Anaplastic carcinoma is a rare pancreatic cancer, and the malignant transformation of a heterotopic pancreas is also rare. We herein report a case of an elderly woman with a mass of unknown origin in the abdominal cavity. Computed tomography identified the extent of the tumor but not the organ of origin. The abdominal tumor eventually metastasized to the liver and lung. An autopsy and immunohistochemical examination revealed an anaplastic carcinoma possibly originating in an ectopic pancreas.

**Key words:** anaplastic carcinoma, cancer of unknown primary, ectopic pancreas, pancreatic cancer

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### Introduction

Anaplastic carcinoma of the pancreas is a rare, frequently aggressive tumor, which displays a variety of growth patterns (1-5). Most cases of heterotopic pancreas are asymptomatic and are found incidentally in the upper gastrointestinal tract (6). Cases of ectopic pancreas have been reported in a variety of other sites, including the omentum, mesocolon, and abdominal lymph nodes (7, 8). Two hypotheses for the development of ectopic pancreas include anomalous separation of the developing pancreatic anlagen and the differentiation of totipotent endodermal cells into pancreatic tissue. Thus, an ectopic pancreas could be found in numerous organs. In addition, the malignant transformation of an ectopic pancreas is also rare (8-10).

We herein report a case of an abdominal neoplasm of unknown origin, which was ultimately diagnosed at autopsy as an anaplastic carcinoma possibly originating in an ectopic pancreas.

### Case Report

An 83-year-old woman was admitted to Sapporo Shirakaba-dai Hospital with a fever and anorexia. She had a previous history of asthma, Hashimoto’s thyroiditis, pseudogout, and dementia.

A physical examination showed mild pyrexia at 38.3°C. The laboratory findings on admission showed leukocytosis (1,381×10⁶/L) with granulocytosis (1,077×10⁶/L), hypoalbuminemia (3.5 mg/dL), renal dysfunction (urea nitrogen, 32.9 mg/dL; creatinine, 1.24 mg/dL), and inflammation (C-reactive protein, 19.67 mg/dL; erythrocyte sedimentation rate, 48 mm/hr; fibrinogen 645 mg/dL). The fever, evidence of inflammation and anorexia continued. Esophagogastro-duodenoscopy showed only mild reflux esophagitis and no evidence of a tumor. Computed tomography (CT) revealed renal cysts, an ovarian cyst, and a solid mass, which was 16 mm in diameter and located near the lesser curvature of the stomach and did not contact any surrounding organs (Fig. 1). Ultrasonography showed a hypoechoic mass (Fig. 2). Although either malignant lymphoma or metastatic lymph node was suspected, neither the patient nor her family wished for further examination. CT on the 161st hospital day revealed that the abdominal mass had enlarged to 56 mm in diameter (Fig. 2). CT also showed multiple liver metastases, bilateral pleural effusion, and small nodules in the lung. Several tumor markers were elevated, including carcinoembryonic antigen (CEA) of 176.2 ng/mL, CA19-9 of 327.2 U/mL, Cypra of 653.0 ng/mL, neuron specific enolase...
Figure 1. An abdominal CT scan 12 days after admission showing an isolated perigastric mass (arrow), which was not in contact with any other organ, including the pancreas (arrow head) and stomach (dashed arrow). The nine images from (a) to (i) are a successive series with 7-mm width.

(NSE) of 118.1 ng/mL, ferritin of 438 U/mL, and interleukin-2 receptor (IL-2R) of 1,188 U/mL. The tumor clinically and radiologically progressed and the patient died on the 196th day. An autopsy was performed.

The main abdominal tumor was located between the stomach and pancreas and had expanded and infiltrated the outer surfaces of stomach and pancreas. However, obvious ectopic pancreatic tissue was not detected around and within the main tumor mass. Sectioning of the tumor revealed necrosis. There were multiple, large metastases in the liver and multiple metastatic nodules in the lung. The tumor cells showed a rounded to pleomorphic histology, and a growth pattern of solid tumor cell nests, in association with a partial sarcomatoid appearance. No osteoclastic giant cells were observed. These data were compatible with the tumor diagnosis of anaplastic carcinoma, the pleomorphic type. An immunohistochemical examination, summarized in Table, showed that both high and low molecular weight keratin (HMWK/LMWK) were positive (Fig. 3). The tumor cells were positive for cytokeratin (CK) 7 but negative for CK20. MUC1, but neither MUC2 nor MUC6, was expressed. MUC5AC showed weak staining in a small number of malignant cells. Neuroendocrine markers including synaptophysin, chromogranin and CD56, but not NSE, were negative. The tumor cells did not expressed CA125, calretinin, estrogen receptor, or progesterone receptor (PgR), suggesting that they were not of Mullerian or mesothelial origin. The expression of CEA further confirmed that the tumor was not a malignant mesothelioma. An extrapancreatic solid pseudopapillary neoplasm (SPN) was excluded by the histological examination and negative reactions with PgR and CD56 antibodies. Moreover, the antibodies against mammary serine protease inhibitor (MASPIN) and insulin-like growth factor (IGF)-II messenger RNA-binding protein-3 (IMP-3), both of which have been demonstrated to be highly expressed in pancreatic ductal carcinoma (11, 12), intensely stained both the cytoplasm and nucleus of the tumor cells but not the normal pancreatic ductal and acinar structures. MASPIN localized to the cytoplasm and the nucleus of the tumor cells, while IPM-3 was expressed in the cytoplasm of the tumor cells. These results suggested that the tumor was an undifferentiated anaplastic carcinoma originating in the ectopic pancreas.

Discussion

Anaplastic carcinoma of the pancreas is rare with an incidence of only 2-7% of all pancreatic cancers (1). Anaplastic carcinomas of the pancreas are divided according to their growth patterns into solid and sarcomatoid types (2, 3). Tu-
Tumor cell morphology is variable, ranging from spindle to pleomorphic cells. The tumor in the present case mainly exhibited a solid growth pattern associated with a partial sarcomatoid appearance and round to pleomorphic histology. The immunohistochemical profile of the tumor in question was comparable with pancreatic anaplastic carcinoma, due to the positivity for LMWK, HMWK, p53 and p63, suggesting a basal-like stem cell origin. MUC1+2- and CK7+20- phenotypes are also comparable with pancreatic ductal carcinoma.

The incidence of anaplastic carcinoma in various organs appears to be very rare, ranging from 1-7%, as revealed in the cases of lung and thyroid cancers similar to the pancreas (1, 3, 13, 14). Both the pancreas and lung have been described to be the most common primary sites among cancers of unknown primary (15, 16). Although anaplastic carcinomas are typically very aggressive, we cannot deny the possibility that the abdominal mass had metastasized, even though the primary cancer nest had disappeared.

An ectopic pancreas is defined as the occurrence of pancreatic parenchyma in aberrant anatomic sites that lack vascular, neural and anatomic continuity with the pancreas proper (6). Pancreatic heterotopia has been found most frequently in the upper gastrointestinal tract, and 70 to 87% of cases are in the stomach, duodenum, or jejunum. Other reported locations also have included the lung, mediastinum, esophagus, gallbladder, bile ducts, splenic hilum, colon, mediastinum, omentum, retroperitoneum, umbilicus, fallopian tubes, mesocolon, and lymph nodes (7-9, 17). Therefore, an ectopic pancreas may be found in numerous organs (18).

Three criteria for a carcinoma arising from a heterotopic pancreas were proposed by Guillou et al.: 1) the tumor must be present within or adjacent to the ectopic pancreatic tissue; 2) the transition between pancreatic elements and carcinoma should be identified; and 3) the non-neoplastic pancreatic tissue must contain acini, epithelial, and ductal structures (19). As we could not detect non-transformed ectopic pancreatic tissue within or around the main tumor mass, we could not confirm the ectopic pancreatic origin of the tumor described (20). Pancreatic tissue may not have been detected.

Figure 2. Sequential abdominal CT scans (according to the days after admission) showing changes in the size of the perigastric mass (arrow), and the mass abutting the stomach (dashed arrow) and pancreas. a: 12 days; b: 68 days; c: 118 days; d: 165 days. (e) Doppler ultrasonography on the 61st day showing a hypoechoic mass with poor blood supply.
in this abdominal mass due to the enlargement of the tumor, resulting in destruction of the ectopic pancreatic tissue. Both MASPIN and IMP-3 have been described as specific markers for pancreatic ductal carcinoma along with S100 P (11, 12), and we detected strong reactivity for both MASPIN and IMP-3 in this tumor. MASPIN is a member of the serpin family of protease inhibitors and associated with the cancer progression of some tumors, including the breast, prostate, oral squamous cell, thyroid, and colorectal carcinomas (11). A battery of additional immunohistochemical stains other than MASPIN and IMP-3, as described, further supported the possibility of its pancreatic origin. It is unlikely that the tumor in question is an extrapancreatic SPN, which has been reported to be entirely negative for MASPIN. We speculate that this anaplastic carcinoma may have originated in the ectopic pancreas located between the stomach and pancreas within the bursa omentalis.

A number of carcinomas, including anaplastic type, have been reported to originate in the ectopic pancreas (8-10). If the ectopic pancreatic tissue is destroyed by tumor growth, then it would be difficult to identify the site of origin of the tumor. We strongly suspect that this is the situation in the present patient, since a battery of tumor markers strongly suggests a pancreatic origin even though the ectopic pancreatic tissue was not identified.

We herein reported a case of a tumor of unknown origin in the peritoneal cavity (bursa omentalis). The tumor was ultimately diagnosed at autopsy to be a pancreatic anaplastic
carcinoma possibly arising in the heterotopic pancreas.

The authors state that they have no Conflict of Interest (COI).

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