Primary Malignant Fibrous Histiocytoma of the Pancreas: an immunohistochemical study

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ABSTRACT

A case of malignant fibrous histiocytoma (MFH) which arose in the pancreas head is presented. Only 4 cases have been documented in the world literature(1-4).

An 86-year-old woman who had chronic congestive heart failure showed signs of anemia and an occasional tarry stool. Computed tomography and ultrasonography indicated the existence of a tumor which was located around the pancreas and suggested invasion to the duodenum.

Postmortem examinations revealed a pancreas head tumor which had a central cystic area containing a muddy-like material and blood. Invasion of the tumor to the duodenal wall was observed and the connection between the duodenal cavity and the central cystic area of the tumor was also demonstrated.

The histological appearance was that of a fine fibrous tissue showing a storiform pattern. Immunohistochemical features also supported the histiocytic cell origin.

Key words: Malignant fibrous histiocytoma, Sarcoma of the pancreas, Immunohistochemistry of pancreatic tumor.

INTRODUCTION

The concept of fibrous histiocytic tumors has been popularized by Weiss and Enzinger as a primitive and pleomorphic sarcoma which shows partial fibroblastic and histiocytic differentiation(5).

Because of the ubiquitous nature of mesenchymal tissue, MFH has the potential of being found in all organs. However, it usually occurs in the deep soft tissue of the lower and upper extremities, retroperitoneum, and the trunk(5, 6). Rare cases of this tumor arising in an unusual site such as the lung(7), kidney (8), bladder(9), scrotum(10), heart(11), aorta(12), stomach(13), small intestine

(14), orbit(15), and nasal cavity(16) have also been reported. Cases arising in the alimentary organs are extremely rare.

Primary malignant neoplasms of a connective tissue origin occur quite rarely in the pancreas(1), and only several cases of MFH have been reported. The present paper reports on a case of MFH with a pancreas head origin, examined immunohistochemically.

CLINICAL SUMMARY

An 86-year-old woman with chronic congestive heart failure complained of chest pain, wheezing, dyspnea, and occasional tarry stool. Serum analysis showed anemia for hemoglobin 6.4 g/d*l*. No particular information was obtained regarding familial and past history.

Examination of the gastrointestinal tract with a fiber scope revealed no obvious lesions in the esophagus, stomach, or colon. No detailed observations were made of the duodenum because of the severe and persistent bleeding in the gastrointestinal tract. Computed tomography showed a tumor localized near the pancreas, and bleeding from a duodenal tumor was suspected. Ultrasonography also supported this observation. Splenomegaly and a liver cyst were also indicated.

A conservative course of therapy was selected for this particular patient. Blood transfusion was given for the occasional tarry stool, but there was no effect upon the anemia. Meanwhile, the congestive heart failure became worse, and thirteen months after admission, it turned decompensative. Pneumonia then developed and administration of antibiotics was not effective. Hepatic and renal dysfunction occured followed by a disturbance of consciousness. She died from pneumonia and an autopsy was performed.

PATHOLOGICAL FINDINGS

The tumor (50×50×40 mm in size), which showed considerable central necrosis, was located in the pancreas head (Fig. 1a, 1b). It was connected with the duodenum and dissociated from retroperitoneal tissue. The cut surface of the tumor was gray-white, well defined and had partly invaded the duodenal wall. The central necrotic area showed bleeding, connecting into the duodenal cavity through tumor invasion at 4cm in the anal side from Vater's papilla. The main pancreatic duct was compressed but not obstructed, and the mucosal surface was smooth and intact. One centimeter thick sagittal serial sections also demonstrated dissociation of the tumor from the retroperitoneum or any other organs (Fig. 1c). They were examined histologically on every cut surface.

The tumor was composed of fine fibroblastoid spindle cells showing a stor-

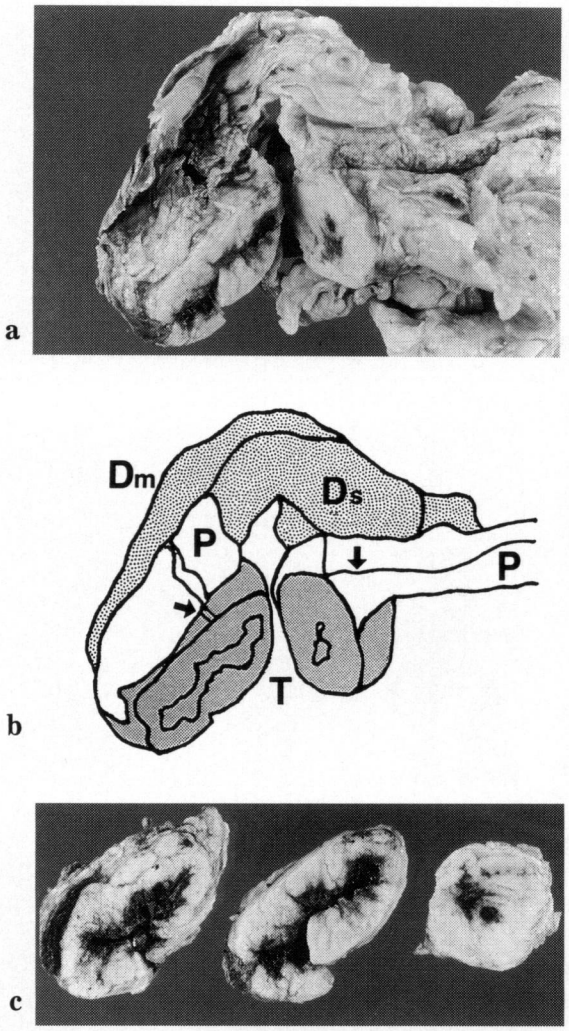

Fig. 1 a : Tumor occupies head of the pancreas. It is encapsulated with a thin connective tissue and no obvious infiltration is seen except in the duodenal wall. The central part of the tumor shows necrosis and bleeding. No connection is observed with the retroperitoneum.

b : Schematic localization of the tumor, pancreas, and duodenum.
T : Tumor
P : Pancreas
Dm : Duodenum, mucosal surface
Ds : Duodenum, serosal surface
→ : Pancreatic duct

c : Sagittal serial sections of the tumor. Its margin is clear and is partially surrounded by compressed pancreatic tissue.

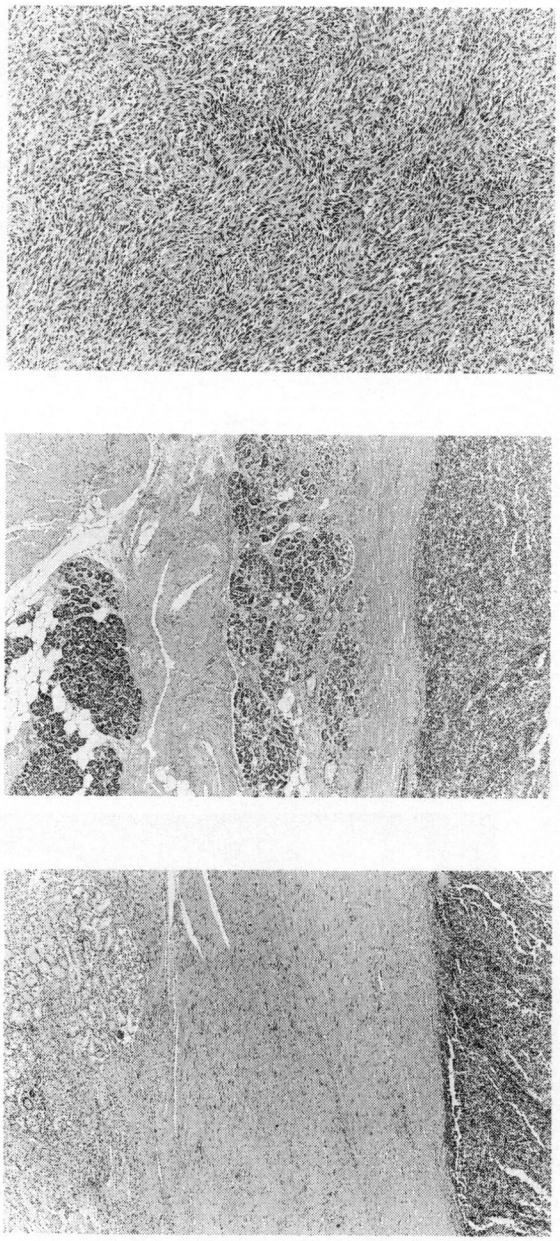

Fig. 2 a: Fibrous spindle cells with a storiform arrangement. Multi- or mono-nucleated giant cells are not found. HE×100
b: Microscopic border of the tumor with pancreatic tissue. HE×40
c: Invasion of the tumor to duodenal wall. Brunner's glands are observed above the smooth muscle of the duodenum. HE×40

iform pattern (Fig. 2a), and it was partially surrounded by a compressed tissue of the pancreas (Fig. 2b). Histological features were almost identical in every cut surface. Nuclear atypism was not evident. Mitotic figures were rare. Multinucleated giant cells and foam cells were seldom seen. Duodenal wall invasion with higher cellularity and slightly enlarged nucleus only suggested the malignant potential of this tumor (Fig. 2c). No evidence of epithelial origin, such as glandular structure, was observed in any field examined.

The lack of granules stained by the Fontana-Masson or Grimerius method indicated, together with the histological features, that this tumor was not of an islet cell origin.

The results from immunohistochemical examination by avidin-biotin peroxidase complex method are summarized in Table 1. It showed positive staining

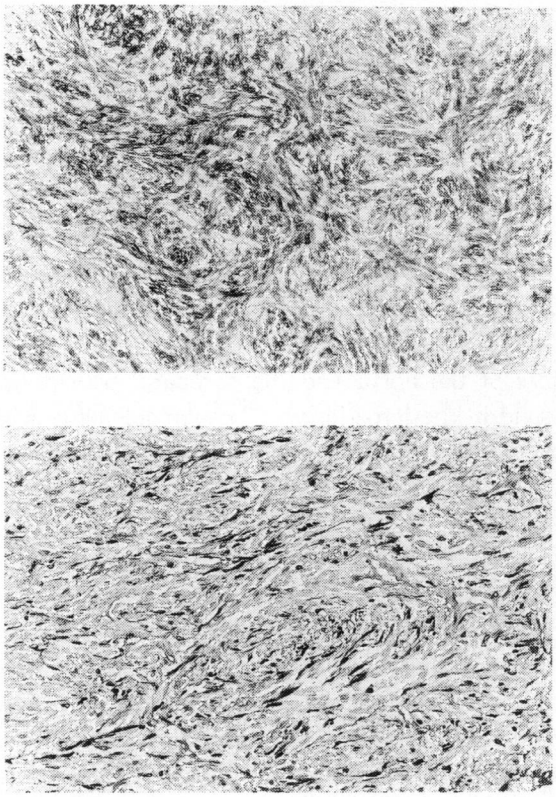

Fig. 3 Immunohistochemical staining with anti-vimentin (a) and anti-α1-antichymotrypsin (b) antibody. Tumor cells exibit a positive reaction for these antibodies.

Table 1 *Immunohistochemical analysis*

Antibody	Source	Dilution	Staining results
Vimentin	Nichirei	1 : 2	+
α1-antichymotrypsin	Nichirei	1 : 1	+
α1-antitrypsin	DAKO	1 : 20	+
Desmin	DAKO	1 : 500	−
S-100	DAKO	1 : 500	−
Lysozyme	DAKO	1 : 50	−
Keratin	DAKO	1 : 300	−
α-sarcomeric muscle actin	DAKO	1 : 50	−
α-smooth muscle actin	DAKO	1 : 50	−
Chromogranin-A	DAKO	1 : 100	−

for vimentin, a marker for cells having a mesenchymal origin, and α1-antichymotrypsin (α1-ACT) and α1-antitrypsin (α1-AT), markers for cells of a histiocytic origin. Staining for desmin, S-100, lysozyme, keratin, α-sarcomeric muscle actin, α-smooth muscle actin, and chromogranin-A were negative. The final diagnosis indicated primary MFH of the head of the pancreas. No metastatic foci were observed.

Other pathological findings of this case were as follows. Jaundice of the skin and bile stasis in bile canaliculi of the liver were observed as a result of the compression of the common bile duct by this tumor. Pleural effusion, 300m*l* in both pleural cavities, were observed as a result of anemia and the conservative therapy.

Atherosclerosis of the aorta and the coronary arteries was evident and an infarction was found in the left kidney. Tubular adenoma with moderate atypia in the ascending colon and nodular goiter of the thyroid gland were also observed.

DISCUSSION

MFH is widely regarded as the most common soft tissue sarcoma found in adulthood, and because of its ubiquitous origin, it may arise in every organ.

The tumor found in the current case consisted of predominantly fibroblastic spindle cells showing a characteristic storiform pattern. However, it is important to discriminate from anaplastic, pleomorphic, or undifferentiated carcinomas of the pancreas, which show various proportions of sarcomatous change. Alguacil-Garcia studied 12 cases of pancreatic carcinoma with sarcoma-like transformation and identified four distinctive histologic types: spindle cell carcinoma, malignant giant cell tumor, pleomorphic giant cell carcinoma, and round cell ana-

plastic carcinoma(17). Among those 12 cases, five were categorized as spindle cell carcinoma, and their histological characteristics were different proportions of large undifferentiated round cells, bizarre cells, and malignant giant cells. Small foci of adenocarcinoma or squamous carcinoma were found by extensive histological examination, which indicated those tumors of a ductal cell origin.

Nevertheless, in extensive examination of multiple sections, no foci of ductal differentiation nor calcification were observed in our case. Multinucleated giant cells or bizarre mononucleated cells were not seen in any sections. Those observations, together with negative staining of keratin, support the diagnosis of this case as an MFH rather than as a sarcomatous part of pleomorphic carcinoma.

Another important point in making the diagnosis is to discriminate from other sarcomas which show MFH like histological features. Fletcher reassessed 159 cases originally diagnosed as pleomorphic sarcoma; and 63% of them proved to be specific sarcomas other than MFH(18). He emphasized that careful histological examination is needed to find small foci of histologic characteristics such as lipoblast, bone, or osteoid synthesis. In addition, immunohistochemical staining to detect tissue specific antigens and electron microcopic examination to demonstrate tissue specific intracellular structures is helpful to make an accurate diagnosis of those cases. However, no case which consisted purely of spindle cells was mentioned in his study. Our current case showed no specific histological features of the other sarcomas as described above.

Immunohistochemical staining, negative for desmine and actin, was used to exclude the possibility of leiomyosarcoma and rhabdomyosarcoma. Negative test for S-100 was also used to exclude malignant peripheral nerve sheath tumor. Among those antibodies we used, α1-ACT, α1-AT, and vimentin were positive in this tumor. Vimentin is broadly expressed in the cells of mesenchymal origin, but its specificity is not strict. Its expression is sometimes observed in poorly differentiated carcinomas(19, 20). α1-ACT and α1-AT are the generally accepted markers for histiocytic origin, however, some other tissue type such as endothelial cells, some carcinomas, RS cells of Hodgkin's disease, and synovial sarcomas(21) are also sometimes positive for these markers. Although there is no strict marker for histiocyte, its histological feature and positivity under α1-AT and α1-ACT, together with its consistent negativity under other tissue type specific markers, should be sufficient to diagnose histiocytic origin.

With its mild nuclear atypism, small number of mitotic figures and infiltration to the duodenal wall, the current case was compatible with the diagnosis of fibrous histiocytoma of a low grade malignancy.

The incidence of sarcoma is extremely low in primary tumors of the pancreas; a review of the literature (1-4) revealed only 4 other cases of MFH

Table 2 *Summary of primary MFH of the pancreas*

Case No.	Reference	Age	Sex	Location	Histology	Immunohistology	Year
1.	Cubilla[1]	?	?	?	Pleomorphic	Not given	1984
2.	Ishiguchi[2]	44	M	Body and tail	Pleomorphic	Not given	1986
3.	Garvey[3]	77	M	Head	Storiform	Not given	1989
4.	Allen[4]	46	M	Body and tail	Pleomorphic	Vimentin(+)	1990
	Current report	86	F	Head	Storiform	Vimentin(+) α1-ACT(+) α1-AT(+)	1992

? : not mentioned in the literature
α1-ACT : α1 antichymotrypsin
α1-AT : α1 antitrypsin

(Table 2). Three of those reports (cases 1, 2, and 3) could be diagnosed only by histopathological findings. The fourth case(4) demonstrated positive for vimentin immunohistologically; however, neither those nor any other previous studies involved an extensive investigation of immunohistological characteristics for distinguishing MFH of the pancreas from that of other organs or tissues.

This report described an extensive investigation of immunohistological characteristics of a very rare MFH arising from the pancreas head. No particular staining or other characteristics were identified to distinguish between an MFH of the pancreas and that of other tissue origin. Histopathological characteristics suggest that the pleomorphic type tends to arise in the body and tail, case 2 and 4, and the striform pattern tends to arise in the head of the pancreas, case 3 and the current case. This suggests a correlation between the cells of origin and localization of the tumor.

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