—Case Reports—

Pancreatic Ductal Adenocarcinoma in Remnant Pancreas after Pancreaticoduodenectomy for Acinar Cell Carcinoma: A Case Report

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We report a case of a pancreatic ductal adenocarcinoma (PDAC) in the remnant pancreas of a 78-year-old man after pancreaticoduodenectomy for acinar cell carcinoma, a relatively rare pancreatic neoplasm. After diagnosis of pancreatic carcinoma, subtotal stomach-preserving pancreaticoduodenectomy was performed. The pathological diagnosis was acinar cell carcinoma of the pancreas (disease stage IA, pT1, pN0, M0), without regional lymph node invasion. Cancer antigen 19-9 levels gradually increased during the 22 months after surgery, and computed tomography showed two solid tumors, 1.1 and 2.1 cm in diameter, at the site of the remnant pancreas. Endoscopic ultrasound fine-needle aspiration revealed pancreatic ductal adenocarcinoma. The tumor cells were not immunoreactive for trypsin. Both tumors were diagnosed as PDAC of the remnant pancreas. The patient declined curative resection, and chemoradiotherapy was started as alternative treatment. The patient died 28 months after surgery. Because this is an extremely rare case, additional cases and studies are needed in order to clarify its pathogenesis. (J Nippon Med Sch 2019; 86: 279–283)

Key words: acinar cell carcinoma, pancreatic ductal adenocarcinoma, pancreaticoduodenectomy, pancreatic cancer

Introduction

Acinar cell carcinoma (ACC) is a relatively rare pancreatic neoplasm. Although the pancreas predominantly consists of acinar cells (82% of total pancreatic volume), ACC accounts for approximately 1% of all pancreatic neoplasms[1,2]. The reason for the low prevalence of ACC is unclear, although some researchers have speculated that acinar cells may undergo metaplasia into ductal cells when they encounter genetic instability. The prognosis for ACC is unclear: some patients have poor outcomes, while others have outcomes better than those for pancreatic ductal adenocarcinoma (PDAC)[3–5]. Outcomes are better for localized disease than for metastatic disease. However, even after curative resection, the rate of recurrence is high[3,6]. Some reports suggest that most patients develop local or liver recurrence[7]. No study has reported other types of carcinoma recurrence in the remnant pancreas. Here, we discuss a case of a PDAC in the remnant pancreas of a patient after pancreaticoduodenectomy for ACC.

Case Report

A 78-year-old man presented with hematuria at our clinic. He had no risk factors for and no family history of pancreatic cancer and no medical history of diabetes, obesity, or alcohol abuse. Enhanced abdominal computed tomography (CT) was performed to identify the cause of hematuria and revealed a mass lesion (diameter 2 cm) in the head of the pancreas (**Fig. 1**). Blood test results showed normal values, as well as normal levels of the tumor markers carcinoembryonic antigen and cancer antigen 19-9 (CA19-9). Endoscopic ultrasound (EUS)

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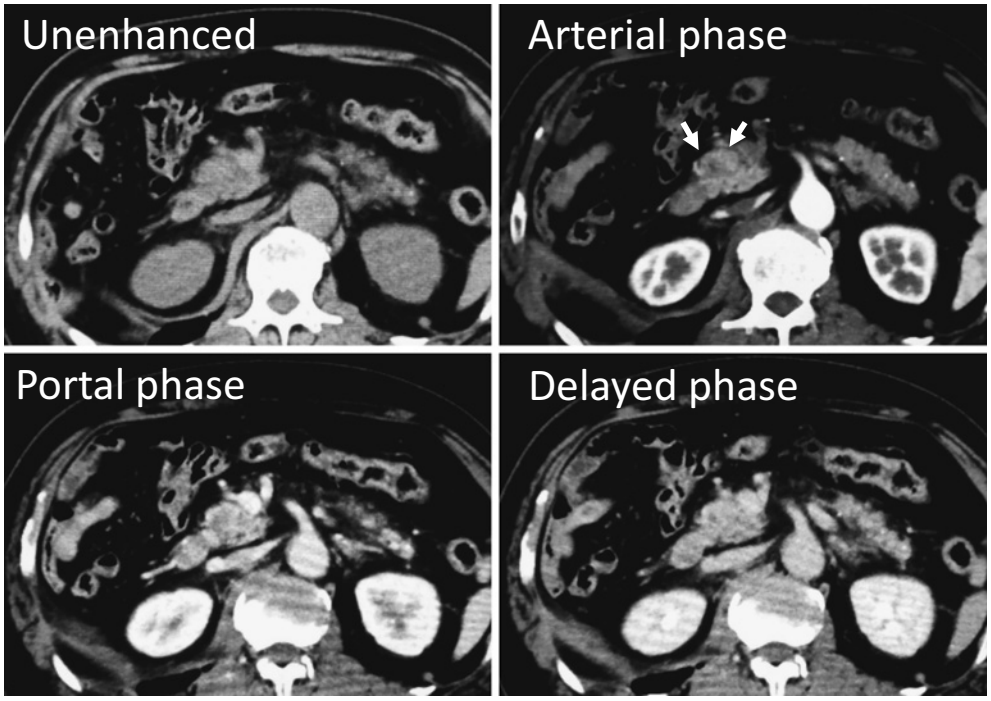

Fig. 1 Dynamic contrast-enhanced CT showing a 20-mm heterogeneous tumor in the head of the pancreas (arrows in the arterial phase image).

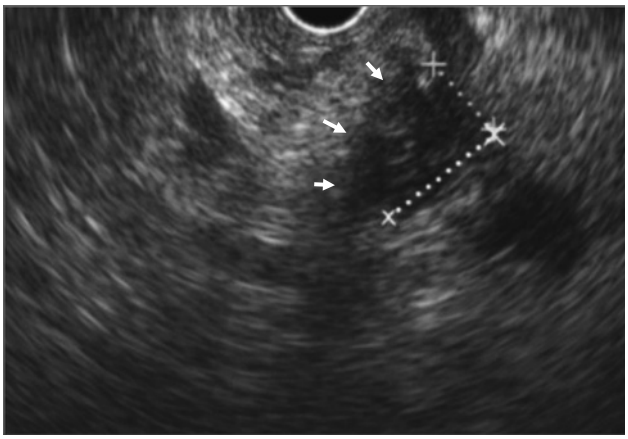

Fig. 2 Endoscopic ultrasound showing a 11 × 17 mm low-echoic mass in the head of the pancreas (arrows).

showed a low-echoic mass in the head of the pancreas (**Fig. 2**). Poorly differentiated carcinoma was suspected on the basis of the results of EUS fine-needle aspiration biopsy. For diagnosis of pancreatic carcinoma, subtotal stomach-preserving pancreaticoduodenectomy was performed.

Macroscopically, the tumor was well circumscribed, and the cut surface showed a solid tumor (**Fig. 3**). Microscopically, tumor cells were arranged in combination patterns, with solid or trabecular anastomosing structures and glandular cells (**Fig. 4a**). Immunohistochemically, the tumor cells were immunoreactive for trypsin and amylase but not in chromogranin, synaptophysin, or CD56 staining (**Fig. 4b**). The non-cancerous region of the pancreas showed chronic pancreatitis, and the dissected peripancreatic tissue margin was negative for carcinoma. The pathological diagnosis was ACC of the pancreas, stage IA pT1, pN0, M0 (Union for International Cancer Control Staging, 8th edition), without regional lymph node invasion.

The postoperative course was uneventful, and the patient was discharged on the 12th postoperative day. He declined postoperative adjuvant therapy. During the 22 months after surgery, CA19-9 levels gradually increased to 163 U/mL. Recurrence of pancreatic cancer was therefore suspected but was not detected on an enhanced abdominal CT scan. Three months later, a CT scan revealed two solid tumors (diameter, approximately 1.1 and 2.1 cm) at the site of the remnant pancreas and invasion of the descending colon (**Fig. 5a**). A positron emission tomography scan showed abnormal accumulation of fluorodeoxyglucose in the remnant pancreas (SUVmax, 5.4), but no evidence of distant metastasis (**Fig. 5b**). EUS confirmed the presence of two low-echoic masses, and EUS fine-needle aspiration revealed ductal adenocarcinoma (**Fig. 6a, 6b, 6c**). The tumor cells were negative for immunoreactivity for trypsin (**Fig. 6d**). We diagnosed both tumors as PDAC of the remnant pancreas.

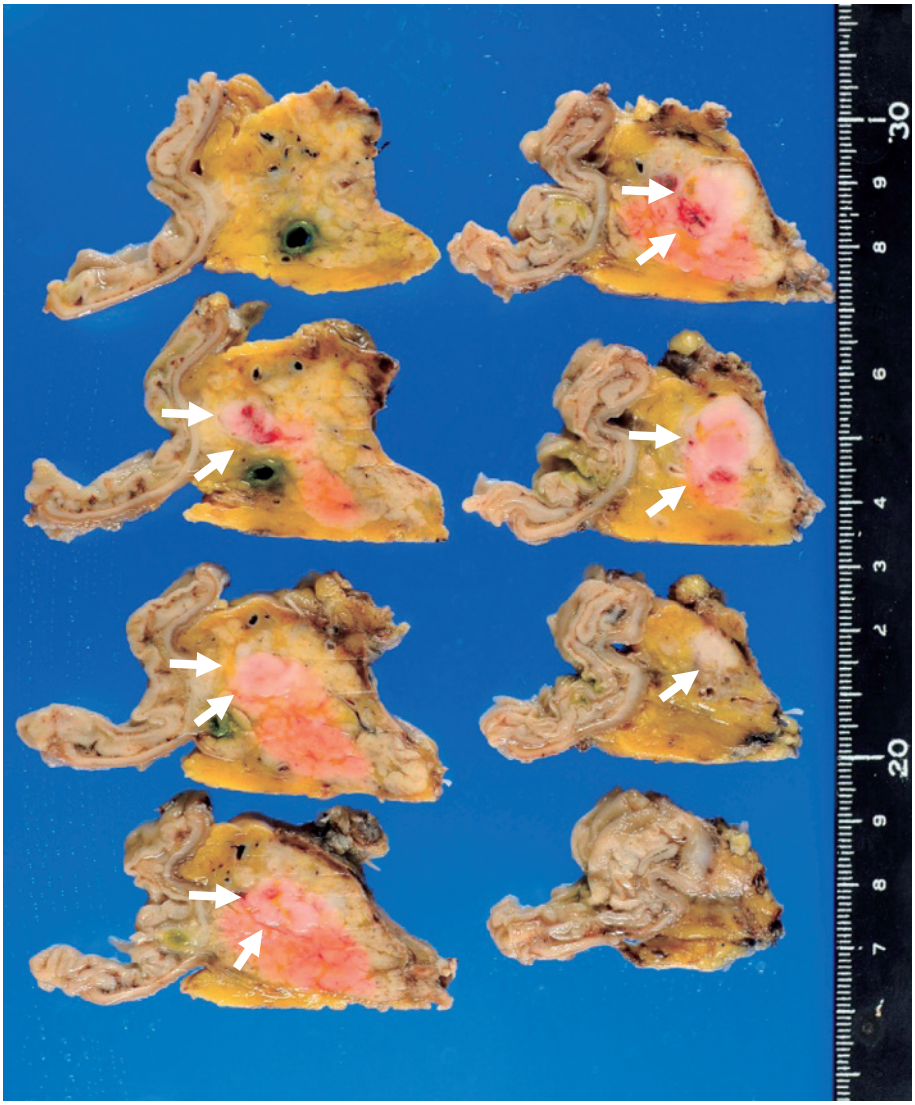

Fig. 3 Cut surface of the resected specimen showing a solid tumor (arrows).

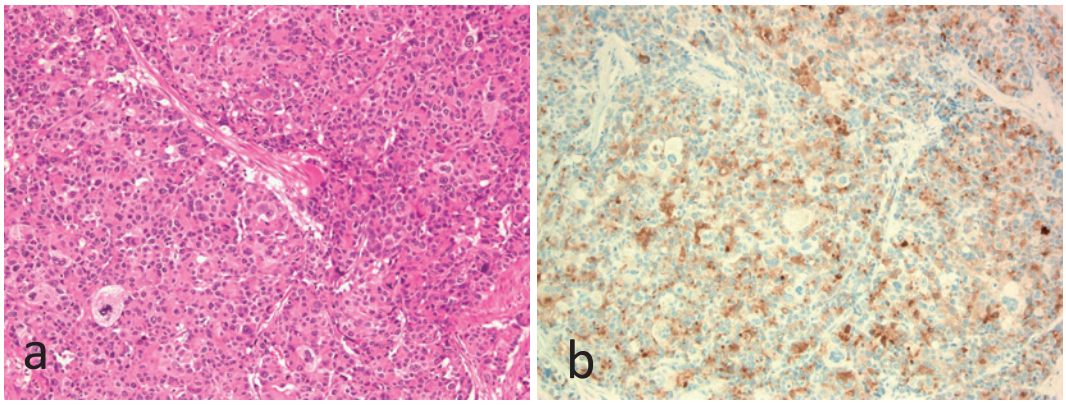

Fig. 4 (a) Hematoxylin and eosin staining showing atypical cells growing in a solid manner, with structured acinar formations. (b) Tumor cells Immunohistochemically stained with trypsin.

The patient declined curative resection, and chemoradiotherapy was started as alternative treatment. Radiation therapy was delivered at a dose of 1.8 Gy per day (total dose 50.4 Gy). On days 1 and 7, chemotherapy with gemcitabine (250 mg/m^2) was administered concurrently with radiation. Despite chemoradiotherapy treatment, CA19-9 level increased to 2,000 U/mL, and he developed weight loss and asthenia. At 28 months after

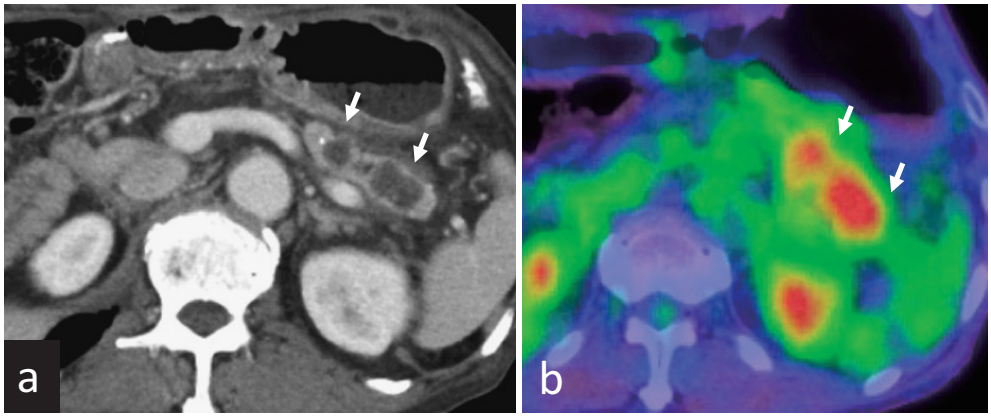

Fig. 5 (a) Enhanced CT showing two hypovascular tumors in the remnant pancreas (arrows). (b) Positron emission tomography showing abnormal accumulation of 18F-fluorodeoxyglucose in the remnant pancreas (SUV max, 5.4).

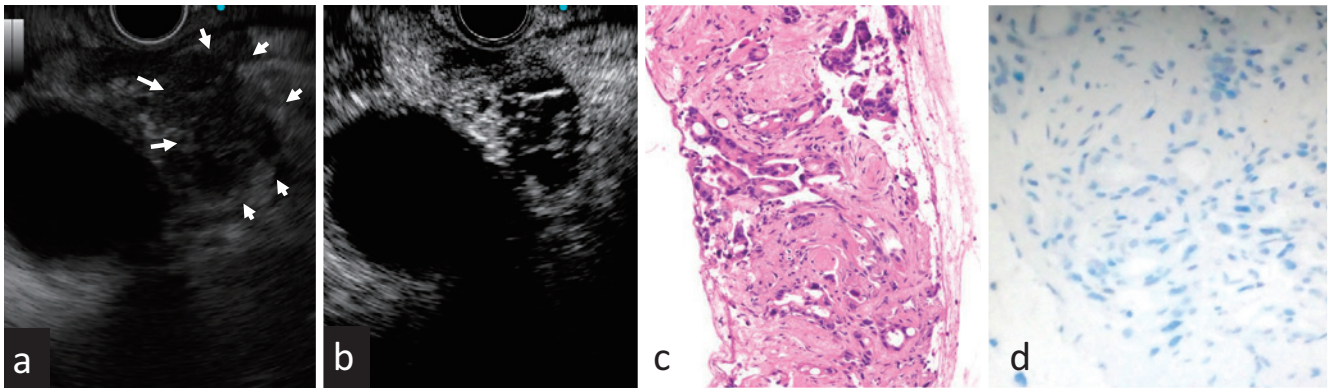

Fig. 6 (a) Endoscopic ultrasound (EUS) showing a low-echoic mass in the remnant pancreas (arrows). (b) Contrast-enhanced EUS with Sonazoid showing a slightly enhanced tumor. (c) Hematoxylin and eosin staining showing a tubular adenocarcinoma composed of irregular glands with marked fibrosis. (d) Immunohistochemical labeling for trypsin shows stained tumor cells.

surgery, the patient was transferred to a palliative care unit, where he died of the disease.

Discussion

ACC is a rare type of malignant tumor. During preoperative evaluation, typical features of CT imaging include a large, exophytic, well-circumscribed, and hypovascular tumor[7]. Lipase hypersecretion syndrome is secondary to lipase hypersecretion by ACC[3,8]. ACC has varied histological features, ranging from acinar structures similar to normal pancreatic acini to solid growths composed of large sheets of poorly differentiated neoplastic cells[9]. Preoperative pathological diagnosis of ACC is rare, and surgeons should thus be cognizant of ACC when evaluating pancreatic cases. The present patient had no specific features. We could not diagnose the tumor as ACC preoperatively, even though EUS-guided fine-needle biopsy and immunohistochemistry are typically utilized for preoperative diagnosis of ACC[10].

Although the prognosis of ACC appears to be better than that of PDAC, it is nevertheless poor because of the risk of metastatic disease and the high rate of recurrence, as described above. The median survival for ACC ranges from 18 to 33 months[3,6,11]. Wang et al.[7] reported a high recurrence rate, 56.3%, in patients who underwent resection. The recurrence sites included both local disease and liver metastasis. ACC is aggressive, like invasive pancreatic carcinoma, and is often a systemic disease with high recurrence rates[3].

When possible, surgical resection with negative margins remains the best initial approach for ACC. Holen et al. and Wang et al. reported that resected patients had significantly better survival than did those not undergoing resection[3,7].

Aggressive surgical resection, with the goal of achieving R0 margins of resection, is associated with long-term

survival[12]. If ACC is unresectable or recurrent, chemotherapy may prove useful; however, few reports have comprehensively examined the effectiveness of chemotherapy for ACC treatment.

Our patient was treated by surgical resection with negative margins for ACC in the head of the pancreas. Twenty-five months after surgery, PDAC developed in the remnant pancreas. The histopathological findings of the first tumor differed from those of the two recurrent masses. Although the tumor was resectable, chemoradiotherapy was performed because the patient declined additional surgical treatment.

Few studies have reported pancreatic carcinoma recurrence in the remnant pancreas after pancreaticoduodenectomy. Ishida reported cumulative 3- and 5-year incidence rates of 3.1% and 17.7%, respectively, for secondary PDAC in the remnant pancreas after pancreatectomy for PDAC[13]. With respect to ACC, no study has reported PDAC development in the remnant pancreas after pancreaticoduodenectomy.

ACC has histological variants, such as mixed acinar-neuroendocrine carcinoma and mixed acinar-ductal adenocarcinoma[9]. In the present case, the first ACC tumor did not exhibit ductal differentiation or a significant neuroendocrine component. However, analysis of a biopsy of the second tumor in the remnant pancreas showed adenocarcinoma.

Diagnosis based on pathological findings is limited. We could not accurately diagnose the tumor in the remnant pancreas because the specimens were partially obtained by fine-needle biopsy and not by surgery or autopsy. Mixed pathological-type tumors can be present in pancreatic cancer, even in secondary tumors. Despite the pathological diagnosis, the remnant pancreatic cancer may have developed from a mixed-type ACC.

The molecular mechanisms underlying ACC are not completely understood. In general, the typical abnormalities of PDAC, including mutations in KRAS, DPC4, p16, and TP53, are absent or very rare in ACC[9,14]. Gene alterations in ACC differ from those in PDAC. In our case, PDAC developed in the remnant pancreas after surgery for ACC. Therefore, genetic alterations in ACC and PDAC might be related, although we did not perform genetic profiling of the present tumors.

We reported the first case of PDAC in the remnant pancreas after pancreaticoduodenectomy for ACC. Because this is an extremely rare case, additional cases and studies are needed in order to clarify its pathogenesis.

Conflict of Interest: None to declare.

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