[症例報告]Metastasis-induced acute pancreatitis caused by small cell lung carcinoma

Metastasis-induced acute pancreatitis caused by small cell lung carcinoma

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ABSTRACT

We report a case of metastasis-induced acute pancreatitis (MIAP) that we successfully treated by chemotherapy based on a cytodiagnosis. A 62-year-old man was diagnosed to have localized small cell lung carcinoma (T1, N3, M0; stage IIIb) and thereafter underwent four courses of chemotherapy accompanied by radiotherapy as follows: 120mg of cisplatinum (CDDP) on Day 1,150mg of etoposide (VP-16) on Days 1 through 3, and 1.5 Gy ×2/day of radiotherapy on Days 5 through 9. The carcinoma went into complete remission (CR), and the patient was then followed up on an outpatient basis. Two years later, the patient was readmitted for left upper abdominal and lumbar pain, and was diagnosed to have mild acute pancreatitis accompanied by neoplastic lesions in the pancreas. Since primary pancreatic carcinoma could not be ruled out by diagnostic imaging, an exploratory laparotomy was performed. An intraoperative cytologic examination confirmed small cell carcinoma. Therefore, four courses of intra-arterial chemotherapy were chosen. The pancreatic tumor disappeared and a cystic lesion remained after completing chemotherapeutic regimen, and a favorable quality of life was thus maintained for nine months. Although unnecessary surgical procedures should be avoided for patients with small cell carcinoma, an exploratory laparotomy for an intraoperative rapid and accurate cytodiagnosis should be performed for the differential diagnosis and thereafter the most appropriate therapeutic modality should be chosen. *Ryukyu Med. J., 19(4)239~243, 2000*

Key words: small cell lung carcinoma, pancreatic metastasis, acute pancreatitis, MIAP, cytodiagnosis

INTRODUCTION

When compared to carcinoma of other organs, lung carcinoma frequently metastasizes early in the course of the disease, and it is one of the malignant cancers with a poor prognosis. Lung carcinoma often metastasizes to the liver or the adrenal gland, but rarely to other organs. Metastasis-induced acute pancreatitis (MIAP) is an uncommon condition and a review of the literature identified few reports. Although tissue diagnosis is difficult, the diagnoses of almost all reported cases were based on clinical, laboratory, and radiologic findings without an autopsy case. We recently encountered a case of MIAP with a cytodiagnosis of small cell carcinoma, while monitoring the post chemo-radiotherapic course of a patient with small cell lung carcinoma. Such a case with an intraoperative cytodiagnosis has not yet been reported to our knowledge.

CASE

Patient: A 62-year-old man.
Chief complaints: Left upper abdominal and lumbar pain.
Past medical history: Nothing worth mentioning.
Family history: Nothing worth mentioning.
present illness: An abnormal shadow was seen on a chest radiograph taken during a periodic physical check-up performed in January 1994. Consequently, the patient received a thorough examination at our institution, and was diagnosed to have localized small cell carcinoma (T1, N3, M0; stage IIIb) (Fig. 1). As a result, four courses of chemotherapy accompanied by radiotherapy were initiated consisting of 120mg of cisplatinum (CDDP) on Day 1, 150mg of etoposide (VP-16) on Days 1-3, and 1.5 Gy × 2/day of radiotherapy on Days 5-9. Thereafter, the lung carcinoma went into complete remission (CR), and subsequently the patient was followed up on an outpatient basis (Fig. 2). About two years later (in

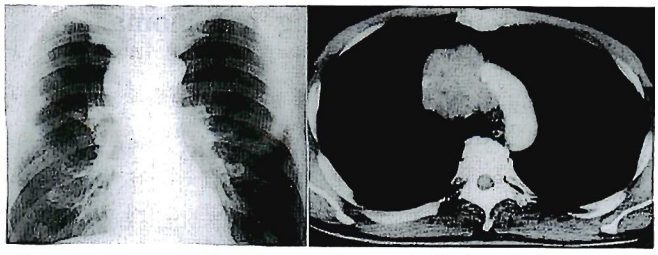

Fig. 1 The initial chest radiograph (left) and CT scan (right). A tumor is seen in the right upper mediastinum.

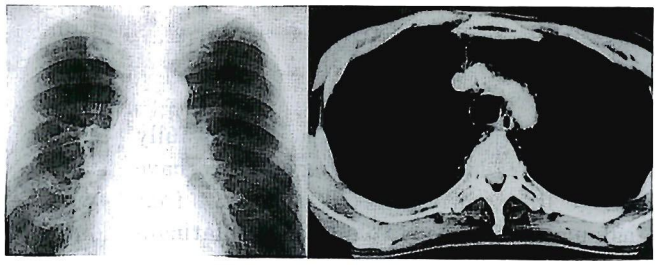

Fig. 2 A plain chest radiograph (left) and a CT scan (right) following chemotherapy. The tumor went into complete remission.

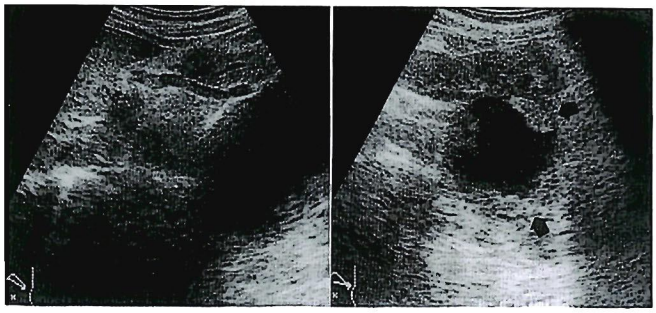

Fig. 3 Abdominal ultrasonogram. A hypoechoic mass was seen in the body of the pancreas (left) and the tail of the pancreas (right). On the dorsal side of the tail of the pancreas, a hypoechoic cystic mass with a clear boundary, accompanied by a mural node (arrow), is seen.

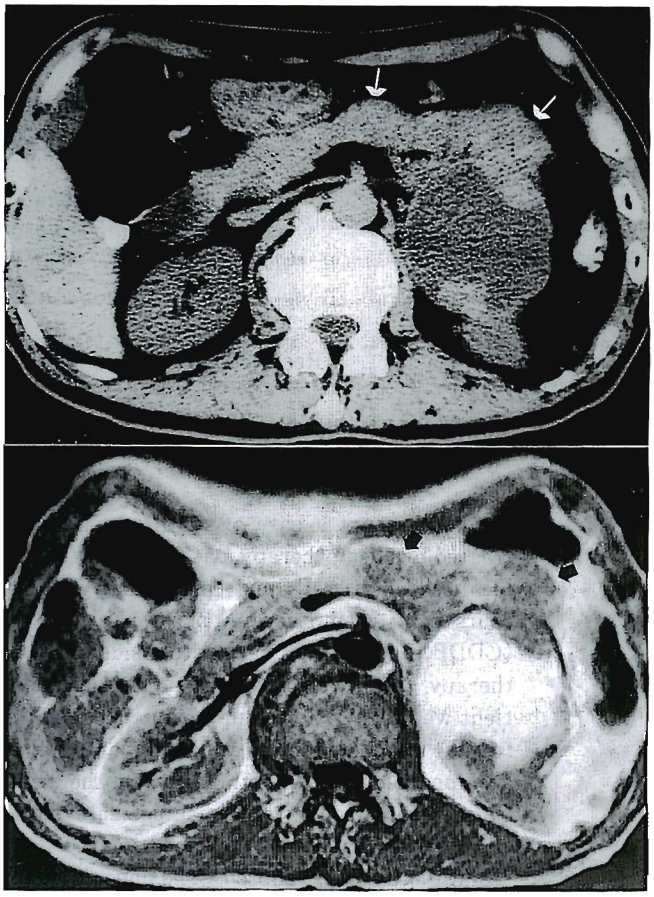

Fig. 4 An abdominal CT scan (top) showing a cystic mass with mural nodules abutting the pancreatic parenchyma. Mural nodules and masses in the pancreatic parenchyma (arrow) have the same attenuation as the pancreas. An abdominal MR image (bottom: T1-weighted image) showing low signal mass (arrow). The internal contents of the cystic tumor showed a high signal, and the signal intensities of mural nodules was the same as those of the pancreatic tumor.

February 1996), the patient was readmitted due to left upper abdominal and lumbar pain.

Physical findings on admission: The patient did not have jaundice or anemia. The abdomen was generally flat and soft, and although lumbar and spontaneous pain and tenderness were detected in the left abdominal region, neither muscle guarding nor rebound tenderness were observed. No masses were palpable.

Laboratory findings on admission: The results of peripheral blood examination were normal. However, the blood and urine chemistry investigations showed a high level of serum amylase (464IU/L) and an increased amount of urinary amylase (1107IU/L). In addition, the levels of CRP and three pancreatic enzymes (elastase, lipase and trypsin) were high (1.21mg/dl (2 +), 1500ng/dl, 108IU/L, and 722ng/ml, respectively). The concentration of the tumor markers were as follows (DUPAN 2 , <25U/ml; SPA N-1 , 12U/ml; CA19-9, 34.9U/ml; ProGRP, 14.1ng/ml; neuron-specific enolase (NSE), 13.0ng/ml; and carcinoembryonic antigen (CEA), 1.3ng/ml). Therefore, except for the slight increase in NSE, the levels of all tumor markers were within the normal range.

Abdominal ultrasonography: A 2 × 2 -cm hypoechoic mass with an isoechoic center was seen in the body of the pancreas. In the tail of the pancreas, a 4 × 3 -cm cystic mass with intramural hyperechoic nodules was detected, and protruded into the peritoneal cavity (Fig. 3).

Abdominal CT and MRI: Abdominal CT revealed masses which had iso attenuation to the pancreatic parenchyma, located in the body and tail of the pancreas. The cystic mass was abutting the tumor in the tail of the pancreas at the site of mural node. Abdominal MRI showed

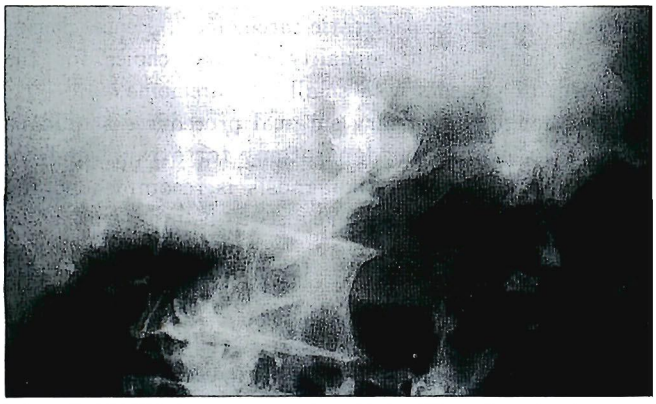

Fig. 5 ERCP demonstrated a slight dilatation in the pancreatic duct and constriction in the body of the pancreas.

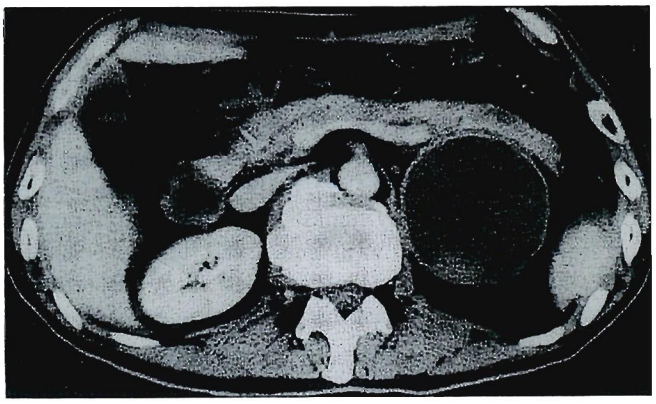

Fig. 6 An abdominal CT scan after the intra-arterial chemotherapy shows that the tumors in the pancreatic parenchyma and intracystic mural nodules have almost resolved. The size of the cyst remains unchainged.

medium signals of the masses in the pancreatic parenchyma and the mural nodules on both the T1 and T2 weighted images, and the internal contents of the cystic mass showed a high signal, thus suggesting bleeding or protein rich fluid related to the pancreatic tumor or cyst (Fig. 4).

Endoscopic retrograde cholangiopancreatography (ERCP): The pancreatic duct was slightly dilated and constricted at the body of the pancreas, probably due to the presence of the tumors (Fig. 5).

Based on these findings, pancreatic metastasis of small cell lung carcinoma was most likely suspected, but chest radiography and CT did not show any signs of recurrence of the primary carcinoma. Although the level of NSE (13.0ng/ml) was slightly above the normal range (<10ng/ml), the concentrations of tumor markers specific for small cell carcinoma and CEA were normal, and thus pancreatic carcinoma could not be ruled out. Hence, an exploratory laparotomy was performed after the pancreatitis had been medically treated.

Surgical findings: A cystic tumor in the tail of the pancreas was strongly attached to the mesocolon, and a tumor partially exposed to the anterior surface of the pancreas was seen in the pancreatic parenchyma extending from the body to the tail of the pancreas. The anterior surface of the tumor in the parenchyma of the tail was fused to the lesser curvature of the stomach, and the lower region was connected to the cystic tumor. Although no abnormalities were found in the head of the pancreas, the caudal pancreatic parenchyma to the tumor in the body of the pancreas was hard and elastic. No ascites was present, while neither any spread nor metastasis was confirmed in the other organs. The results of an aspiration cytodiagnosis of the tumor in the tail of the pancreas confirmed the presence of small cell carcinoma. A resection was not performed since the tumor in the tail of the pancreas was strongly attached to the surrounding tissues and the results of the cytodiagnosis confirmed small cell lung carcinoma.

Postoperative course: In order to treat the pancreatic metastases, an arterial catheter was inserted from the left femoral artery into the celiac artery. Subsequently, 80mg of CDDP and 100mg of VP-16 were administered intra-arterially four times every three weeks. After completing this therapy, the level of NSE (that was slightly elevated at the time of admission) was normalized and the tumor in the pancreatic parenchyma disappeared. Although the cystic tumor in the tail of the pancreas did not shrink, it did not increase in size (Fig. 6). Since both the abdominal and lumbar pains significantly improved, the patient was discharged. Thereafter, on an outpatient basis, 300mg of UFT was administered orally and 5 mg of CDDP was given intra-arterially once a week for nine weeks. For about eight months, the patient remained asymptomatic, and no recurrent or metastatic tumors in the lung or other organs were detected, and he was thus able to maintain a high quality of life. Then, on the ninth month, the patient was readmitted due to insomnia, loss of appetite, and mild abdominal pain caused by recurrence of the pancreatic metastasis. As the tumor increased in size, the patient's condition deteriorated markedly, and he eventually died 5 months later.

DISCUSSION

The prevalence of lung carcinoma is on the rise, and has recently become the leading cause of death in Japan[1]. Lung carcinoma frequently metastasizes early in the course of the disease, and its prognosis is poor. It is generally accepted that lung carcinoma often metastasizes to the liver and adrenal gland, but much less often to the pancreas or the digestive tract. The results of postmortem examinations have shown that the prevalence of digestive tract metastasis among lung carcinoma patients was 12% according to Burbige *et al*[2]. Among patients of

lung carcinoma, although pancreatic metastasis was detected in 20-40% of patients with small cell carcinoma[3,4], tumor-induced acute pancreatitis only rarely developed. The occurrence rate of MIAP was reported to be 3.3% by Chowhan and Madajewicz[5] and 7.5% by Yeung *et al*[6] among patients with small cell lung carcinoma, and only 0.12% in lung carcinoma[7]. On the other hand, 60% of MIAP were caused by small cell lung carcinoma[5]. Therefore, in patients with small cell lung carcinoma, even when the primary cancer goes into CR, careful follow-up is needed because of the risk of metastasis to the abdominal organs (in particular the pancreas).

At our institution, we have treated five patients with acute abdomen caused by digestive tract metastasis[8,9]. However, we had not yet treated any patient with pancreatic metastasis of lung carcinoma before encountering this case, and there have been only few documented cases of lung carcinoma with some sort of clinical manifestations attributed to disorders in the pancreas or bile duct caused by pancreatic metastasis. The prevalence of digestive tract metastasis may be higher if the asymptomatic patients were also included[10].

Although the primary pancreatic carcinoma and metastatic pancreatic tumor are difficult to distinguish by diagnostic imaging[11-14] without a clinical information in conjunction with CT characteristics such as multiplicity of tumors or hypervascularity[15], once a carcinoma is histologically diagnosed to be small cell carcinoma, it is safe to assume that lung carcinoma is the primary carcinoma. Small cell carcinoma that originates in the pancreas is rare. It is often difficult to make a histological diagnosis in such seriously ill patients with pancreas tumor and pancreatitis due to the high morbidity and false negative rates of pancreatic biopsy[16]. Therefore, diagnosis of MIAP is made usually based on the clinical, laboratory, and radiologic findings in combination with evidence of disease progression elsewhere. In almost all previous reports a histologic diagnosis could only be made at autopsy.

In our case, general chemotherapy was chosen to treat small cell carcinoma, and thereafter the carcinoma went into CR. When the abdominal pain appeared, no recurrent tumors were found in the chest, and since primary pancreatic cancer could not be ruled out, exploratory laparotomy was performed. The results of an aspiration cytodiagnosis confirmed small cell carcinoma, and thus chemotherapy was selected instead of resection.

A pancreatectomy is contraindicated for patients with pancreatic metastasis once a definite diagnosis has been made. When an exploratory laparotomy is performed to distinguish pancreatic carcinoma from pancreatic metastasis, a resection of the tail of the pancreas may be performed for a biopsy examination, however, a total pancreatectomy or pancreatoduodenectomy should be avoided[7]. The primary reason for performing an exploratory laparotomy is to make a rapid intraoperative cytodiagnosis. It has been reported that chemotherapy for small cell lung carcinoma is also effective for small cell pancreatic carcinoma[14]. Hence, chemotherapy should be the modality of first choice for the treatment of patients with small cell carcinoma.

Although unnecessary surgical procedures should be avoided, an exploratory laparotomy for a rapid and accurate intraoperative cytodiagnosis is recommended for the differential diagnosis and also to help determine the most appropriate therapy.

CONCLUSION

The present paper described a case with pancreatic metastasis of small cell lung carcinoma exhibiting MIAP, and also discussed the patient's diagnosis and treatment while considering the relevant references.

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