Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.6143-20
Intern Med 60: 1377-1381, 2021
http://internmed.jp

【 CASE REPORT 】

The First Case of Metastatic Pancreatic Leiomyosarcoma Derived from the Urinary Bladder Diagnosed Using an Endoscopic Ultrasound-guided Fine-needle Biopsy

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Abstract:
We herein report the first case of metastatic pancreatic leiomyosarcoma derived from the urinary bladder diagnosed by an endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) in a 65-year-old woman. The patient had undergone total cystectomy for bladder leiomyosarcoma. Four years thereafter, a nodule was observed in her left lung on chest computed tomography. Suspecting primary lung cancer, pulmonologists at our hospital recommended a thoracoscopic lung biopsy, which the patient refused. Five years post-cystectomy, fluorodeoxyglucose positron emission tomography revealed enlargement of the left lung nodule and a new mass in the pancreatic head. She was referred to our department for the pathological diagnosis of a pancreatic head mass by an EUS-FNB. The EUS-FNB yielded adequate pancreatic tissue for an immunohistochemical analysis. A diagnosis of metastatic pancreatic lesion originating from the urinary bladder was made. In atypical pancreatic tumors, the utilization of an EUS-FNB and immunohistochemical analysis can help establish an accurate diagnosis.

Key words: pancreas, leiomyosarcoma, neoplasm metastasis, urinary bladder neoplasms

(Intern Med 60: 1377-1381, 2021)
(DOI: 10.2169/internalmedicine.6143-20)

Introduction

The use of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) has increased rapidly since it was first reported by Vilmann et al. (1) in 1992. It is currently considered a safe, minimally invasive, and reliable technique for pathologically examining solid masses. The main target lesions of EUS-FNA are upper abdominal masses, such as pancreatic neoplasms, upper gastrointestinal subepithelial lesions, and mediastinal neoplasms. Recent advances in EUS-FNA have made the pathological diagnosis of previously undiagnosed diseases possible without surgical resection. Furthermore, recently developed fine-needle biopsy (FNB) needles are able to collect a sufficient volume of sample to establish a diagnosis histologically. These needles have attracted substantial attention owing to their advanced diagnostic capabilities and superiority relative to conventional FNA needles (2-8).

We herein report our experience with a patient who had metastatic leiomyosarcoma of the pancreas that was diagnosed by an EUS-FNB. To our knowledge, this is the first case report describing the diagnosis of metastatic pancreatic leiomyosarcoma derived from the urinary bladder by an EUS-FNB.

Case Report

A 65-year-old woman underwent total (radical) cystectomy for bladder leiomyosarcoma. At the four-year follow-up, chest computed tomography (CT) showed a pulmonary nodule in her left lung. Suspecting primary lung cancer, pul-

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Received: August 19, 2020; Accepted: October 12, 2020; Advance Publication by J-STAGE: November 30, 2020
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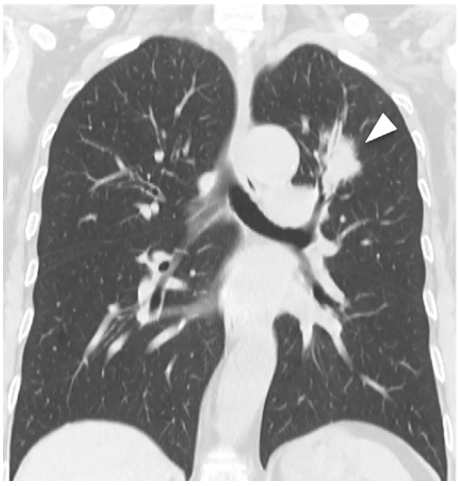

Figure 1. Computed tomography of the chest. An irregular nodular lesion with spiculated margins, 28 mm in size, is visible in the upper left lung (arrowhead).

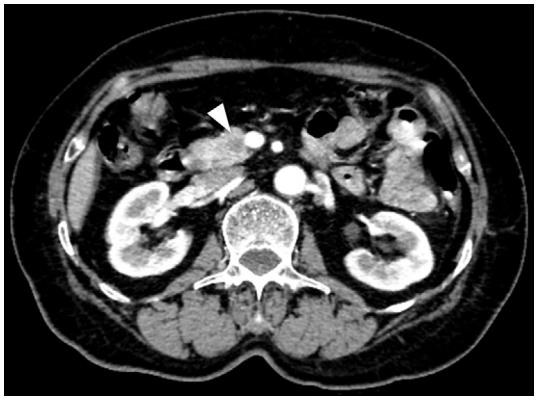

Figure 2. Computed tomography of the abdomen. A 9-mm, low-density area with relatively clear margins was observed in the arterial phase of abdominal enhanced CT (arrowhead).

monologists at our hospital recommended a thoracoscopic lung biopsy, which the patient refused.

Five years post-cystectomy, an intracranial tumor was observed on CT, which had been performed to investigate complaints of paresthesia of her right arm and leg. Doctors diagnosed her with an intracranial metastasis from pulmonary carcinoma, and she underwent radiation therapy. Fluorodeoxyglucose positron emission tomography (FDG-PET) performed around the same time revealed enlargement of the left lung nodule and a new mass in the pancreatic head. She was referred to our department for a pathological diagnosis of the pancreatic head mass by an EUS-FNB.

The medical history of the patient and her family was unremarkable. In addition, the only unusual physical finding was right-sided paresis. Her alkaline phosphatase levels were slightly elevated. She tested negative for all tumor markers examined (carcinoembryonic antigen, carbohydrate antigen 19-9, duke pancreatic monoclonal antigen type 2, progastrin-releasing peptide, and squamous cell carcinoma). An irregular 35-mm nodule was noted on chest CT with a spiculated margin in the upper field of the left lung (Fig. 1). A 9-mm, low-density area with relatively clear margins was observed in the arterial phase of abdominal enhanced CT (Fig. 2). On FDG-PET, areas with an increased uptake were noted in the upper left lung field and pancreatic head (Fig. 3). EUS revealed the mass on the pancreatic head to be 10×9 mm in size. In addition, the pancreatic head had a distinct border, irregular margin, and uniformly hypoechoic interior (Fig. 4A). No main pancreatic duct dilatation was observed caudal to the mass. Doppler ultrasound revealed the mass to be ischemic (Fig. 4B). On contrast-enhanced EUS, the mass exhibited an avascular pattern in the initial phase (Fig. 4C). These findings made us suspect pancreatic metastasis from either primary pulmonary carcinoma or urinary bladder leiomyosarcoma.

To confirm the diagnosis, we performed an EUS-FNB via a trans-duodenal access route using a 22-gauge FNB needle (Acquire™; Boston Scientific, Marlborough, USA) (Fig. 4D). The obtained histological sections are shown in Fig. 5. Proliferation of spindle cells with nuclear atypia was noted on Hematoxylin and Eosin (H&E) stained sections. In the immunohistochemical analysis, neoplastic cells were positive for α-smooth muscle actin (αSMA) and vimentin and negative for AE1/3, CD34, S-100 protein, c-kit, and discovered on GIST1. The cells had an MIB-1 labeling index of 20%. These findings indicated the mass to be a malignant mesenchymal tumor with smooth muscle differentiation and high proliferative potential, leading us to diagnose the patient with a leiomyosarcoma (metastatic recurrence of bladder leiomyosarcoma).

After the EUS-FNB, spindle cells were also observed in tissue collected from the pulmonary lesion via a transbronchial route, which tested negative for TTF-1, Napsin A, p40, and CK5/6. Based on the findings of the immunohistochemical analysis, we concluded that the nodule was most likely a metastatic lesion originating from urinary bladder leiomyosarcoma.

Discussion

Non-epithelial tumors account for less than 5% of bladder malignancies, and leiomyosarcomas are even rarer, accounting for only 0.1% of bladder malignancies (9). In a study of postoperative outcomes of bladder leiomyosarcoma, Spiess et al. noted local recurrence in 16% of cases and distant metastases in 53%, most frequently to the lungs, bones, liver, or brain (10). However, the occurrence of metastatic pancreatic cancer is extremely rare. Indeed, in a review conducted in 2004 using data collected from records of autopsy records and surgical resections, Adsay et al. observed secondary tumors of the pancreas in 1.6% and 3.9% of such cases, respectively (11). According to Minni et al., the primary origins of metastatic pancreatic cancer are most frequently renal cell carcinoma (45%), followed by lung carcinoma (14.7%), breast carcinoma (7.5%), and colonic carcinoma (6.6%) (12). In addition, Adler et al., in a review of 399

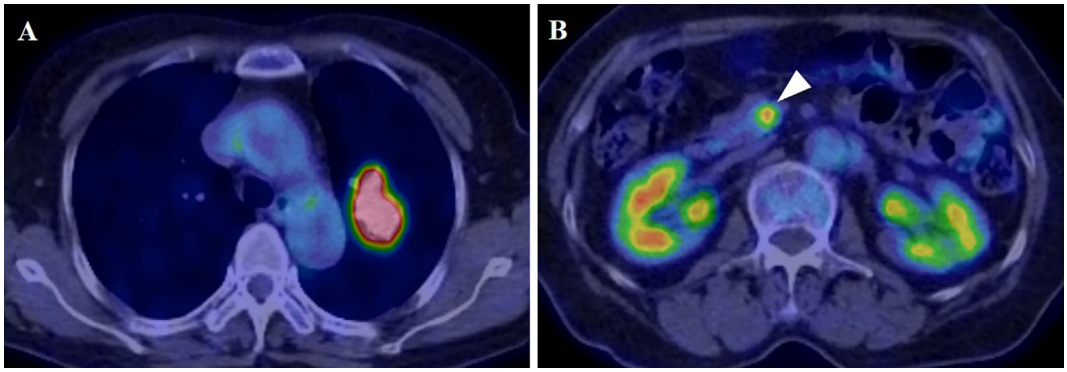

Figure 3. **Fluorodeoxyglucose (FDG) positron emission tomography. A: An increased FDG uptake is apparent in the 35-mm mass in the upper left lung. B: An increased FDG uptake is visible in the micronodular lesion at the pancreatic head (arrowhead).**

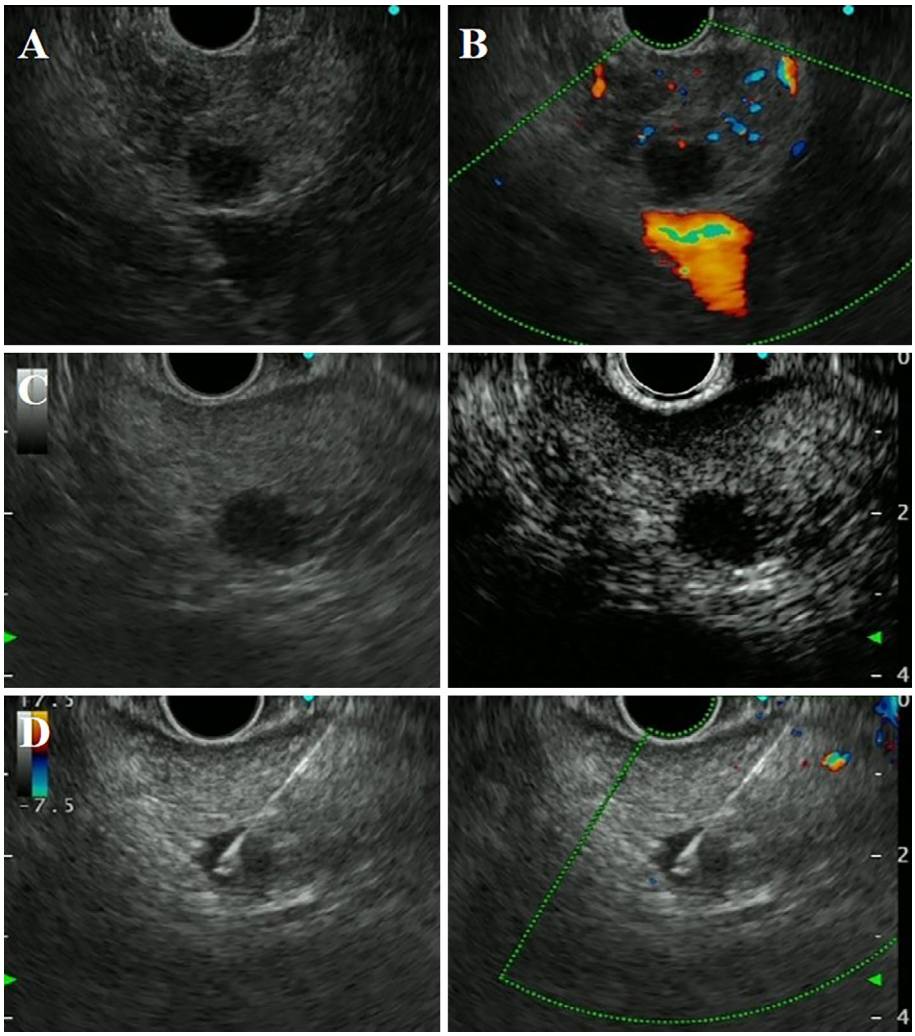

Figure 4. **Endosonography and EUS-guided fine-needle biopsy findings. A: A 10-mm mass is visible in the pancreatic head, characterized by a distinct border, irregular margin, and uniformly hyperechoic interior. B: A poor blood flow is indicated by the weak Doppler ultrasound signal. C: On contrast-enhanced EUS, the mass presents with an avascular pattern in the initial phase. D: The mass is punctured by a 22-gauge biopsy needle. EUS: endoscopic ultrasound**

such cases, found renal cell carcinoma to be the most common origin (62.6%), followed by sarcoma (7.2%) and colorectal carcinoma (6.2%) (13). To our knowledge, no case of metastatic pancreatic cancer originating from urinary bladder leiomyosarcoma has been reported previously.

Adsay et al. classified 81/190 pancreatic tumors in

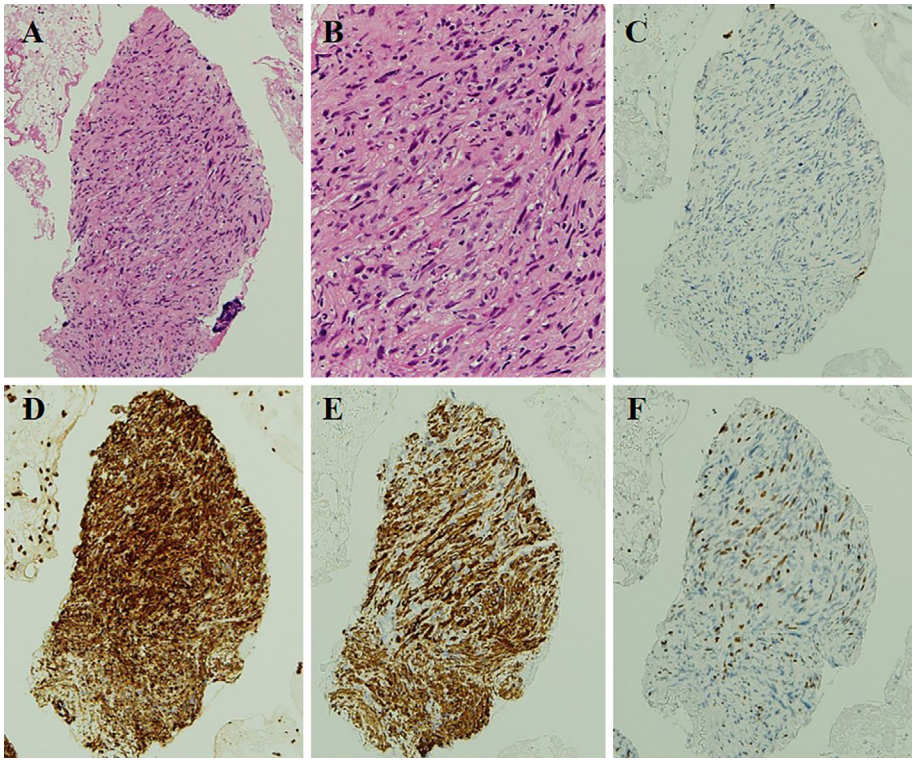

Figure 5. **Histological sections of specimens obtained by an EUS-FNB. A: 100× magnification of a histological specimen of the tumor stained with Hematoxylin and Eosin (H&E) staining. Spindle-shaped tumor cells with nuclear variants were present. B: 200× magnification of a histological specimen of the tumor stained with H&E staining. C: Staining for AE1/3 was negative (100× magnification). D: Staining for vimentin was positive (100× magnification). E: Staining for α-smooth muscle actin was positive (100× magnification). F: The MIB1-index was 20% (100× magnification). EUS-FNB: endoscopic ultrasound-guided fine-needle biopsy**

autopsy cases as metastases from other organs, including a single case of urinary bladder origin (11). However, their work did not include any information on the histopathology. A literature search using PubMed/MEDLINE indicated that cases of metastatic pancreatic leiomyosarcoma derived from the urinary bladder had not been reported previously. This is the first case of metastatic pancreatic leiomyosarcoma derived from the urinary bladder diagnosed by an EUS-FNB.

In this case, the nodule was observed in the patient's lung, an area prone to postoperative (metastatic) recurrence of urinary bladder leiomyosarcoma, before the appearance of the pancreatic mass. Therefore, the most plausible diagnosis seemed to be metastatic lung and pancreatic cancer originating from primary bladder leiomyosarcoma. However, the CT findings in our patient were consistent with primary lung cancer. It is well known that primary lung cancer frequently metastasizes to the pancreas, and this led us to consider primary lung cancer along with metastatic pancreatic cancer in our differential diagnosis. We concluded that pancreatic duct carcinoma was unlikely for several reasons. First, her blood biochemical profile was negative for all tumor markers specific to this condition. Second, there was no associated dilation caudal to the mass of the main pancreatic duct. Finally, her contrast EUS presentation lacked hypoenhancement, a characteristic feature of pancreatic duct carcinoma proposed by Kitano et al. (14). Eventually, using a biopsy needle, a method which is reportedly useful for making a diagnosis (2-8), we collected sizable quantities of tumor tissue, allowing us to perform a wide variety of immunostaining tests needed for a differential diagnosis. Pancreatic carcinoma was ruled out based on the proliferation of spindle cells with nuclear atypia identified by H&E staining. In addition, the tumor cells were negative for cytokeratin (AE1/AE3) and positive for vimentin and αSMA on immunohistochemistry. We diagnosed the mass as a leiomyosarcoma: a mesenchymal malignancy exhibiting smooth muscle differentiation and a high proliferative potential, confirmed based on an MIB-1 proliferation index of 20%. Despite the small size of the tumor, the EUS-FNB facilitated the collection of a sufficient sample to obtain a pathological diagnosis by an immunohistochemical analysis. Previous studies have reported that the recently developed biopsy needle enables the collection of more tissue than previously existing puncture needles (15). In line with this, we recommend using a biopsy needle for the diagnosis of small tumors, such as the one reported in the present case.

Of note, spindle cells were also observed in tissue collected from the pulmonary lesion via a transbronchial route, and these tested negative for both adenocarcinoma and squamous cell carcinoma markers. The grade of nuclear

atypia was lower in the connective tissue-like spindle cells than in the pancreatic lesions, so a definitive diagnosis could not be established. Based on the findings of the immunohistochemical analysis, we concluded that the nodule was most likely a metastatic lesion originating from urinary bladder leiomyosarcoma. To obtain a definitive diagnosis of whether the pulmonary mass originated from a primary pancreatic tumor or some other organ, it would have been necessary to check for pathological similarities between the EUS-FNB-sampled pancreatic tissue and the previously resected bladder leiomyosarcoma. However, this was not feasible in the present case, as the patient had moved to a different country.

Metastatic pancreatic tumors are often discovered at an end-of-life stage when malignancies spread throughout the body. However, some patients with these malignancies remain physically active, which is an important criterion to be eligible for surgical resection or chemotherapy. Based on the accurate diagnosis confirmed by an EUS-FNB, the patient in the present case was administered doxorubicin chemotherapy (75 mg/m^2). When practitioners encounter an atypical pancreatic tumor, the proactive performance of an EUS-FNB and immunohistochemical analysis can provide accurate pathological findings, which may help establish a diagnosis that can guide and result in the proper treatment of such malignancies.

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

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