicating rapid disease progression (Fig. 1D).

This retrospective case report was prepared in accordance with the ethical principles of the Declaration of Helsinki.

DISCUSSION

Non-functional PanNETs have a higher potential for malignancy than functional tumors, such as insulinomas, due to the absence of endocrine symptoms. Consequently, preoperative diagnosis typically relies solely on imaging modalities (1). PanNETs usually appear as well-circumscribed masses with hyperenhancement during the arterial phase and mild hyperattenuation during the portal-venous and delayed phases. However, the degree of enhancement and homogeneity varies according to the tumor grade. Smaller tumors tend to be homogeneous, whereas larger tumors often exhibit heterogeneous enhancement due to internal necrosis and degenerative changes, including calcification. Typical PanNETs demonstrate expansile growth, and deviation or displacement of the MPD is frequently observed. Unlike pancreatic ductal adenocarcinoma, invasion of the ductal system by the tumor is rare.

Pancreatic neoplasms that predominantly exhibit intraductal growth are generally rare. These include intraductal papillary mucinous neoplasms, intraductal tubular neoplasms, and intraductal tubulopapillary neoplasms (4). On rare occasions, acinar cell carcinomas may also exhibit intraductal growth with a well-distinguished margin (5). In contrast, typical pancreatic ductal adenocarcinomas present with poor enhancement and irregular margins, often invading the pancreatic or bile ducts and adjacent structures (1). Our case presented a relatively well-defined large mass with homogeneous enhancement and expansile growth, devoid of necrosis. However, the mass primarily occupied the MPD, resulting in upstream parenchymal atrophy and adjacent vascular invasion. Therefore, it could mimic the aforementioned tumors, except adenocarcinoma.

Intraductal growth of PanNETs with venous invasion is extremely rare. To the best of our knowledge, only 15 cases, including this one, have been reported to exhibit intraductal growth (Table 1) (1, 2, 4-9). Although the underlying mechanisms are not entirely clear, two hypotheses exist regarding the intraductal growth of PanNETs. First, a parenchymal lesion near the MPD may extend into and along the duct. Alternatively, PanNETs may arise from totipotent stem cells in the epithelium of the major duct, forming a polypoid mass within the lumen (10). While the origin remains controversial, it is strongly believed that the tumor originated from islet or ductal cells near the MPD.

Preoperative differentiation between benign and malignant variants is challenging, particularly in patients without lymphadenopathy or aggressive invasion of adjacent organs. However, studies have suggested that intraductal growth and vascular invasion in non-functional PanNETs may be indicative of malignancy. Furthermore, PanNETs involving the MPD are associated with a higher risk of nodal metastasis and poorer clinical outcomes (3). Pathological examinations have shown that cases involving the MPD display an invasive growth pattern with fibrosis, distinct from classical NETs (3). Moreover, macrovascular venous invasion, such as venous tumor thrombus or direct wall invasion, has been linked to elevated levels of

Table 1. Summary of the Previous 14 Cases

Case	Age, yrs	Sex	Size, mm	Site	Biopsy Specimen		Surgical Specimen			Outcome
					Ki-67 Index, %	Grade	Ki-67 Index, %	Mitotic Count, /10 HPFs	Grade	
1	44	F	NA	H	Necrotic tissue		<5	NA	Low-grade malignant	NA
2	57	M	15	T	NA		15	NA	Malignant	Survived for 2 years
3	43	M	25	B	NA		<5	NA	Malignant	Survived for 1 year
4	36	M	16	H	NA		NA	NA	Malignant	Survived for 6 months
5	68	M	29	H	NA		NA	NA	Malignant	Dies from tumor recurrence (multiple liver metastasis)
6	47	F	75	H-T	NA		30–40	NA	NEC	Survived for 2 years
7	46	F	30	H	NA		Low	Low	NA	NA
8	26	F	NA	H-B	NA		NA	NA	G2	NA
9	78	M		H-T	60	G3	70–80	48	G3	Referred to another hospital
10	48	F	25	B	NA		5	NA	G2	Alive
11	83	F	37	H	NA		6	NA	G2	NA
12	50	F	18	B-T	NA		NA	NA	NA	NA
13	52	M	NA	H	NA		95	25	Adenoca. with NEC	NA
14	69	M	70	T	NA		<2	NA	Low-grade	Alive

B = pancreatic body, F = female, H = pancreatic head, HPF = high power field, M = male, NA = not available, NEC = neuroendocrine carcinoma, T = pancreatic tail

tumor circulating cells in the portal vein and a higher risk of metastasis.

In general, pancreatic NETs are known to grow slowly and are associated with prolonged survival compared to pancreatic ductal adenocarcinoma, which has a poor prognosis. However, in this case, despite the well-differentiated and homogeneous enhancing mass, the absence of necrosis, lymphadenopathy, or intra-abdominal metastasis, distant metastases were found, and the patient had a poor prognosis despite systemic chemotherapy. Imaging findings of intraductal growth and venous invasion, even in the presence of other benign features such as well-defined tumor margins and the absence of lymphadenopathy, suggest that an aggressive diagnostic and therapeutic approach should be considered.

In conclusion, we report an extremely rare case of a non-functional PanNET primarily located within the MPD, accompanied by venous invasion. Although the lesion in this patient was well-demarcated, with no regional lymphadenopathy or intra-abdominal metastasis, the patient developed aggressive bone metastases and had an unfavorable prognosis. Therefore, intensive and aggressive treatment should be pursued in cases involving intraductal growth and venous invasion.

Author Contributions

Conceptualization, P.H.J.; data curation, J.Y.K., P.H.J., R.R.R.; formal analysis, J.Y.K., P.H.J., L.E.S.; investigation, J.Y.K., P.H.J., R.R.R.; methodology, P.H.J., H.H.W., L.E.S., R.R.R.; supervision, P.H.J., H.H.W., L.E.S., R.R.R.; validation, P.H.J., L.E.S.; visualization, P.H.J.; writing—original draft, J.Y.K., P.H.J.; and writing—review & editing, J.Y.K., P.H.J., H.H.W.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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췌관내 발생 및 정맥 침범을 동반한 췌장 신경내분비 종양의 영상 소견: 증례 보고 및 문헌 고찰

정윤경¹ · 박현정^{1*} · 황혜원² · 이은선¹ · 유래림¹

췌관내 성장을 보이는 췌장 신경내분비 종양은 매우 드물며, 신경내분비 종양의 췌관 침범은 공격적인 병의 진행과 관련이 있다고 보고된다. 67세 남성 환자가 췌장 종양으로 병원에 내원하여 초음파, 조영증강 CT 및 MRI, 내시경 초음파를 시행하였다. 병변은 주췌관 내에 위치한 경계가 좋은 췌장 종양으로 간문맥 침범을 동반하고 있었다. 내시경 초음파 유도생검 결과 3등급의 고분화 신경내분비 종양으로 확인되었다. 환자는 수술 예정이었으나 양전자단층촬영 검사에서 추가적인 다발성 골전이가 확인되었다. 췌장 신경내분비 종양에서 췌관내 성장 및 정맥 침범이 발견되는 것은 일반적이지 않지만, 이러한 환자에 대해서는 좀 더 적극적인 검사와 치료가 필요하다.

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