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CASE REPORT

Metastasis-Induced Acute Pancreatitis in a Patient with Small Cell Carcinoma of the Lungs

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ABSTRACT

Context Pancreatic metastases are relatively common in advanced lung cancers (both small cell lung carcinoma and non-small cell lung carcinoma), but metastasis-induced acute pancreatitis is very unusual. **Case report** A 51-year-old woman with small cell carcinoma of the lung developed acute pancreatitis as the initial manifestation. Abdominal ultrasonography revealed multiple pancreatic metastases which were confirmed by magnetic resonance imaging. Conventional treatment did not improve her condition. However, aggressive chemotherapy resulted in a dramatic recovery from the acute pancreatitis and significant improvement in her general condition. **Conclusion** When cases of acute pancreatitis in patients with small cell lung carcinoma are encountered, we must consider the possibility of metastasis-induced acute pancreatitis and that, should pancreatic metastases be found in these patients, chemotherapy may provide substantial benefit.

INTRODUCTION

A variety of tumors have been reported to metastasize to the pancreas, including prostatic carcinoma, renal cell carcinoma, squamous cell carcinoma of the skin, carcinoma of the breast, hepatoma, a variety of sarcomas, Hodgkin's disease, small cell lung carcinoma and non-small cell lung carcinoma, and pancreatic metastases are relatively common in advanced small cell lung carcinoma and non-small cell lung carcinoma [1, 2, 3, 4]. Metastasis-induced acute pancreatitis, however, is very unusual. In this report, we documented a case of metastasis-induced acute pancreatitis as an initial manifestation of small cell lung carcinoma, and reported dramatic improvement of the patient's condition after using chemotherapy to treat the metastases. We concluded that, when cases of acute pancreatitis in patients with small cell lung carcinoma are encountered, the patient should be screened for pancreatic metastases and, if found, these metastases should be treated aggressively.

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Key words Acute Disease; Adult; Carcinoma; Carcinoma, Non-Small-Cell Lung; Female; Humans; Lung Neoplasms; Neoplasm Metastasis; Pancreatic Neoplasms; Pancreatitis; Small Cell Lung Carcinoma

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CASE REPORT

A 51-year-old woman was admitted to Nagoya City University Hospital with severe epigastralgia. She had been smoking 20 cigarettes a day for 30 years. There was no history of excessive alcohol consumption, medication or cholelithiasis. On admission to Nagoya City Hospital, pertinent physical findings were confined to the abdomen, the patient exhibiting abdominal tenderness and guarding over the epigastrium. Laboratory data were as follows: WBC count, 6,100 mm^{-3} (reference range: 3,000-8,500 mm^{-3}); RBC, 411 $x10^4$ mm^{-3} (reference range: 378-499 $x10^4$ mm^{-3}); hemoglobin, 12.6 g/dL (reference range: 10.8-14.9 g/dL); BUN, 10 mg/dL (reference range: 8-22 mg/dL); creatinine, 0.7 mg/dL (reference range: 0.4-0.7 mg/dL); and calcium, 9.4 mEq/L (reference range: 8.7-10.3 mEq/L). The pancreatic enzymes were elevated: serum amylase, 135 U/L (reference range: 37-125 U/L); lipase, 276 U/L (reference range: 13-49 U/L); and elastase-1, 2,000 ng/dL (reference range: 100-400 ng/dL). Urophanic amylase was elevated to 887 U/L (reference range: 0-650 U/L). Small cell lung carcinoma markers were elevated: neuron-specific enolase, 24 ng/mL (reference range: 0-10 ng/mL) and pro-gastrin-releasing peptide, 2,310 ng/mL (reference range: 0-46 ng/mL).

Plain chest X-ray films revealed a left parahilar tumor (Figure 1). Chest computed tomography (CT) showed multiple diffuse parahilar lymphadenopathy and a 44x33 mm mixed density lung mass with irregular margins at the left hilum (Figure 2a). Abdominal US

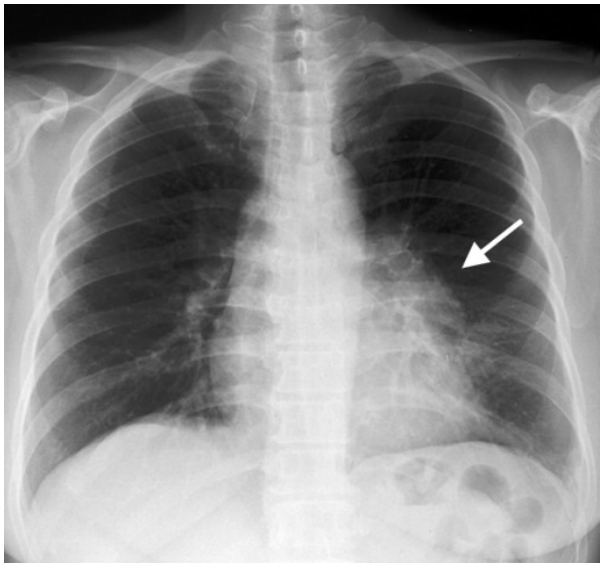

Figure 1. Chest X-ray films revealed a left parahilar tumor (arrow).

disclosed 1-3 cm multiple low echoic masses within the swollen pancreatic body and tail (Figure 3a). Magnetic resonance imaging (MRI) confirmed the US findings (Figure 4ac), but abdominal CT demonstrated only a swollen pancreas. Because the pancreatic duct

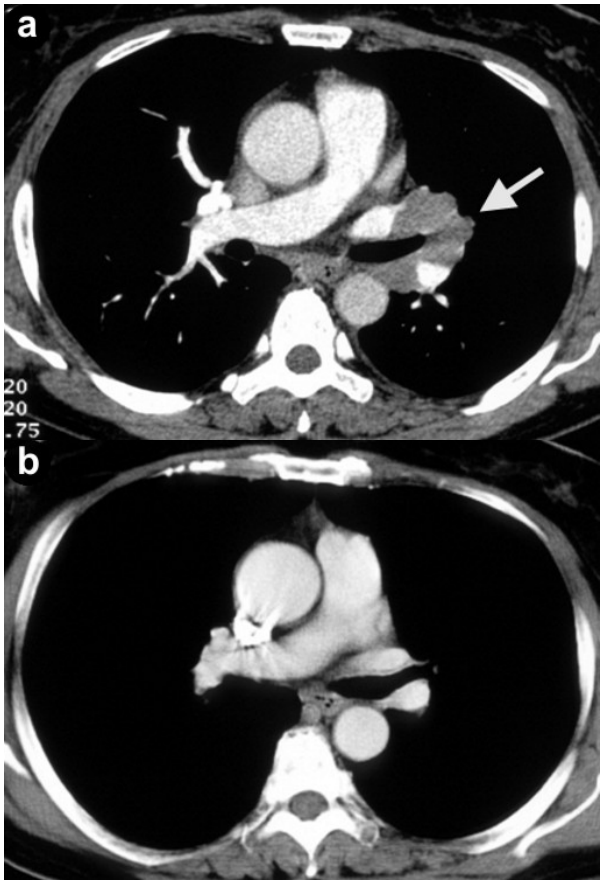

Figure 2. a. Contrast-enhanced chest computed tomography showed ultiple diffuse parahilar lymphadenopathy and a 44x33 mm mixed density lung mass with irregular margins at the left hilum (arrow). **b.** After two courses of chemotherapy, the lung tumor disappeared.

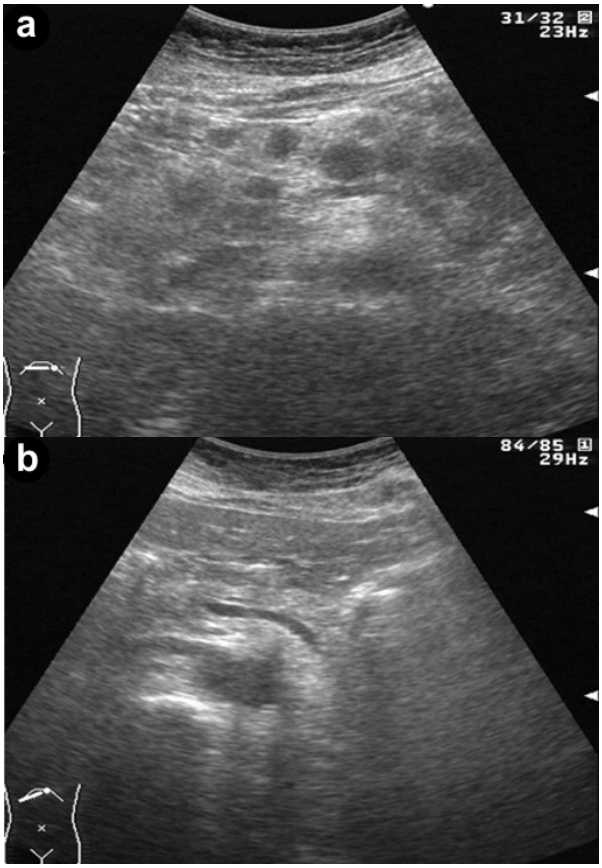

Figure 3. a. Abdominal ultrasonography disclosed 1-3 cm multiple low echoic masses within the swollen pancreas body and tail. **b.** After two courses of chemotherapy, the pancreas metastatic tumors disappeared.

was normal in the US, CT and MRI images, the MRCP image was not diagnostic at that time. Bone scintigraphy revealed a hot spot in the right arm. A head MRI was normal. A cytological diagnosis of the sputum revealed small cell carcinoma. Since the acute pancreatic symptom was severe, bronchoscopy, endoscopic retrograde pancreatography and endoscopic US-guided fine needle aspiration biopsy (EUS-FNA) were not performed.

The patient received conventional treatment of a fasting couplet with an anti-pancreatic exocrine enzyme (gabexate mesylate 600 mg/day) and antibiotics (meropenem, 1 g/day). However, the treatment did not improve her condition. Therefore, ulinastatin (150,000 U/day) was added to her treatment after one week. Still, her condition remained unchanged. Thus, aggressive combination chemo-therapy with two courses of PVP-IAV therapy was performed (CDDP+VP16 therapy was modified to PVP-IAV therapy at the Department of Pulmonology in our hospital at the time). PVP and IAV therapy were scheduled alternatively once every 3 weeks. Each procedure was performed twice over the course of 12 weeks. At the time the patient was treated, the standard PVP therapy at Nagoya City University Hospital was cisplatin 36 mg/m^2 days 1, 2, 3 plus etoposide 100 mg/m^2 days 1, 2, 3, and the standard IAV therapy was

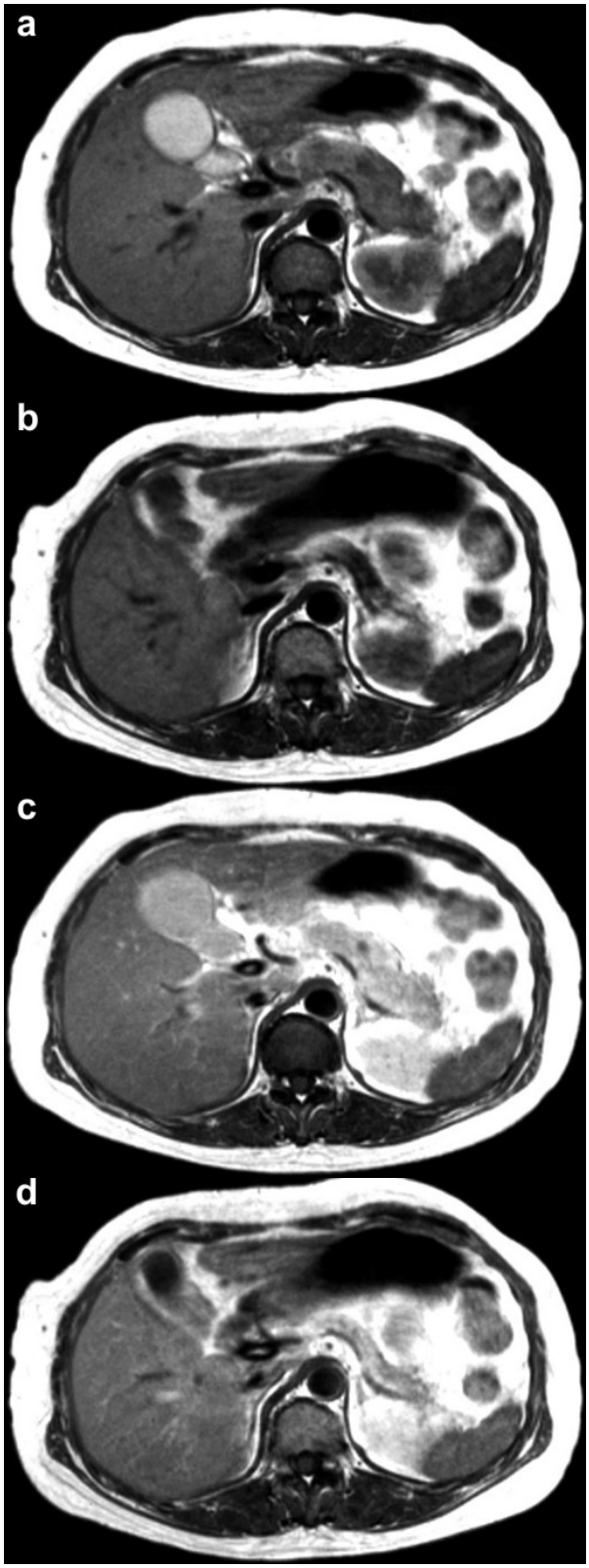

Figure 4. a. T1 weighted magnetic resonance imaging (MRI) confirmed the ultrasonography findings. MRI showed multiple low intensity masses within the swollen pancreas body and tail. **b.** After two courses of chemotherapy, the pancreas metastatic tumors disappeared in T1-weighted MRI. **c.** Gadolinium-enhanced MRI showed multiple low intensity masses. **d.** After two courses of chemotherapy, the pancreas metastatic tumors had disappeared in gadolinium-enhanced MRI.

ifosfamide 1,500 mg/m^2 day 1 plus adriamycin 40 mg/m^2 day 1 plus vincristine 1.5 mg/m^2 day 1. After two courses of chemotherapy, the lung tumor and the parahilar lymphadenopathy had disappeared on the chest X-ray and CT (Figure 2b). The pancreas metastatic tumors had also disappeared on abdominal US (Figure 3b) and MRI (Figure 4bd). Chemotherapy also caused a rapid and dramatic improvement in her condition and a significant decrease in follow-up amylase levels. The same combination chemotherapy was continued in another hospital near the patient's home. However, she died due to multiple brain metastatic tumors 8 months after her initial presentation with pancreatitis. Permission for a postmortem was not granted.

DISCUSSION

Prospective confirmation of a diagnosis of metastasis-induced acute pancreatitis is difficult in the absence of EUS-FNA or exploratory laparotomy with pancreatic biopsy. Since permission for a postmortem was not granted, we could not confidently diagnose the pancreatic masses found in this patient as metastases. However, chemotherapeutic treatment for small cell carcinoma was effective against the pancreatic masses of this patient, suggesting that the pancreatic masses were small cell carcinoma. In addition, metastases to the pancreas from small cell lung carcinoma are frequent and are found in 24% of patients at post-mortem [3]; primary small cell carcinoma of the pancreas is very rare, only 1-1.4% of pancreatic cancers [5, 6]. Finally, while 96% of small cell cancers are of pulmonary origin, only about 4% arise in extra-pulmonary sites [7]. Taken together, these data suggest that it is likely that the pancreatic tumors were metastatic small cell lung carcinoma in this patient, and that the acute pancreatitis was induced by these metastases.

Metastasis-induced acute pancreatitis can occur as an initial manifestation of a carcinoma or later in the course of the disease (Table 1). There are no standard treatment approaches to metastasis-induced acute pancreatitis due to the rarity of this disease and its grim prognosis. Reported survival times range from 8 days to 8 months (the present case) with a mean survival of approximately 2.2 months from the onset of the pancreatitis (Table 2). However, only in the nine cases in which acute pancreatitis manifested as an initial symptom of small cell lung carcinoma [8, 9, 10, 11, 12, 13, 14, 15] did treatment with chemotherapy have a significant effect on patient survival time; patients treated with chemotherapy survived an average of 3.9 months while patients with only supportive therapy survived an average of 22.4 days (Table 2). Perhaps of greater importance, however, the chemotherapeutic treatment of the patient reported here resulted in a rapid and significant regression of her pancreatitis symptoms and a dramatic improvement in her general condition.

Table 1. Metastasis-induced acute pancreatitis with lung cancer.

Cases	Age (years) [a]	Sex	Initial manifestation	Histology	Treatment	Survival	References
1	51	Female	MIAP	Small cell lung carcinoma	Chemotherapy	8 months	Our case
2	58	Male	MIAP	Small cell lung carcinoma	Chemotherapy	5-6 weeks	[14]
3	55	Female	MIAP	Small cell lung carcinoma	Chemotherapy	14 days	[15]
4	44	Male	MIAP	Small cell lung carcinoma	Chemotherapy	Over 6 months	[8]
5	67	Male	MIAP	Small cell lung carcinoma	Supportive	12 days	[9]
6	58	Male	MIAP	Small cell lung carcinoma	Supportive	46 days	[10]
7	45	Female	MIAP	Small cell lung carcinoma	Supportive	8 days	[11]
8	56	Female	MIAP	Small cell lung carcinoma	Supportive	37 days	[12]
9	68	Female	MIAP	Small cell lung carcinoma	Supportive	9 days	[13]
10	58	Male	MIAP	Large cell carcinoma	Chemotherapy	8 months	[16]
11	59	Male	MIAP	Bronchogenic carcinoma	Supportive	8 weeks	[17]
12	55	Male	MIAP	Adenocarcinoma	Supportive	13 days	[1]
13	53	Male	Lung cancer [b]	Small cell lung carcinoma	Chemotherapy	162 days	[23]
14	53	Male	Lung cancer [b]	Small cell lung carcinoma	Chemotherapy	155 days	[23]
15	37	Female	Lung cancer [b]	Small cell lung carcinoma	Chemotherapy	114 days	[23]
16	73	Female	Lung cancer [b]	Small cell lung carcinoma	Supportive	5 days	[19]
17	63	Male	Lung cancer [b]	Small cell lung carcinoma	Supportive	N/A	[20]
18	52	Male	Lung cancer [b]	Small cell lung carcinoma	Supportive	3 weeks	[21]
19	67	Male	Lung cancer [b]	Small cell lung carcinoma	Supportive	12 days	[19]
20	48	Male	Lung cancer [b]	Small cell lung carcinoma	Supportive	11 days	[15]
21	45	Female	Lung cancer [b]	Small cell lung carcinoma	Endoscopic stenting	N/A	[22]
22	45	Male	Lung cancer [b]	Small cell lung carcinoma	Supportive	2 months	[18]
23	37	Male	Lung cancer [b]	Anaplastic bronchial carcinoma	Chemotherapy	N/A	[24]
24	48	Male	Lung cancer [b]	Bronchogenic carcinoma	Supportive	7 weeks	[18]
25	57	Male	Lung cancer [b]	Squamous cell carcinoma	N/A	N/A	[24]

[a] Small cell lung carcinoma: cases 1-9: mean 55.8 years (range: 44-68 years); cases 13-22: mean 53.6 years (range: 37-73 years)
[b] Acute pancreatitis during treatment of lung cancer
MIAP: metastasis-induced acute pancreatitis; N/A; data not available

Notably, while therapy directed against pancreatic metastases dramatically improved the condition of the patient, the conventional treatment of fasting coupled with intravenous therapy with gabexate mesylate/nafamostat mesilate and antibiotics had no effect on the patient's condition. We concluded that when cases of acute pancreatitis in patients with small cell lung carcinoma are encountered, the possibility of metastasis-induced acute pancreatitis must be considered and that, should pancreatic metastases be found in these patients, chemotherapy may provide substantial benefit.

Conflict of interest The authors have no potential conflicts of interest

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Table 2. Cases of acute pancreatitis as the initial manifestation of bronchogenic carcinoma.

Treatment	Number of cases	Survival			References
		Mean	Median	Range	
Small cell lung carcinoma					
- Chemotherapy	4	3.9 months	3.7 months	14 days - 8 months	Our case, [8, 14, 15]
- Supportive	5	22.4 days	12 days	8 days - 12 days	[9, 10, 11, 12, 13]
Total	**9**	**2.2 months**	**1.2 months**	**8 days - 8 months**	**Our case, [8, 9, 10, 11, 12, 13, 14, 15]**
Non-small cell lung carcinoma					
- Chemotherapy	1	8 months			[16]
- Supportive	2	13 days, 8 weeks			[1, 17]
Total	**3**	**Range: 13 days - 8 months**			**[1, 16, 17]**

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