Official Case Reports Journal of the Asian Pacific Society of Respirology
Respirology Case Reports
OPEN ACCESS

Metastatic pancreatic carcinoma masquerading as cystic lung disease: a rare presentation

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Keywords
Air trapping, cystic lung disease, lepidic growth, pancreatic adenocarcinoma.

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Received: 21 March 2017; Revised: 8 May 2017; Accepted: 11 May 2017; Associate Editor: Conroy Wong.

***Respirology Case Reports*, 5 (5), 2017, e00246**

doi: 10.1002/rcr2.246

Abstract

This 52-year-old male ex-smoker presented with a six-month history of progressive breathlessness and weight loss. He deteriorated acutely, and was admitted with severe type 1 respiratory failure. Apart from diffuse coarse crackles on chest auscultation, physical examination was unremarkable. High-resolution computed tomography (HRCT) showed diffuse cystic changes throughout the lungs. A diagnosis of pulmonary Langerhans cell histiocytosis (PLCH) was considered. Further workup identified a coincidental pancreatic lesion of uncertain significance, which remained indeterminate on magnetic resonance imaging (MRI) and on positron emission tomography (PET). Transbronchial biopsy revealed enteric differentiated adenocarcinoma exhibiting lepidic spread, and autopsy later confirmed primary pancreatic malignancy. This case demonstrates that metastatic pancreatic malignancy can present with severe respiratory failure and masquerade as cystic lung disease.

Introduction

This case report describes a patient with pancreatic adenocarcinoma with lepidic pulmonary metastases presenting with cystic lung disease and severe respiratory failure, which to our knowledge has not previously been described in the literature.

Case Report

A 52-year-old male living in a rural area was interviewed via telehealth, with a six-month history of progressive dyspnoea, 20 kg weight loss, and recent minimally productive cough with clear sputum. His exercise tolerance was reduced but he could still walk 1–2 km at his own pace. Past medical history was unremarkable, apart from a 35-pack year smoking history and heavy alcohol use, both of which ceased four months prior to presentation. Occupational exposure included cement and concrete. High-resolution computed tomography (HRCT) performed one month prior to the interview demonstrated multiple pulmonary cysts, nodules with a stellate pattern, and preserved lung volumes (Fig. 1). A low-density lesion in the head of the pancreas was seen and which, on subsequent cross-sectional abdominal imaging with magnetic resonance cholangiopancreatography (MRCP), could not be further characterized as a benign or malignant pancreatic process.

A provisional diagnosis of pulmonary Langerhans cell histiocytosis (PLCH) was considered based on the smoking history and HRCT findings. Malignancy required exclusion; the pulmonary infiltrates were, however, atypical for metastatic malignancy. In view of the patient's age, wishes and the potential of a disease treatable with transplantation, urgent investigations were organized.

However, the patient was transferred urgently to a hospital by Flying Doctor one week later after an acute deterioration with severe breathlessness and type 1 respiratory failure requiring 25 L/min oxygen to maintain his SaO_2 above 90%. His cough was unchanged, he was afebrile,

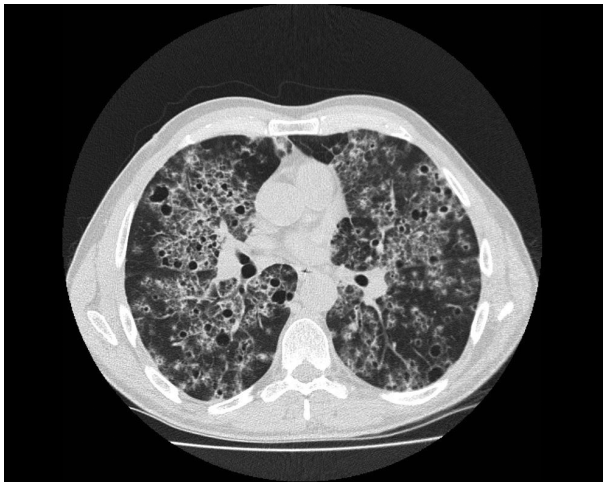

Figure 1. Initial high-resolution computed tomography (HRCT) showed multiple cysts and nodules with a stellate pattern suggestive of pulmonary Langerhans cell histiocytosis.

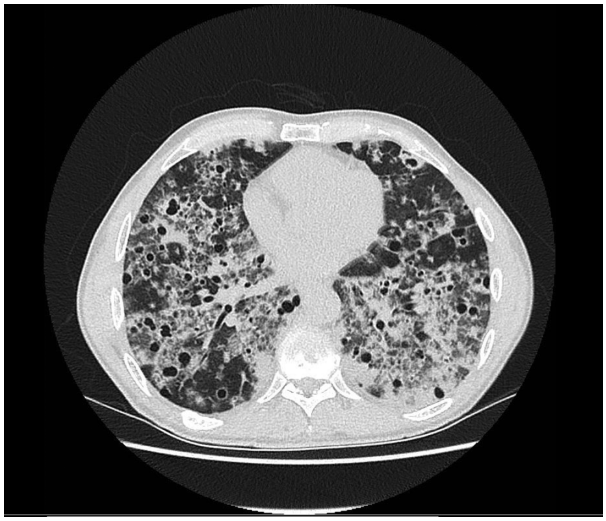

Figure 2. Subsequent high-resolution computed tomography (HRCT) showed extensive ground-glass and consolidation on the background of multiple lung cysts.

and the only abnormal finding on examination was widespread crackles on chest auscultation. Apart from a mild leucocytosis (white cell count 13.30×10^9/L (normal $4.00 - 11.00 \times 10^9$/L)) and a raised C-reactive protein (213 mg/L (normal <10 mg/L)) which rapidly normalized, blood work including autoimmune markers were non-diagnostic. There was no evidence of infection on sputum microscopy and culture. Sputum cytology showed atypical glandular cells of uncertain significance. Carcinoembryonic antigen was normal (2 ng/mL (normal <2.5 ng/mL)) and carbohydrate antigen 19–9 mildly elevated at 240 (normal 37 kU/L).

Repeat HRCT revealed marked deterioration with extensive ground-glass infiltrates and dense consolidation on the background of the cystic lung disease (Fig. 2). Positron emission tomography showed patchy non-uniform fluorodeoxyglucose (FDG) avidity in the lungs that was not high grade, suggestive of inflammation or patchy infection but atypical for metastatic malignancy. The only high-grade uptake was in muscles, in particular the inter-costals, reflecting his significant work of breathing. The ill-defined hypodense lesion in the head of the pancreas showed low-grade uptake and there was no FDG avid lymphadenopathy.

Broad-spectrum antibiotics were commenced to cover the possibility of a superadded infection, but the patient continued to deteriorate with increasing oxygen requirements up to 40 L/min (FiO_2 80%). Pulsed methylprednisolone was administered which resulted in a moderate improvement in breathlessness with reduced oxygen requirements down to 15 L/min, which facilitated bronchoscopic examination.

Transbronchial biopsy of the right lower lobe showed a well-differentiated mucinous adenocarcinoma with enteric differentiation and lepidic spread. Microscopy and culture showed no evidence of infection. After discussion with the patient, treatment was withdrawn and with palliative management, he died 4 h later.

Autopsy examination identified an invasive ductal adenocarcinoma in the head of the pancreas. Although there were some background emphysematous changes in the lungs, the predominant pattern was extensive parenchymal involvement by moderately differentiated adenocarcinoma in a lepidic growth pattern, showing similar cytomorphology and immunohistochemical profile to the pancreatic primary site (cytokeratin (CK) 7, CK19, CDX2, CK20 positive, and thyroid transcription factor 1 (TTF1) negative). The cut surface of each lung demonstrated abundant mucinous material, pooling in innumerable cystic spaces ranging from 5 to 10 mm in diameter. Where there was wall-to-wall mucin and some adenocarcinoma glands, air-trapping was seen creating small air filled cysts, some of which were lined by mucin. Peribronchiolar lymphoid aggregates did not obstruct airways although most bronchioles were filled with mucin. There were no features of infection and there were no discrete solid lesions in the lungs.

Discussion

Most cases of pulmonary metastases from pancreatic adenocarcinoma are nodular with well-demarcated or

irregular/spiculated margins. Less commonly, they may cause lymphangitis carcinomatosis [1]. Rarely, lung metastases from pancreatic adenocarcinoma may grow in a lepidic pattern, where they replace alveolar epithelial cell and produce an abundance of mucin which results in radiological patterns including air-space nodules, parenchymal consolidation, focal or extensive ground glass opacity, and nodules with a halo sign [2]. In this case, diagnosis was hampered because HRCT initially showed lung cysts, and subsequently added consolidation, which to our knowledge has not been correlated with any pancreatic metastasis growth pattern.

We hypothesize that the air filled cystic change seen on HRCT and at autopsy represented air trapping by surrounding mucin. Infiltration and obstruction of lymphatics and small airways is described in lymphangioleiomyomatosis and thought to cause cysts through a "ball-valve" effect [3]. While lymphatic and small airway obstruction was not evident at autopsy in this case, obstruction by mucin filled alveoli may have contributed to a similar effect. An alternate explanation could be "pseudocavitation," whereby the central bubble-like low attenuating regions within pulmonary nodules represented patent small airways or distended alveolar spaces under traction from malignant cells growing along alveolar walls [4].

We attribute the patient's acute clinical deterioration to aggressive lepidic tumour growth with rapid inter-alveolar tumour transition and abundant pooling of mucinous material within the lungs. This correlates with the dense infiltrate and air space opacification seen on the second HRCT (Fig. 2), and findings at autopsy. Such progression would be sufficient to worsen gas exchange and increase work of breathing. Interestingly, despite the abundance of mucin found at autopsy, the patient had surprisingly little sputum production.

Although infection or significant inflammation secondary to the tumour may have contributed to the marked deterioration and worsening consolidation, apart from an elevated C-reactive protein on admission (for which there was no recent comparison and which rapidly fell to normal) there was no other clinical, microbiological, or pathological evidence during life or at autopsy to support this. Indeed, there was no clinical improvement with broad-spectrum antibiotics. In light of this, we cannot explain the elevated CRP that rapidly normalized in the absence of clinically effective treatment.

The significance of the mottled FDG avidity of the lungs on positron emission tomography (PET) is not clear. The role of PET in the diagnosis of pancreatic cancer is unclear with significant false positives and negatives [5]. The improved oxygenation following methylprednisolone therapy may have related to decreased oedema and secretions such as seen when used with lymphangitis carcinomatosis [6] or to the anti-inflammatory and tumour angiogenesis suppressive effects of corticosteroids [7].

In summary, we encountered a case of lepidic metastasis from adenocarcinoma of pancreas that at initial presentation, clinically and radiologically resembled cystic lung disease. This case, in a man who presented late with severe respiratory failure and unusual clinical and radiological presentation and subsequent equally unusual pathology, posed a diagnostic conundrum with possibilities ranging from treatable to terminal. Atypical pulmonary metastasis should be included in the differential for multiple cystic lung disease.

Disclosure Statements

No conflict of interest declared.
Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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