SVC syndrome managed immediately after on site diagnosis of EUS-guided sampling for metastatic small-cell carcinoma of the pancreas presenting as acute pancreatitis

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Small-cell lung cancer (SCLC) is an aggressive malignancy with a high propensity for early regional and distant metastasis. However, acute pancreatitis due to pancreatic metastasis in lung cancer, including SCLC, is very rare.[1] Lung cancer is a leading cause of superior vena cava (SVC) syndrome. SVC syndrome is a medical emergency, but appropriate management can be delayed a few days to confirm the biopsy result after a lymph node (LN) or lung biopsy. In this respect, because endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) can offer rapid onsite diagnosis, it is useful for immediately deciding the optimal management for SVC syndrome. We urgently treated a patient with acute pancreatitis, having a pancreatic mass, with SVC syndrome caused by SCLC, based on onsite results of an emergency EUS-FNB.

A 45-year-old male presented with epigastric pain, which radiated to back pain over 3 days. He had no history of gallstone disease or alcohol abuse. He also had no history of recent infection, trauma, or an endoscopic procedure, and was taking no regular medication. Amylase and lipase levels were 1,225 U/L (normal range 28-100) and 2,243 U/L (normal range 7-60), respectively. Computed tomography (CT) showed a diffuse enlargement of pancreas. CT severity index was 6, grading of pancreatitis was multiple fluid collections, and pancreatic necrosis was less than 33%. CT findings was compatible with acute pancreatitis, but needed for differentiating malignancy such as pancreatic cancer [Figure 1]. The next day, patient complained of headache, facial swelling, and shortness of breath. Engorged neck and chest veins were evident on physical examination without palpable neck LNs and mediastinal widening was observed on a chest X-ray. We suspected SVC syndrome based on the clinical symptoms and findings of the physical examination, but no additional CT could be performed because of contrast-induced nephropathy in a previous abdominal CT. Because the patient needed an emergency histopathological diagnosis to decide on the optimal management of the SVC syndrome, we planned to perform EUS for the purpose of evaluating the mediastinal widening and a subsequent EUS-FNB of the pancreatic mass in the same procedure. EUS-FNB using a linear array echoendoscope (GF-UCT240; Olympus Medical Systems Co. Ltd, Tokyo, Japan) was immediately performed on the pancreatic mass. Enlarged mediastinal and subcarinal LNs were also revealed on EUS. After using color-Doppler ultrasound, EUS-FNB was

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performed using a 22-gauge (G) FNB needle (Procore; Wilson-Cook Medical, Winston-Salem, NC, USA) for the pancreatic body mass and subcarinal LNs [Figure 2]. The part of tissue obtained from the EUS-FNB was air dried and stained with Diff-Quik (International Reagents Co., Ltd., Kobe, Japan) for an immediate onsite diagnosis. The remaining tissues were fixed with alcohol for cytological analysis using Papanicolaou staining and formalin for histological analysis. In the onsite examination of the pancreatic mass and subcarinal LN, small-cell carcinomas were suspected [Figure 3a]. Based on our onsite examination of the EUS-FNB, appropriate radiotherapy and chemotherapy were started immediately to help reduce the mass effect of SVC syndrome due to the small-cell carcinoma. The small-cell carcinoma was finally confirmed from the Papanicolaou-stained cytology [Figure 3b] and histology using hematoxylin and eosin (H & E) staining [Figure 3c]. Immunohistochemistry (IHC) for neuroendocrine markers, including chromogranin, synaptophysin, and CD56, showed positivity in the tumor cells. In addition, tumor cells showed nuclear staining of thyroid transcription factor 1 (TTF-1), consistent with metastatic pulmonary adenocarcinoma [Figure 3d]. We finally confirmed the diagnosis of pancreatic and LN metastases from the SCLC. SVC syndrome and symptoms were improved dramatically by chemotherapy for SCLC. The pancreatitis was treated successfully with conservative treatment and the patient was treated with radiotherapy for the metastatic lesion.

DISCUSSION

Metastatic tumors of the pancreas are uncommon. The incidence of metastases to the pancreas has been reported to range from 3 to 10.6% at autopsy in patients with a malignant neoplasm.[2]

The most common histological type of metastatic lung cancer in the pancreas is small-cell carcinoma. This is because small-cell carcinoma of the lung is characterized by diffuse metastases, with lymphatic and hematogenous spread. Not all cases of pancreatic metastases present with clinical pancreatitis. Typically, it occurs in patients known to have advanced carcinomas. A tissue biopsy should be performed to confirm the diagnosis of metastases, including pancreatitis.[3,4]

In our case, the patient had no pulmonary symptoms and was admitted for evaluation and treatment of acute pancreatitis combined with a pancreatic mass. Although the diagnosis of pancreatic cancer was correct, we performed the EUS-FNB for the pancreatic mass more quickly because SVC syndrome was suggested from an unknown origin and we needed to make a histopathological diagnosis for the optimal management of the SVC syndrome. SVC syndrome is caused by extrinsic compression or intraluminal blockade of the SVC due to mediastinal lymphadenopathy or a right upper lobe lung tumor with mediastinal invasion. Timely diagnosis of the condition underlying the SVC syndrome is essential for starting appropriate treatment, especially if small-cell carcinoma or lymphoma is confirmed. A histological diagnosis can sometimes be achieved by bronchoscopy, LN biopsy, or a transvenous biopsy. Unfortunately, the diagnostic yield for these studies is often low.[5] Previous studies showed that when these less-invasive techniques failed, cervical mediastinoscopy or anterior mediastinotomy was more often successful in obtaining a tissue diagnosis in

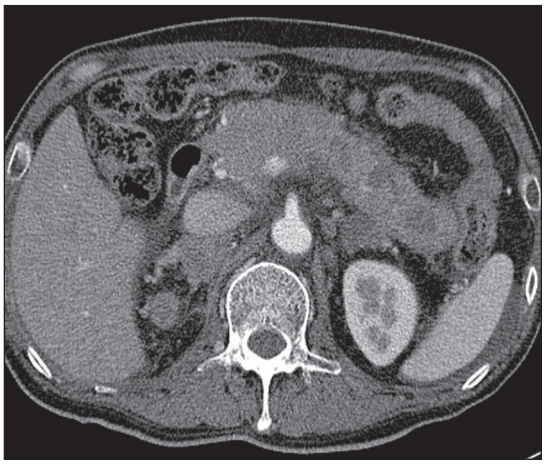

Figure 1. Computed tomography (CT) showing a diffuse enlargement of pancreas. CT severity index was 6, grading of pancreatitis was multiple fluid collections, and pancreatic necrosis was less than 33%

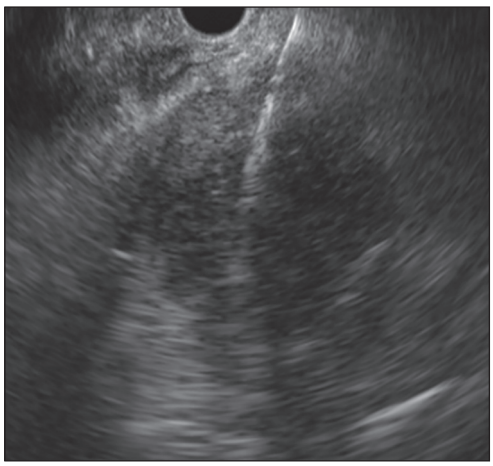

Figure 2. Endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) of pancreas' body mass and subcarinal lymph node

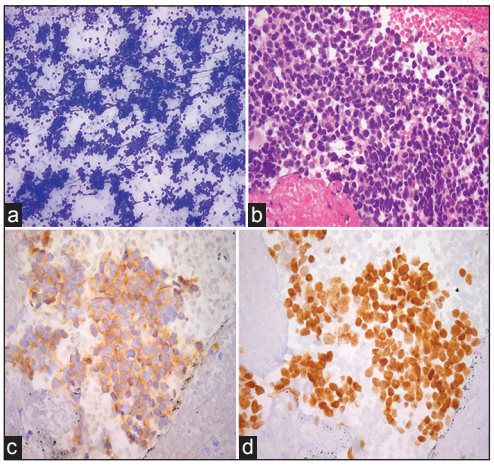

Figure 3. Metastatic adenocarcinoma from the lung diagnosed by EUS-FNB. (a) Tumor cells with variable nuclear size and salt and pepper chromatin (Diff-Quik, ×400). (b) The cytological smears were very cellular, with cells singly or in loose clusters (Papanicolaou, ×400). (c) The tumor cells were small cells with round, irregular nuclei, little or no cytoplasm, and individual necrosis (H & E, ×400). (d) Tumor cells show nuclear staining of thyroid transcription factor 1 (TTF-1), consistent with metastatic pulmonary adenocarcinoma (IHC, ×200). H & E = Hematoxylin and eosin. IHC = immunohistochemistry

SVC syndrome. However, because these procedures involve the dissection and biopsy of tissue in the presence of distended neck veins and collateral circulations, they involve the risk of hemorrhage and other complications. One review article reported the overall morbidity associated with these more invasive procedures was 8.2%.[6]

Since the advent of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) as a relatively safe procedure for establishing the diagnosis of a mediastinal mass, there is a good clinical rationale for its application in SVC syndrome. In a previous study of EBUS-TBNA for the diagnosis of SVC syndrome, malignancy was confirmed in 16 of 17 patients (diagnostic yield 94.1%) and there was no major complication, including significant bleeding or pneumothorax, related to the procedures.[7] EUS-FNB is also a safe and accurate method used in the diagnosis of primary pancreatic cancer.[8] Additionally, EUS-FNB for diagnosis of pancreatic metastasis was reported to be as useful as an EUS-guided Trucut biopsy (EUS-TCB).[9]

In the present case, EUS-FNB was useful in three ways. First, SCLC was diagnosed immediately using onsite diagnosis of a specimen acquired by EUS-FNB and this facilitated starting disease management more quickly; suitable chemotherapy for SCLC was begun as treatment for the SVC syndrome. Second, we performed a histological analysis with ICH in addition to a cytological analysis, and the final histopathological diagnosis and the primary origin of the malignancy were confirmed by EUS-FNB as pancreatic metastasis. Third, we performed EUS-FNB on the subcarinal LN and pancreas in the same procedure and could diagnose the SCLC. Based on these advantages, EUS-FNB with onsite diagnosis could be considered a method for the histopathological diagnosis of SVC syndrome, and could be especially useful when an urgent pathological diagnosis is required. Based on onsite results of EUS-FNB, we diagnosed small-cell carcinoma, so we could determine the cancer's primary origin. We could then begin suitable early management for SCLC, such as radiotherapy and chemotherapy. In conclusion, EUS-FNB is a safe, reliable, and accurate tissue-sampling method that can be helpful in establishing a diagnosis for acute-phase management, as in our case.

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