



A rare case of pulmonary lepidic metastasis in patient with branch-type intraductal papillary mucinous carcinoma of the pancreas

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Abstract

Pulmonary lepidic metastasis from intraductal papillary mucinous carcinoma (IPMC) of the pancreas is extremely rare. The patient was a 50s-year old male who was hospitalized in the department of respiratory in our hospital for the evaluation of ground-glass opacities in both lungs on computed tomography (CT) imaging. Steroid therapy was administered, as interstitial pneumonia was suggested; however, there was no improvement. A transbronchial lung biopsy (TBLB) revealed the possibility of distant lung metastases. Abdominal CT revealed pancreatic cystic lesions; the patient was, therefore, referred to our department for further evaluation. Endoscopic ultrasound revealed large multi-cystic lesion with mural nodule and wall thickness. A subsequent pancreatic juice cytology under endoscopic retrograde cholangiopancreatography revealed adenocarcinoma. As this was consistent with the pathological findings shown on TBLB, IPMC metastasis to the lung was diagnosed. In this case, it was considered that pulmonary lepidic metastasis from IPMC by CT imaging and pathological findings. Although the cases of pulmonary lepidic metastasis from gastrointestinal cancer are rare, we should consider these pathological conditions when pneumonia-like infiltration observed on imaging studies does not respond to treatment.

Keywords Lepidic metastasis · Lung metastasis · IPMC

Introduction

Intraductal papillary mucinous carcinoma (IPMC) of the pancreas is recognized as a tumor that progresses gradually. When the tumor worsens, it shows infiltrative growth, metastasizes to other organs, and has a poor prognosis. Although lung metastasis from IPMC is comparatively rare, it is easy to diagnose because the metastatic lesion is usually recognizable as a mass form, such as solitary or multiple nodular densities with smooth margins, or lymphangitic carcinomatosis. However, there is also a rarely observed

mode of spread to the lung called lepidic metastasis, where the alveolar structure is retained, while tumor cells replace the alveolar epithelium as the metastasis expands. In such cases, a pneumonia-like radiographic image similar to alveolar epithelial carcinoma is shown, making a diagnosis of the metastasis difficult. We here in reported a rare case of IPMC with pulmonary lepidic metastasis.

Case report

A 50s-year old man who was being treated for diabetes and dyslipidemia, presented with cough and exertional dyspnea, which had persisted from a few months prior. A computed tomography (CT) image of the chest revealed ground-glass opacities in the lung fields bilaterally; bacterial pneumonia was diagnosed, and the patient was administered antibiotics, however, there was no improvement. At that point, cryptogenic organizing pneumonia was considered, and steroid treatment was administered without improvement.

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Therefore, he was referred to our hospital and admitted for further treatment. The increase in the patient's leukocyte count to 18,500/ μ L was considered to be due to the effect of the steroid. Meanwhile, CA19-9 was 12,000 U/mL, which was markedly elevated (Table 1). CT showed patchy consolidation, predominantly in the periphery of both lungs, and ground-glass opacity in the surrounding area (Fig. 1a–c). Simultaneously, the cystic lesions in the pancreatic body and tail were seen (Fig. 1d). Transbronchial lung biopsy (TBLB) revealed mucus-producing columnar epithelial cells with papillary hyperplasia replacing the alveolar epithelium (Fig. 2a). Immunohistochemical staining was positive for cytokeratin 7 (CK7) (Fig. 2b), and negative for cytokeratin 20 (CK20) (Fig. 2c) and thyroid transcription factor-1

(TTF-1) (Fig. 2d). Given these findings, the possibility of lung metastases from another organ was suspected. Because the previous CT showed the pancreatic cystic lesions, it was considered that pancreatic cystic neoplasm might be origin. An MRCP revealed a multicystic mass 45 mm in diameter and in continuity with the main pancreatic duct in the pancreatic body/tail; the branch-type IPMN was suspected (Fig. 3a). An endoscopic ultrasound (EUS) (Fig. 3b) also revealed a multicystic mass 45 \times 37 mm in size in the pancreatic body/tail; intra-cystic nodules were present and partial wall-thickening was observed. Endoscopic retrograde cholangiopancreatography (ERCP) showed communication between the cystic lesion and the main pancreatic duct (Fig. 3c), and pancreatic juice cytology revealed atypical cells with mucus and mucilaginous vacuoles (adenocarcinoma) (Fig. 4a). Thus, based on these findings, pancreatic cystic mass was diagnosed as the intraductal papillary mucinous carcinoma (IPMC).

The obtained atypical cells from pancreatic juice were consistent with the findings seen on TBLB; immunohistochemical staining was positive for CK7 (Fig. 4b) and negative for CK20 (Fig. 4c). Mucin (MUC) staining was positive for MUC5AC and MUC6, and negative for MUC1 and MUC2, consistent with gastric type (Fig. 5a–d). Retrospective MUC staining of the TBLB specimen showed a similar staining pattern to those from the pancreatic juice (Figs. 5e–h). From the above results, IPMC with pulmonary lepidic metastasis was diagnosed. Chemotherapy was considered, however, the patient died on day 49 after admission to our hospital due to respiratory failure caused by rapid progression of the pulmonary lesion.

Discussion

Generally, imaging findings of metastatic pulmonary tumors are commonly distinct solitary or multiple nodular densities with smooth margins, or lymphangitic carcinomatosis. However, cancer rarely progresses beyond the alveolar wall, therefore, a pneumonia-like image is presented. Bronchioloalveolar carcinoma (BAC) is a type of pulmonary adenocarcinoma that is known to present with pneumonia-like infiltration on plain radiography. In the case presented here, the CT imaging was suspicious for bacterial or organizing pneumonia, making it a very difficult case to correctly diagnose. As the patient did not respond to antibiotic or steroid treatment, TBLB was performed and tumor cells were confirmed. Immunohistochemical staining with TBLB specimen was negative for TTF-1 which is positive for more than 80% of primary lung adenocarcinomas [1], and metastatic pulmonary tumors were suspected.

Gaeta et al. [2] retrospectively investigated CT imaging of pulmonary metastatic lesions in 65 cases of primary

Table 1 Laboratory findings on admission

<i>Blood exam</i>		WBC	18,500/ μ L
AST	18 IU/L	Neutrophils	90.4%
ALT	37 IU/L	Eosinophils	0%
ALP	143 IU/L	Basophils	0.7%
LDH	279 IU/L	Monocytes	5.8%
GGT	62 IU/L	Lymphocytes	5.2%
Total bilirubin	0.3 mg/dL	RBC	344 \times 10 ⁴ / μ L
Total protein	5.7 g/dL	Hb	9.9 g/dL
Albumin	2.4 g/dL	Ht	30.1%
Glucose	206 mg/dL	Plt	22.5 \times 10 ³ / μ L
BUN	15 mg/dL	Bronchoalveolar lavage fluid exam	
Cre	1.02 mg/dL	Total cells	200/ μ L
Amylase	42 U/L	Macrophages	91%
Na	135 mEq/L	Neutrophils	4.4%
K	4.3 mEq/L	Lymphocytes	4.2%
Cl	101 mEq/L		
Ca	7.8 mEq/L		
CRP	5.76 mg/dL		
HbA1c	9.6%		
(1,3)- β -D-glucan	6.0 pg/mL		
SP-D	89.8 ng/mL		
KL-6	320 ng/mL		
Ferritin	439.5 U/mL		
SCC	0.7 ng/mL		
CYFRA	11.0 ng/mL		
NSE	24.5 ng/mL		
Pro-GRP	41.2 pg/mL		
CEA	7.7 pg/mL		
SLX	33 U/ml		
CA19-9	12,000 U/ml		

SP-D: pulmonary surfactant protein-D; KL-6: sialylated carbohydrate antigen KL-6; SCC: squamous cell carcinoma antigen; CYFRA: soluble cytokeratin 19 fragment; NSE: nerve specific enolase; Pro-GRP: gastrin discharge peptide precursor; CEA: carcinoembryonic antigen; SLX: sialyl Lewis-x-i antigen; CA19-9: carbohydrate antigen 19-9

Fig. 1 Computed tomography (CT) showed patchy consolidation predominantly in the periphery of both lungs with ground-glass opacities in the surrounding area (a–c). Abdominal CT revealed a cystic lesion in the pancreatic body and tail (d)

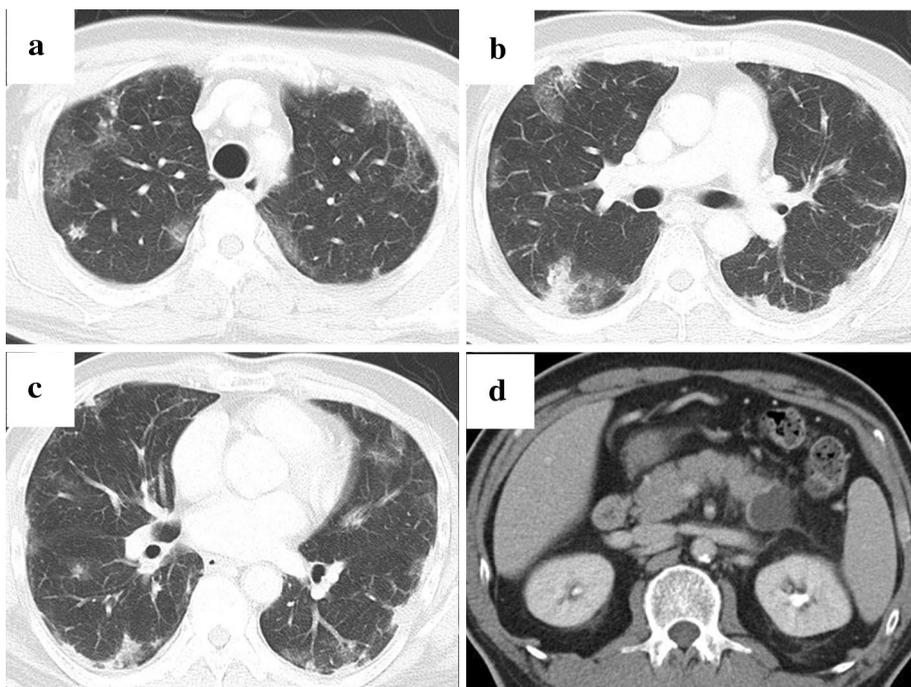
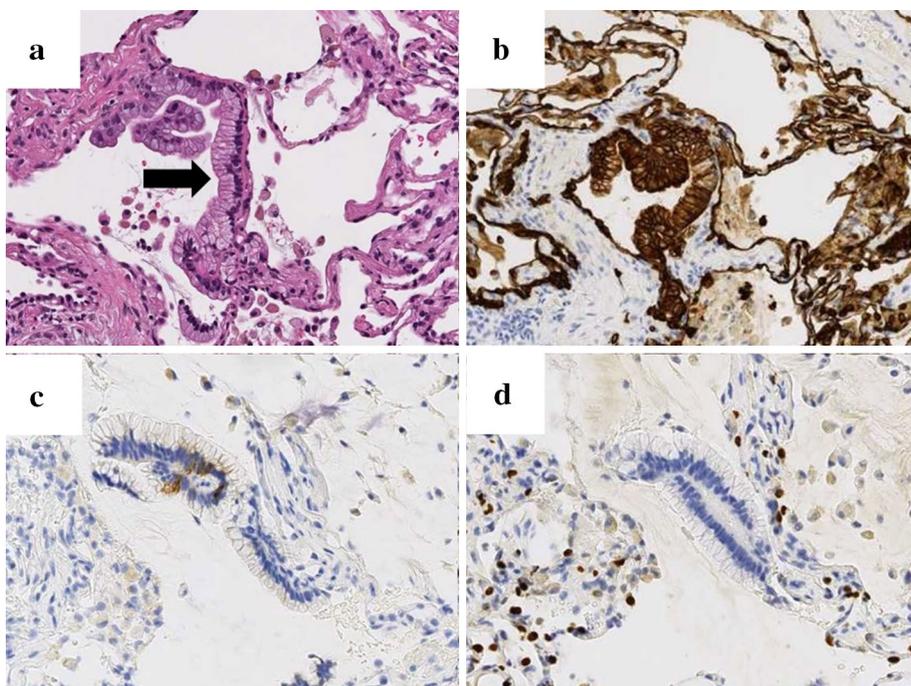


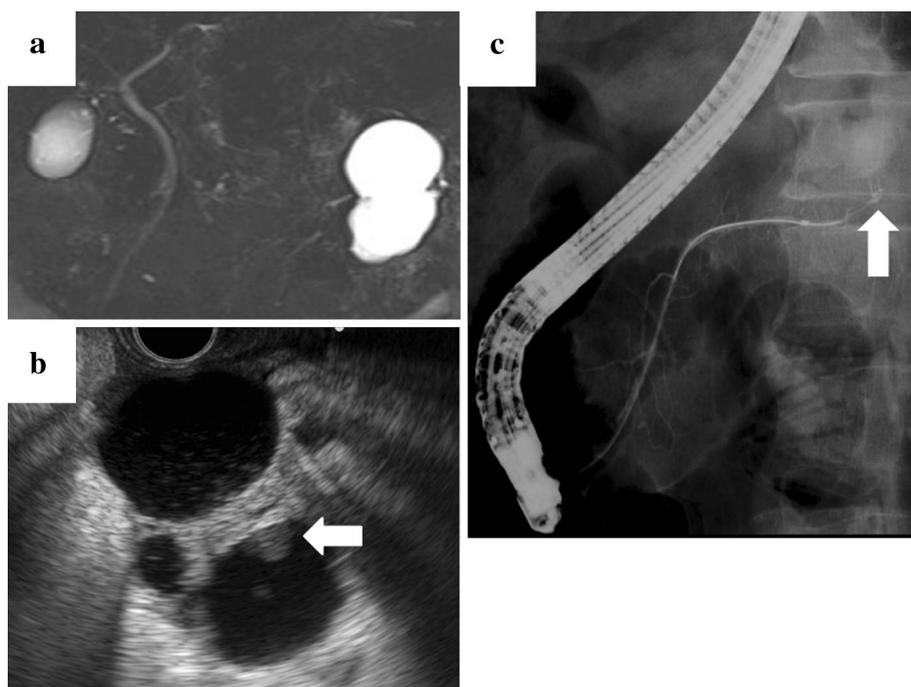
Fig. 2 Microscopic findings of lung tumor. (hematoxylin and eosin stain, 10×). Mucus-producing columnar epithelial cells with papillary hyperplasia replacing the alveolar epithelium were observed (arrow) (a). Immunohistochemical staining was positive for CK7 (b), and negative for CK20 (c) and TTF-1 (d)



gastrointestinal adenocarcinoma, and used CT features to classify lesions into 4 characteristic lepidic patterns: (a) air-space nodules; (b) parenchymal consolidation containing air bronchogram and/or showing angiogram sign; (c) focal or extensive ground-glass opacities; and (d) nodules with a “halo” sign. The presented case showed mixed findings of (b) and (c). Moreover, in their investigation, 6 (9.2%) of the

65 cases showed lepidic metastasis morphology, with the primary cancers as follows: pancreatic cancer in 3 cases, colon cancer in 2 cases, and duodenal cancer in 1 case. In addition, Mito et al. [3] reported a case of pancreatic cystadenocarcinoma with lepidic metastasis. In our case, the immunohistochemical staining of CK7/CK20 and the MUC staining pattern matched between the samples of lung and

Fig. 3 **a** Magnetic resonance cholangiopancreatography image. A cystic lesion suspected to be in continuity with the main pancreatic duct was seen in the pancreatic body and tail. **b** Endoscopic ultrasound image. A multilocular cyst 45×37 mm in size was seen in the pancreatic body and tail. Nodules were present in the interior (arrow), and thickening was seen in part of the wall. **c** Endoscopic retrograde cholangiopancreatography image. There was communication between the cystic lesion of the pancreatic body and tail and the main pancreatic duct (arrow). There was no dilatation of the main pancreatic duct



pancreatic juice. In addition, the CK7 positive/CK20 negative staining pattern is common in lung adenocarcinomas, however, even in pancreatic cancers, a similar staining pattern is seen in approximately 26% [4]. Moreover, MAC5AC was positive; regardless of the histological subtype of IPMN, this is a characteristic common to IPMNs [5]. As such, we concluded IPMC with pulmonary lepidic metastasis.

Cases of pulmonary lepidic metastasis from gastrointestinal cancers have also been reported previously; the frequency of pancreatic cancer is known to be relatively high [6]. Lepidic metastasis cases with air-space nodular appearance on CT imaging after surgery for cholangiocarcinoma have been detected relatively early. Surgical resection is then typically performed for the metastasis, with a

Fig. 4 In the pancreatic juice cytology, atypical cells with mucus and mucilaginous vacuoles in the cytoplasm were seen as a mild invagination (Papanicolaou stain, $40\times$) (**a**). Immunohistochemical staining was positive for CK7 (**b**) and negative for CK20 (**c**)

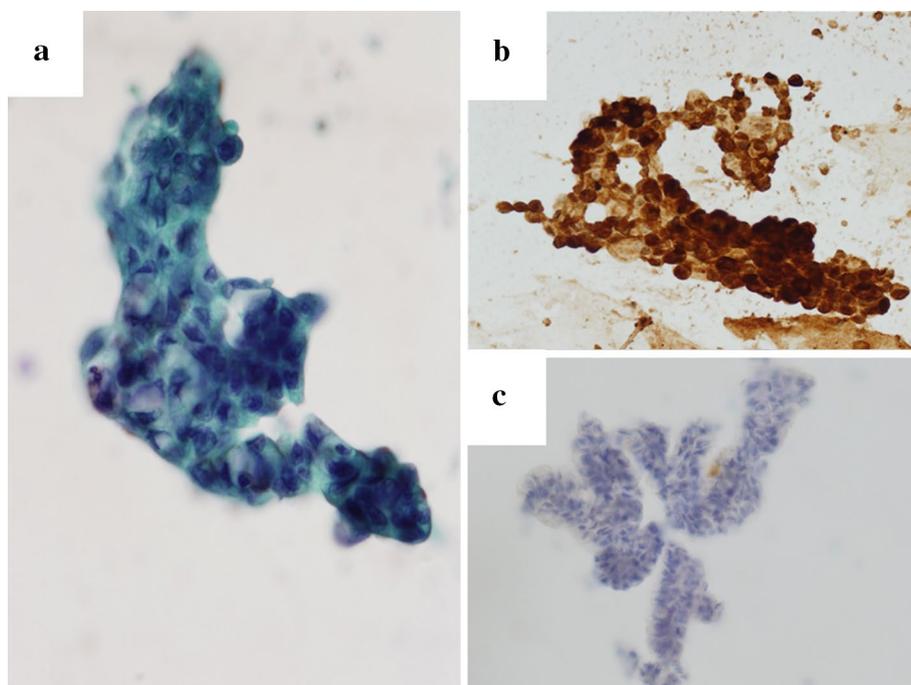
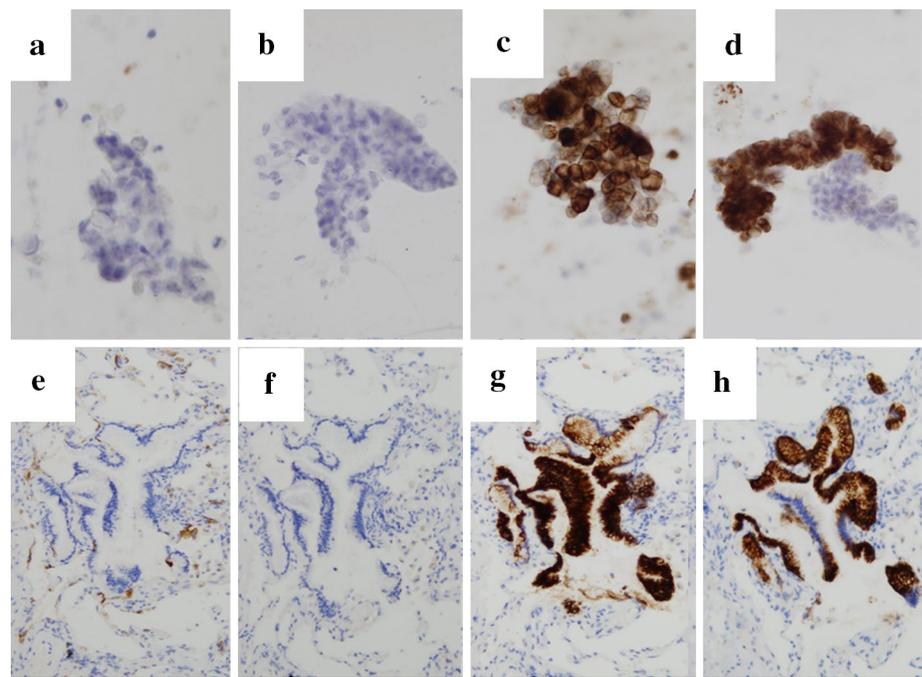


Fig. 5 Both pancreatic juice cytology and the lung tumor showed the same mucin (MUC) staining pattern: MUC1 (–) (a, e, respectively); MUC2 (–) (b, f, respectively); MUC5AC (++) (c, g, respectively); MUC6 (+) (d, h, respectively)



good outcome [7]. On the other hand, rapid progression to respiratory failure, as in our case, has also been reported [2, 8]. In patients with alveolar epithelial carcinoma, the formation of a bronchial fistula occurs in 6–21%; fistula formation may be involved in lepidic metastasis, with a mode of spread similar to that of alveolar epithelial cancer [2]. Moreover, obstruction due to the copious amount of metastasis-related mucus production and subsequent inflammatory reaction is highly likely to worsen respiratory failure [9]. In our case, these mechanisms were likely involved in triggering rapid respiratory failure.

When pneumonia-like infiltration that does not respond to antibiotics is encountered on imaging studies, metastasis from gastrointestinal carcinoma (especially mucinous carcinoma, such as pancreatic cancer) should be considered in the differential diagnosis, in addition to benign lung disease and primary lung tumor; close examination is required. In known IPMN/IPMC cases, as well as pancreatic carcinoma in general, routine surveillance chest CT imaging can detect lepidic metastasis early to allow surgical treatment before respiratory failure occurs. Although rare, pulmonary lepidic metastasis should be kept in consideration.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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