

[CASE REPORT]

Primary Pulmonary Colloid Adenocarcinoma: How Can We Obtain a Precise Diagnosis?

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Abstract:

A 76-year-old asymptomatic man was found to have a mass in the right lower lung field. Although the presence of a mucinous component in the majority of the tumor was shown by magnetic resonance imaging, the presence of cancer cells was suspected by contrast enhancement on computed tomography (CT) and based on the partial accumulation in the marginal regions of the tumor on fluorodeoxyglucose-positron emission tomography (FDG-PET). A transbronchial lung biopsy was non-diagnostic, but resection of the mass resulted in a diagnosis of colloid adenocarcinoma. The findings from combined contrast CT and FDG-PET may raise the suspicion of colloid adenocarcinoma and prompt the consideration of surgical resection.

Key words: colloid adenocarcinoma, lung cancer, contrast computed tomography (CT), fluorodeoxyglucose-positron emission tomography (FDG-PET)

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Introduction

Colloid adenocarcinoma, which is classified as a variant of invasive adenocarcinoma, is histologically characterized by the presence of abundant mucus in the tumor (1). Colloid adenocarcinoma is extremely rare, accounting for 0.24% of all lung cancers (2). It is recognized as a mass with poor contrast enhancement on computed tomography (CT); whereas the findings on magnetic resonance image (MRI) are characterized by low intensity on T1-weighted imaging (WI) and high intensity on T2WI, which might be from the mucus component of the tumor (3). However, CT and MRI findings frequently cannot discriminate between benignity and malignancy.

We herein report a rare case of colloid adenocarcinoma that was suspected of being mucinous adenocarcinoma by a combination of contrast CT and fluorodeoxyglucose-positron emission tomography (FDG-PET).

Case Report

A 76-year-old Japanese man visited our hospital because of a pulmonary mass that was detected on chest radiograph during an annual health examination. He did not have any respiratory symptoms, such as cough, sputum production, or dyspnea, but he had noted a weight loss of 2.5 kg within the past 2 months. He had a history of pulmonary tuberculosis at 20 years of age. He had a 46-pack-year smoking history and had been engaged in shipbuilding work for 45 years.

A physical examination showed a body temperature of 36.3°C, no superficial lymphadenopathies, and the absence of crackles on chest auscultation. Chest radiography showed a mass in the right lower lung field (Fig. 1a). His laboratory findings showed 4,400/ μ L white blood cells, 3.2 g/dL albumin, 20.2 mg/dL blood urea nitrogen, 1.07 mg/dL creatinine, 9.4 ng/mL carcinoembryonic antigen (CEA), and 2.52 ng/mL cytokeratin 19 fragment (CYFRA 21-1). Other

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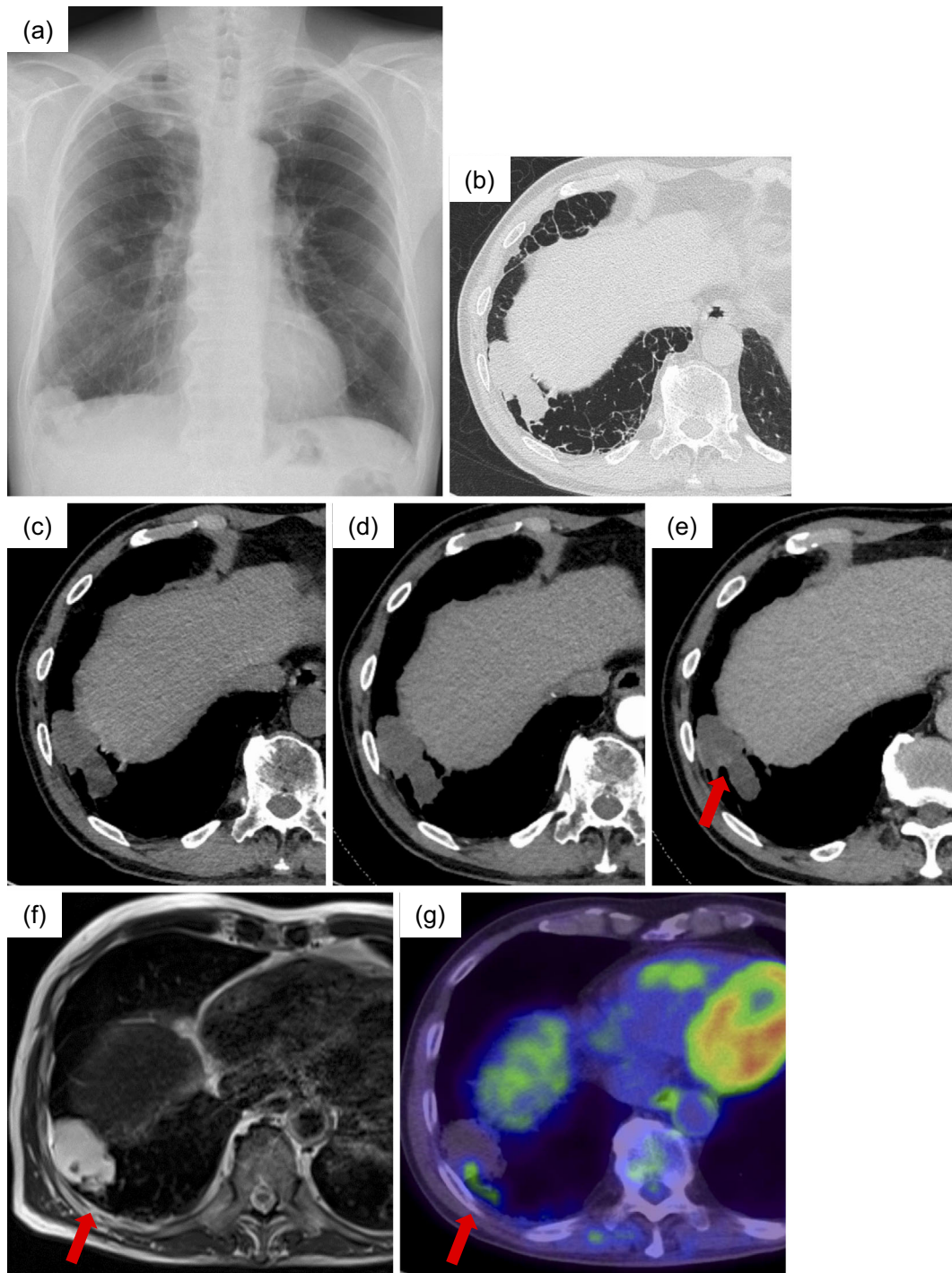


Figure 1. Radiologic findings in a 76-year-old man with primary pulmonary colloid adenocarcinoma. (a) Chest radiograph shows a mass in the right lower lung field. Chest CT reveals a 55-mm lobulated mass (b) on the lung window. Contrast CT on the mediastinal window shows a low-attenuation mass in (c) the non-contrast and (d) arterial phases and (e) slight septal enhancement (red arrow) only in a limited area in the delayed phase. (f) MRI shows a high-intensity mass on T2-weighted imaging with a low-intensity area in the marginal region (red arrow). (g) FDG-PET shows a low accumulation in the pulmonary mass with a high accumulation in the marginal region (red arrow).

examinations, including a urinalysis, coagulation profile, and arterial blood gas, were within the normal range. Chest CT showed a cystic mass lesion, measuring 55 mm in diameter, in the right lower lobe on the background of extensive emphysematous lesions (Fig. 1b). The mass showed low attenuation on non-contrast CT (Fig. 1c). Dynamic CT showed a

delayed slight septal enhancement only in a limited area of the mass (Fig. 1d and e). No hilar or mediastinal lymphadenopathies were seen. On chest MRI, the mass was seen as a multilobular cystic mass lesion with a focal low-intensity area on T2WI, which corresponded to the region with delayed enhancement on CT (Fig. 1f). FDG-PET revealed a

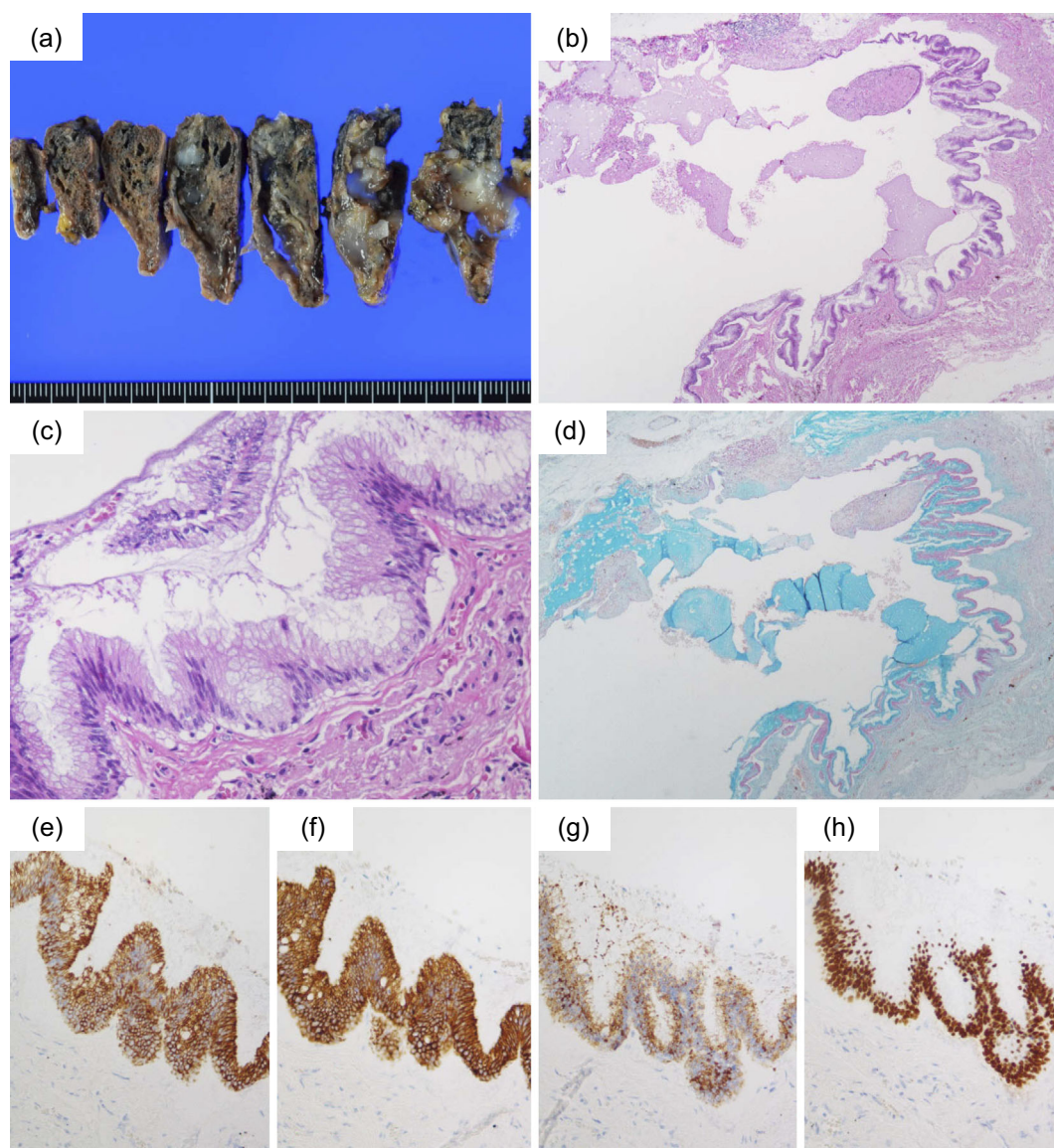


Figure 2. Pathological findings of the resected specimen in a 76-year-old man with primary pulmonary colloid adenocarcinoma. (a) The cut surface of the resected specimen shows a cystic lesion with pooling of mucin. (b) The cyst wall is covered by tumor cells producing abundant mucin [Hematoxylin and Eosin (H&E) staining, $\times 20$]. (c) The tumor cells have cytoplasmic mucin and significant nuclear atypia, which indicate adenocarcinoma (H&E staining, $\times 200$). (d) Both the cytoplasmic and pooled mucin contents are positive on Alcian blue staining ($\times 20$). Photographs of the immunohistochemistry staining ($\times 200$) show tumor cells that are positive for (e) CK7, (f) CK20, (g) MUC2, and (h) CDX2. There is abundant mucus content in the mass (H&E staining, $\times 40$). (b) Lining epithelial tumor cells (H&E staining, $\times 400$). (c) The abundant mucus also stained positive with Alcian blue ($\times 40$). Immunohistochemistry examinations showed positive staining with (d) MUC2, (e) CK20, and (f) CDX2 ($\times 400$).

minimal accumulation in most parts of the pulmonary mass, but a relatively high accumulation was observed in a focal region, with a maximum standardized uptake value (SUV max) of 2.14 in the early phase and 2.17 in the delayed phase (Fig. 1g). The patient underwent a transbronchial lung biopsy (TBLB), which revealed no malignant cells. Since the possibility of lung cancer with mucinous features could not be excluded, right lower lobectomy and regional lymph node dissection were performed. For the differential diagnosis, we considered a primary mucus-producing tumor, metas-

tatic tumor from gastrointestinal tract, and a fungal infection.

On a pathological examination, the cut surface of the resected specimen showed a cystic lesion with significant mucin pooling (Fig. 2a). Histologically, the cyst wall was partly covered by tumor cells with nuclear atypia and abundant mucin (Fig. 2b and c), which was positive on Alcian blue staining (Fig. 2d). From the histological findings, colloid adenocarcinoma, invasive mucinous adenocarcinoma, enteric adenocarcinoma, and metastatic mucinous adenocarcinoma

from the gastrointestinal tract were initially considered as pathological differential diagnoses. Immunohistochemically, these tumor cells were positive for CK7, CK20, MUC2, and CDX2 (Fig. 2e-h); these characteristics were consistent with colloid adenocarcinoma. The immunoprofile of colloid adenocarcinoma has been reported to overlap with that of enteric adenocarcinoma or metastatic mucinous adenocarcinoma from the gastrointestinal tract (4). However, we considered that the findings of abundant pooling of extracellular mucin and scant tumor cells were typical histological features of colloid adenocarcinoma. The possibility of metastatic mucinous adenocarcinoma from the gastrointestinal tract was ruled out based on the absence of any gastrointestinal tumor lesions on a postoperative examination.

Given these findings, he was ultimately diagnosed with primary pulmonary colloid adenocarcinoma, T3N0M0, stage IIB. No epidermal growth factor receptor (EGFR) or KRAS mutations were detected in the present case. At one year after the operation, he remained free from any lung cancer recurrence.

Discussion

In the latest World Health Organization (WHO) classification of lung and pleural tumors, the diagnosis of colloid adenocarcinoma was based on the findings of neoplastic cells floating in large pools of mucus and focally lining the alveolar spaces (1, 5). In a previous case series, 13 patients (7 men and 6 women) with pulmonary colloid adenocarcinoma and a mean age of 64.5 years (range, 50-79 years) showed presenting symptoms of cough (5 cases), hemoptysis (2 cases), and chest pain (1 case) (2). Similar to our case, five cases in that report were asymptomatic and detected on a routine health examination.

Colloid adenocarcinoma tumors have been described as well-defined nodules or masses in the peripheral lung field, with sizes ranging from 1.8 to 6.5 cm (4). Previous reports have described findings of low attenuation and poor enhancement on contrast CT, low intensity on T1WI, and high intensity on T2WI on MRI, with a low uptake on FDG-PET; these findings may be attributed to the abundant mucin occupying the majority of the tumor (3, 6, 7). However, these findings were insufficient for a definitive diagnosis. Furthermore, as shown in the present case, contrast enhancement on CT and a high focal accumulation on FDG-PET can also suggest the presence of colloid adenocarcinoma cells. In our case, the margin of the tumor was smooth, and no invasive tendency was noted on CT. However, it should be noted that the margin of the tumor had likely been modified by the severe emphysematous changes.

In the present case, the pathological findings were characterized by tumor cells floating in large pools of mucus and focally lining the alveolar spaces, with positive immunohistochemistry staining for MUC2, CK20 and CDX2. Of note, a previous study on 13 patients with colloid adenocarcinoma showed that the prognosis tended to be better in patients

with CDX2-/MUC2-positive expression than in those with CDX2-/MUC2-negative expression (2).

Pulmonary colloid adenocarcinoma is difficult to diagnose by a TBLB because of the abundant amount of mucus and few malignant cells in the tumor, and most cases require surgical resection for the diagnosis. Therefore, the preoperative assessment of the probability of malignancy is important for making decisions regarding surgery, and obtaining the precise diagnosis of a pulmonary mass may eventually require surgery when radiologic examinations raise the suspicion of colloid adenocarcinoma. In the present case, the suggestive contrast CT and FDG-PET findings in the marginal region of the tumor were useful for obtaining a preoperative diagnosis. Russell et al. estimated the 5-year survival to be 51% in 9 patients with pulmonary colloid adenocarcinoma who underwent surgical resection; that study included 1 stage IA case, 3 stage IB cases, 1 stage IIA cases, and 4 stage III cases (8). Of note, several papers have reported lymphogenous and hematogenous metastases in pulmonary colloid adenocarcinoma (3, 9).

In conclusion, physicians should be aware of the clinical presentation of colloid adenocarcinoma and should consider surgical resection of pulmonary masses with a large mucinous component and findings suggestive of malignant cells on radiologic examinations, such as contrast CT and FDG-PET.

Written informed consent was obtained from the patient for the publication of this case report.

The authors state that they have no Conflict of Interest (COI).

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