

# Refractory bronchorrhea and mucinous pleural effusion caused by lung metastasis of pancreatic cancer

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## Abstract

Our case indicates that when bronchorrhea and mucinous pleural effusion with pancreatic cancer are observed, bronchorrhea due to malignant disease should be taken into consideration and, bronchorrhea derived from not bronchial asthma but lung metastasis of pancreatic cancer could lead to be refractory.

## Title page:

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## Key Clinical Message:

Our case indicates that when bronchorrhea and mucinous pleural effusion with pancreatic cancer are observed, bronchorrhea due to malignant disease should be taken into consideration and, bronchorrhea derived from not bronchial asthma but lung metastasis of pancreatic cancer could lead to be refractory.

Key words: Bronchorrhea, Mucinous pleural effusion, Pancreatic tumor.

## (2)Text:

### Introduction:

Bronchorrhea is a clinical condition in which more than 100 ml of sputum is discharged in one day[1]. Massive amount of sputum leads to severe cough and continuous difficulty in expectoration, and daily life gets remarkably affected. Bronchial asthma, bronchioloalveolar adenocarcinoma, and chronic bronchitis are several causes of bronchorrhea. Reports of bronchorrhea caused by pulmonary metastases of pancreatic cancer are

rare. Our case was also accompanied by mucinous pleural effusion. Here, we describe a therapeutic course of pulmonary metastases of pancreatic cancer with bronchorrhea and mucinous pleural effusion.

#### Case Report:

**Case:** A 76-year-old man presented at our hospital in 2016 with a complaint of left back pain and sputum. Chest X ray showed pleural effusion on left lung and mediastinal displacement(Figure 1A).

Enhanced chest-abdominal computed tomography revealed a solid tumor and partial atelectasis, pleural effusion in the left lung, and a multiloculated cystic mass on the head of the pancreas(Figure 1B,1C). Fluorodeoxyglucose (FDG) accumulation was observed in the same location during PET-CT (Figure 1D, 1E). The sputum was faint white and viscous. The total volume of sputum in 24 hours was over 300 ml (Figure 2A). He was therefore diagnosed with bronchorrhea. According to a blood test, his white blood cell (WBC) count was relatively elevated. Hb, Plt, liver enzyme, and AMY levels were normal.CA-19-9,sIL2receptor, and HbA1c levels were elevated(Table 1).

Although thoracentesis of the left lung was attempted, pleural effusion was not aspirated because of excessive viscous.

The patient experienced dyspnea and had a large amount of left pleural effusion.Chest drainage was performed. Biochemical assessment of pleural effusion could not be performed because of excessive viscous.

The cytodiagnosis of pleural effusion showed adenocarcinoma, and pancreatic cancer and lung cancer were suspected. For the purpose of diagnosis, transbronchial lung biopsy was performed on the lower left lobe of the lung.Amount of viscous sputum was confirmed inbronchial lumen (Figure 2B,2C). Hematoxylin–eosin staining revealed adenocarcinoma, which showed progression from papillary and mucosal fluid production. On immunostaining, cytokeratin 7, MUC5AC, MUC6, CA19-9, and mesothelin were positive, while napsin A and TTF-1 were negative (Fig3). Epidermal growth factor receptor mutations and the ALK fusion gene were also negative. Bacterial culture of the bronchoalveolar lavage was negative. Therefore, the diagnosis was believed to be metastasis of invasive pancreatic cancer after a course of therapy upon admission. Although chest drainage was performed,over 1000 ml of pleural effusion was drained each day. Although pleurodesis was performed twice, the pleural effusion did not decrease. A trend toward dehydration appeared and was accompanied by drainage. In addition, as a systemic chemotherapy, gemcitabine monotherapy was administered, but the pleural effusion did not decrease. Afterward, the patient experienced bacteremia, and his dyspnea worsened.

This patient exhibited a poor performance status and he died of his illness. The bronchorrhea did not improve during the entire course of his illness.

#### Discussion:

Bronchorrhea is a condition in which a large amount of sputum is discharged (over 100 ml per day). Simply, this term is used to describe airway hypersecretion with a large volume of sputum<sup>[1]</sup>. Bronchorrhea is thought to be derived from malignant disease in 5%–20% of the cases<sup>[2]</sup>.In non-small cell lung carcinoma, the frequency of bronchorrhea is less than 1%. It is well known that bronchorrhea is a characteristic of alveolar epithelial cancer and therefore the frequency of bronchorrhea is 6%–24% in these cancers<sup>[1]</sup>. In terms of lung cancer and metastatic lung cancer, bronchorrhea has only been reported in the adenocarcinoma type. Furthermore, it was reported that cultured cells derived from lung tumors exhibited exocrine function.

As a result, secretion hyperactivity of epithelial cell-derived tumor cells is thought to be a cause of bronchorrhea<sup>[3]</sup>. Bronchorrhea with colon cancer, cervical cancer, and pancreatic cancer, such as in our case, has also been reported <sup>[4]</sup> <sup>[5]</sup> <sup>[6]</sup>. Our case had symptoms characteristic of mucinous pleural effusion. Because mucinous pleural effusion with intrathoracic progression of pseudomyxoma peritonei is relatively common, lung adenocarcinoma is rarely associated with mucinous pleural effusion. In this case, it is believed that direct invasion of the pleura by the lung cancer led to the mucinous pleural effusion. In our case, the mucinous pleural effusion was thought to be derived from lung metastasis of pancreatic cancer.

With regard to the treatment of the tumor-induced bronchorrhea, the decrease in bronchorrhea after inhalation of indomethacin in alveolar epithelial cancer has been reported<sup>[7]</sup>. Moreover, it has been reported that epidermal growth factor controls mucin secretion in airway epithelium in alveolar epithelial cancer. Presumably, epidermal growth factor receptor directly suppresses the secretory function of tumors<sup>[8]</sup>. In the lung cancer experiment, it was demonstrated that gefitinib exhibited anti-tumor effects and that it directly suppressed exocrine function. In our case, because of the difficulty in internal use and lower performance status, this patient had no choice except anticancer drug infusion. Unfortunately, the anticancer treatment was refractory to bronchorrhea and mucinous pleural effusion. Characteristically, the dehydration trend appeared to be accompanied by drainage. In conclusion, we experienced a case of bronchorrhea and mucinous pleural effusion derived from lung metastasis of pancreatic cancer. The anticancer treatment was refractory to bronchorrhea and the mucinous pleural effusion.

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The authors declare that they have no conflicts of interest (COI).

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Figure legends:

Figure 1. A chest X-ray showed pleural effusion in the left lung (A). Enhanced chest-abdominal computed tomography showed the presence of a solid tumor and partial atelectasis as well as pleural effusion in the left lung (B, C). FDG accumulation was observed in the same location during PET-CT (D, E).

Table 1. Laboratory findings on admission.

Figure 2. The total volume of sputum over 24 hours was over 300 ml (A).

The properties of the sputum were endobronchially observed during bronchoscopic examination (B, C).

Figure 3. On immunostaining, cytokeratin 7, MUC5AC, MUC6, CA19-9, and mesothelin were positive, whereas napsin A and TTF-1 were negative.

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