CASE REPORT

A Rare Case of Duodenal Metastasis from Anaplastic Carcinoma of the Pancreas

Akira Yamamiya[1], Mimari Kanazawa[1], Keiichi Tominaga[1], Kenichi Goda[1], Shuhei Noda[2], Kazuyuki Ishida[2], Atsushi Irisawa[1]

[1]Department of Gastroenterology, Dokkyo Medical University School of Medicine, Mibu, Tochigi 321-0293, Japan

[2]Department of Diagnostics Pathology, Dokkyo Medical University School of Medicine, Mibu, Tochigi 321-0293, Japan

ABSTRACT

Anaplastic carcinoma not only infiltrates the surrounding tissue but also rarely metastasize to the gastrointestinal tract. Thus far, there are no reported cases of distant metastasis to the duodenum. Herein, we report a case of duodenal metastasis in a 65-year-old man. He had loss of appetite for a month, and his previous upper gastrointestinal endoscopy results revealed multiple sub-epithelial lesions with depression in the duodenum. Contrast-enhanced computed tomography then showed an intra-abdominal tumor with internal necrosis approximately 80 mm in size between the ventral segment of the pancreatic body, the lateral segment of the liver, and the lesser curvature of the stomach, multiple enlarged lymph nodes between the mediastinum and pelvic cavity, multiple intramuscular mass, and ascites. Biopsies taken from the duodenal lesion, intra-abdominal tumor, enlarged cervical lymph nodes, and immune-histology, revealed AE1/3 positive, maspin positive, CK7 negative, CK20 negative, and CA19-9 negative. We considered the possibility of a primary origin in the pancreas but failed to reach a definite diagnosis. We also considered chemotherapy for carcinoma of unknown primary origin, but the patient's general health deteriorated rapidly, and he died on day 35 of admission. Pathological autopsy revealed that the intra-abdominal tumor contained a mixture of giant cells and spindle cells. Finally, we diagnosed the tumor as an anaplastic pancreatic carcinoma with rare duodenal metastasis.

INTRODUCTION

Anaplastic carcinoma of the pancreas is a type of cancer that manifests with sarcomatoid growth patterns. The first case was reported by Sommers et al. in 1954 [1]. This neoplasm infiltrates the surrounding tissue and generates many hematogenous metastases, thereby leading to a much poorer prognosis than that in more common pancreatic carcinomas [2, 3, 4]. Apart from direct infiltration, they rarely metastasize to the gastrointestinal tract, and only a few cases of colorectal metastasis have been reported [5, 6, 7, 8]. However, to date, there are no reported cases of distant metastasis to the duodenum. We herein report a rare case of duodenal metastasis from anaplastic carcinoma of the pancreas.

Received April 15th, 2020 - Accepted May 16th, 2020
Keywords Pancreatic cancer; Neoplasm metastasis; Endoscopic Ultrasound-Guided Fine Needle Aspiration
Abbreviations WBC White Blood Cells; RBC Red Blood Cells; Hb Hemoglobin; Ht Hematocrit; PLT Platelet; TP Total Protein; Alb Albumin; T-bil Total Bilirubin; D-bil Direct Bilirubin; Cr Creatinine; Ca Calcium; AST Aspartic Aminotransferase; ALT Alanin Aminotransferase; LDH Lactate dehydrogenase; ALP Alkaline Phosphatase; γ-GTP γ-glutamyltransferase; Amy Amylase; SCC Squamous Cell Carcinoma; NSE Neuron-Specificenolase; CYFRA Cytokeratin Fragment; CEA Carcinoembryonic Antigen; CA19-9 Carbohydrate Antigen 19-9; DUPAN-II Pancreatic Cancer Associated Antigen-2; PSA Prostate Specific Antigen; AFP α-Fetoprotein; PIVKA-2 Protein Induced By Vitamin K Absence Or Antagonist-II; sIL2-R Soluble Interleukin-2 Receptor; EGD Esophagogastroduodenoscopy; EUS-FNA Endoscopic Ultrasound-guided Fine-Needle Aspiration; EMR Endoscopic Mucosal Resection; ESD Endoscopic Submucosal Dissection

Correspondence Atsushi Irisawa
Department of Gastroenterology,
Dokkyo Medical University
880 Kitakobayashi, Mibu,
Tochigi 321-0293, Japan
Tel +81-282-87-2147
Fax +81-282-86-7761
E-mail irisawa@dokkyomed.ac.jp

CASE PRESENTATION

A 65-year-old man experienced loss of appetite for about a month and was examined at another hospital. Esophagogastroduodenoscopy (EGD) revealed multiple sub-epithelial lesions with ulceration in the duodenum. Abdominal CT showed intra-abdominal masses. The patient was therefore referred to our hospital for admission and detailed examination. The patient had a history of liver cirrhosis due to hepatitis C and alcohol, diabetes mellitus, and left putaminal hemorrhage. The patient had a history of smoking and alcohol abuse for about 40 years. On admission, the patient was lucid, with no abnormal findings of the abdomen. Blood test

revealed an elevated serum C-reactive protein level (CRP 5.45 mg/dL), reduced hemoglobin (Hb 9.6 g/dL), and hypoalbuminemia (Alb 2.5 g/dL). Tumor marker tests revealed CYFRA of 5.6 ng/mL (normal range: <3.5 ng/mL), AFP of 174 ng/mL (normal range: <8 ng/mL), PIVKA-II of 2114 mAU/mL (normal range: 9.1-27.8 mAU/mL), and SIL-2 of 2060 U/mL (normal range: 220–230 U/mL) **(Table 1)**.

In a second EGD, multiple elevated sub-epithelial-like lesions with a depression along the descending part from the superior duodenal angle were identified **(Figure 1)**. Based on the morphology, we suspected malignant lymphoma or metastatic tumors and performed a biopsy at that site. Although metastatic carcinoma was diagnosed from pathological examination, we could not reach a definite diagnosis. A subsequent contrast-enhanced CT examination of the thoracic, abdominal, and pelvic regions revealed an intraabdominal tumor with internal necrosis approximately 80 mm in size between the ventral segment of the pancreatic body, the lateral segment of the liver, and the lesser curvature of the stomach, multiple enlarged lymph nodes between the mediastinum and pelvic cavity, multiple intramuscular mass, and ascites **(Figure 2)**. An Endoscopic Ultrasound-guided Fine-Needle Aspiration biopsy (EUS-FNA) was performed on the large intra-abdominal tumor to further investigate the primary tumor. The findings showed structural atypia. The immunohistological findings were as follows; lymphoid marker negative, AE1/3 strongly positive, maspin positive, uroplakin-2 negative, uroplakin-3 positive, TTF-1 negative, CK7/17/20 negative, CK18/19 positive, CD38 positive, AFP negative, CDX2 negative, and hepatocyte negative. Based on the above results from pathological examination, lymphoma was negative and epithelial malignancy or carcinosarcoma was suspected, but a definitive diagnosis could not be obtained.

Table 1. Laboratory Data on admission.

Peripheral Blood	WBC	5,ooo/μL
	RBC	326x104/μL
	Hb	9.6 g/μL
	Ht	29.50%
	PLT	16.8x104/μL
Biochemistry	TP	6.6 g/dL
	Alb	2.5 g/dL
	T-bil	0.9 mg/dL
	D-bil	0.5 mg/dL
	BUN	12 mg/dL
	Cr	0.77 mg/dL
	Ca	8.4 mg/dL
	AST	13 IU/L
	ALT	9 IU/L
	LDH	124 IU/L
	ALP	221 IU/L
	γ-GTP	41 IU/L
	Amy	33 IU/L
	P-Amy	21 IU/L
	Na	133.0 mEq/L
	K	4.6 mEq/L
	Cl	102 mEq/L
	CRP	5.45 mg/dL
Tumor Marker	SCC	1.0 ng/mL
	NSE	12.6 ng/mL
	CYFRA	5.6 ng/mL
	CEA	1.8 ng/mL
	CA19-9	14 U/mL
	DUPAN-2	41 U/mL
	SPAN-1	26 U/mL
	PSA	0.183 ng/mL
	AFP	174 ng/mL
	PIVKA-2	2114 mAU/mL
	sIL-2R	2060 U/mL

As we were unable to identify the primary tumor based on imaging and pathological examination, we considered chemotherapy for a cancer of unknown primary origin. However, the patient experienced rapid deterioration in general health, and he passed away on day 35 of admission. A pathologic autopsy was performed after obtaining informed consent from the patient's family. We found a 70-mm in size between the ventral segment of the pancreatic body, the lateral segment of the liver, and the lesser curvature of the stomach as well as the CT findings. Based on the absence of marked changes in the biliary epithelium and its location, we diagnosed the tumor in the pancreatic head. Histological examination of the tumor revealed severe dysplastic cells with a large nucleus and prominent nucleoli, and the cells were arranged in a tubular pattern. We also found many highly atypical giant cells and spindle cells, characteristic of invasive anaplastic carcinoma of the pancreas **(Figure 3)**. Immunohistology revealed that the tumor was AFP negative, naspin A negative, TTF-1 negative, CK7 negative, CK20 positive, hepatocyte negative, and maspin positive, all of which did not contradict an origin in the pancreas.

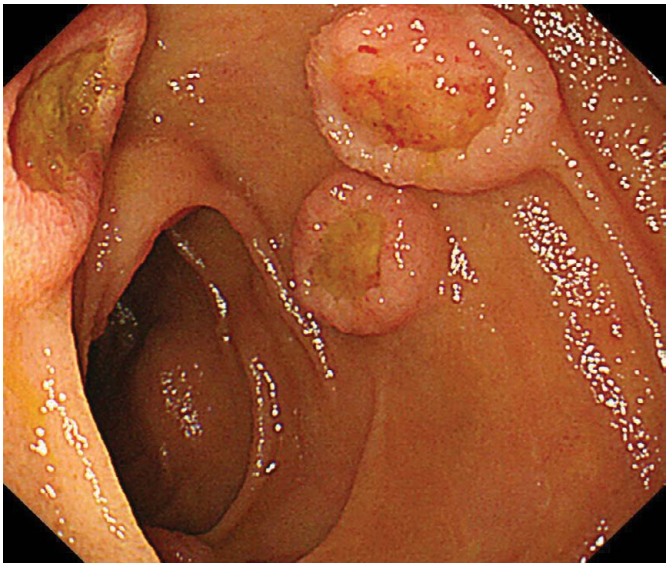

Figure 1. Esophagogastroduodenoscopy (EGD) findings. Multiple elevated subepithelial-like lesions with a depression were observed along the descending part from the superior duodenal angle.

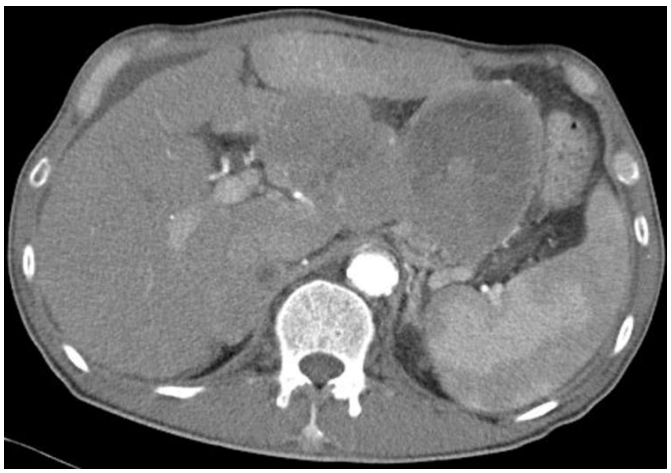

Figure 2. Contrast-enhanced computed tomography (CE-CT) findings. A large intraabdominal tumor was observed between the ventral segment of the pancreatic body, the lateral segment of the liver and ascites.

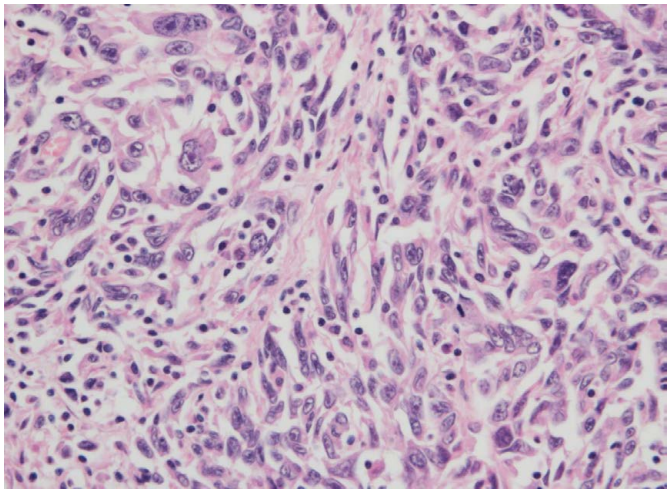

Figure 3. Pathologic autopsy findings of the tumor showed spindle and multinuclear giant cells, indicating an anaplastic carcinoma of the pancreas (HE stain×40).

DISCUSSION

Distant metastases of pancreatic cancer commonly arise in the liver, lungs, peritoneum, and lymph nodes, with rare cases of metastasis to the gastrointestinal tract [5, 9, 10]. We encountered a case of pancreatic anaplastic carcinoma with distant duodenal metastasis. In a study of autopsy reports, duodenal metastases were reported to account for 6% of duodenal malignant tumors [11], and duodenal metastasis from pancreatic carcinoma is speculated to be extremely rare.

There are three patterns of metastasis to the gastrointestinal tract:

1. Hematogenous metastasis,
2. Lymphogenous metastasis, and
3. Direct infiltration or secondary infiltration from peritoneal seeding

The majority of cases involve direct infiltration from an adjacent organ, which also accounts for most duodenal metastases from pancreatic carcinoma. Characteristic patho-histological findings of anaplastic carcinomas are tumor cells with a highly non-uniform nucleus in various forms and often loose cell adhesion [12]. These characteristics are assumed to give rise to reduced cell adhesion, tumor enlargement, and early hematogenous metastasis. Given these observations, the duodenal lesions in our case probably arose by hematological metastasis.

In this case, we failed to reach a definite pathological diagnosis before the patient's death. For conventional pancreatic carcinomas, a definite diagnosis can often be achieved using EUS-FNA, but cases of pancreatic anaplastic carcinoma are mostly diagnosed based on postoperative specimens, with few reports of cases diagnosed using EUS-FNA. Hoshimoto et al. reported a definite diagnosis in only 3 of 60 cases (5%) of pancreatic anaplastic carcinoma using endoscopic biopsy or EUS-FNA [13]. This result is believed to be due to a strong tendency toward necrosis and the difficulty of harvesting a viable specimen from the tumor. In our case, a specimen by EUS-FNA for the primary intra-abdominal tumor did not provide a definitive diagnosis.

In this case, we had difficulty in identifying the primary tumor based on CT findings and reaching an overall diagnosis using EGD both due to the atypicality of the metastasis from the primary pancreatic lesion and due to inadequate biopsied tissue for diagnosis. In this case, the findings suggest a metastatic tumor in the gastrointestinal tract. Therefore, if a diagnosis cannot be reached by normal biopsy, it is probably advisable to consider Endoscopic Mucosal Resection/Endoscopic Submucosal Dissection (EMR/ESD) or another method of obtaining as large a specimen as possible [14, 15]. We did not use EMR/ESD in this case, but when a EUS reveals a tumor located within the submucosal or mucosal layer, obtaining a "jumbo" biopsy using EMR/ESD can potentially help in reaching a definite diagnosis.

CONCLUSION

We experienced a rare case of anaplastic carcinoma of the pancreas with distant metastasis to the duodenum. We should at least be mindful of the existence of cases of distant metastasis to the duodenum from anaplastic carcinoma of the pancreas, which is, by itself, a rare type of pancreatic cancer. We should also consider that immunehistochemical analysis and unconventional methods of biopsy (EMR/ESD) will assist in making a definite diagnosis in such cases.

Conflicts of Interest

All named authors hereby declare that they have no conflicts of interest to disclose.

REFERENCES

1. Sommers SC, Meissner WA. Unusual carcinomas of the pancreas. AMA Arch Pathol 1954; 58:101-111. [PMID: 13170907]

2. Paal E, Thompson LD, Frommelt RA, Przygodzki RM, Heffess CS. A clinicopathologic and immunohistochemical study of 35 anaplastic carcinomas of the pancreas with a review of the literature. Ann Diagn Pathol 2001; 5:129-140. [PMID: 11436166]

3. Strobel O, Hartwig W, Bergmann F, Hinz U, Hackert T, Grenacher L, et al. Anaplastic pancreatic cancer: presentation, surgical management, and outcome. Surgery 2011; 149:200-208. [PMID: 20542529]

4. Cubilla AL, Fitzgerald PJ. Classification of pancreatic cancer (nonendocrine). Mayo Clin Proc 1979; 54:449-458. [PMID: 221755]

5. Bellows C, Gage T, Stark M, McCarty C, Haque S. Metastatic pancreatic carcinoma presenting as colon carcinoma. South Med J 2009; 102:748-750. [PMID: 19488001]

6. Ogu US, Bloch R, Park G. A rare case of metachronous skip metastasis of pancreatic cancer to the colon. Am Surg 2012; 78:E342-E343. [PMID: 22748524]

7. Kahl R, George K, Patel K, Stawick L. Pancreatic adenocarcinoma with rare sigmoid colon metastasis. ACG Case Rep J 2019; 10:e00132.

8. Kelley KM, Myer BS, Berger JJ. Malignant large bowel obstruction: a rare presentation of metastatic pancreatic cancer. Am Surg 2016; 82:206-208. [PMID: 27657570]

9. Roland CF, van Heerden JA. Nonpancreatic primary tumors with metastasis to the pancreas. Surg Gynecol Obstet 1989; 168:345-347. [PMID: 2928909]

10. Inada K, Shida D, Noda K, Inoue S, Warabi M, Umekita N. Metachronous colonic metastasis from pancreatic cancer seven years post-pancreatoduodenectomy. World J Gastroenterol 2013; 19:1655-1658. [PMID: 23539549]

11. Yokoyama T, Saitou D, Kondou H, Shiroto M, Hosokawa K, Siroo K, et al. Endoscopic diagnosis of duodenal malignant tumor. Stomach and Intestines 1993; 28:641-649.

12. Vilmann P, Jacobsen GK, Henriksen FW, Hancke S. Endoscopic ultrasonography with guided fine needle aspiration biopsy in pancreatic disease. Gastrointest Endosc 1992; 38:172-173. [PMID: 1568614]

13. Hoshimoto S, Matsui J, Miyata R, Takigawa Y, Miyauchi J. Anaplastic carcinoma of the pancreas: case report and literature review of reported cases in Japan. World J Gastroenterol 2016; 22:8631-8637. [PMID: 27784976]

14. Çolak Ş, Gürbulak B, Çakar E, Bektaş H. Evaluation of endoscopic mucosal resection and endoscopic submucosal dissection in submucosal lesions of the colon and rectum. Wideochir Inne Tech Maloinwazyjne 2018; 13:448-453. [PMID: 30524614]

15. Liu B, Chen H, Zhang W, Zhang G. A novel technique for removing large gastric subepithelial tumors with ESD method in the subcardia region. Oncol Lett 2019; 18:5277-5282. [PMID: 31612037]