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THE GREAT MIMICKER: PULMONARY ADENOCARCINOMA WITH INTERSTITIAL LUNG DISEASE-LIKE PRESENTATION

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ABSTRACT

A 52-year-old female with a significant smoking history and newly diagnosed chronic obstructive pulmonary disease (COPD) presented to the emergency department with shortness of breath and blood-tinged sputum. Following a prior hospitalization for a COPD exacerbation, imaging revealed atypical features prompting autoimmune evaluations that were negative. A decline in pulmonary function led to admission for bronchoscopy, which revealed invasive mucinous adenocarcinoma (IMA). This case underscores the diagnostic challenges of IMA, which can mimic interstitial lung disease (ILD), resulting in delayed diagnosis and mismanagement. The high false-negative rate of bronchoalveolar lavage cytology in mucinous adenocarcinoma highlights the need for prompt tissue sampling in similar presentations for timely intervention.

KEYWORDS

Interstitial lung disease (ILD), invasive mucinous adenocarcinoma (IMA), bronchoalveolar lavage (BAL), biopsy, pulmonary function test (PFT)

LEARNING POINTS

- Invasive mucinous adenocarcinoma, a rare subtype of lung adenocarcinoma, often presents with discrete tumours rather than diffuse interstitial involvement, leading to difficulties in diagnosis, which can mimic benign lung conditions.
- Initial imaging findings such as cystic changes and ground-glass opacities may suggest interstitial lung disease, potentially resulting in an unnecessary autoimmune workup. This emphasizes the importance of considering lung cancer in patients with significant smoking history and worsening respiratory symptoms.
- Bronchoalveolar lavage cytology may fail to identify malignant cells in cases of mucinous adenocarcinoma due to its lepidic growth pattern. This highlights the need for histopathological confirmation through biopsy to avoid false negatives and ensure appropriate management.

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INTRODUCTION

Lung cancer remains a significant global health challenge, with lung adenocarcinoma being the most prevalent subtype of non-small cell lung cancer (NSCLC), accounting for approximately 40% of all lung cancer cases[1]. The clinical presentation of lung adenocarcinoma is often varied, frequently mimicking benign or inflammatory lung conditions. This can lead to delays in diagnosis and treatment, particularly in cases involving the rare subtype known as invasive mucinous adenocarcinoma (IMA). Unlike more typical solid or acinar variants, IMA often exhibits a diffuse, interstitial-like involvement in the lungs rather than forming distinct tumours. The diagnostic challenges posed by IMA are exemplified in patients with a significant smoking history or worsening respiratory symptoms, such as decreased oxygen requirements and atypical interstitial lung disease (ILD) patterns. Initial imaging studies may reveal scattered cystic changes, ground-glass opacities, and interstitial thickening, which can easily lead to an autoimmune workup that may return negative. This scenario illustrates a common predicament in clinical practice, where the resemblance of IMA to conditions like cryptogenic organizing pneumonia or nonspecific interstitial pneumonia complicates early diagnosis and management. As observed in our case study, there is a critical need for early tissue sampling in patients presenting with these atypical ILD patterns. The limitations of bronchoalveolar lavage (BAL) in identifying malignant cells in IMA further contribute to the challenges in timely and accurate diagnosis. With BAL cytology having a notable false-negative rate, histopathological confirmation through biopsy often becomes necessary. Understanding the distinct growth patterns and presentation of invasive mucinous adenocarcinoma is essential in refining diagnostic approaches and improving outcomes for patients presenting with respiratory symptoms.

CASE DESCRIPTION

A 52-year-old female with a history of newly diagnosed chronic obstructive pulmonary disease (COPD), a 30 pack-year smoking history, and multiple allergies, including Ragweed, presented to the emergency department complaining of shortness of breath and cough with blood-tinged sputum production. She was admitted a month ago when she was treated for COPD exacerbation secondary to flu with oseltamivir, dexamethasone, and antibiotics, and was discharged on 2 l O_2, which was a new oxygen requirement. She had also reported blood-tinged sputum production. At that time, computed tomography angiography (CTA) of the chest was performed, which showed diffusely scattered cysts and ground glass densities in the lungs suspicious for interstitial lung disease (ILD) *(Fig. 1)*; therefore, she was tested for anti-neutrophil antibodies, rheumatoid factor, and SSA/SSB antibodies to rule out causes of ILD, which came back negative. Of note, the patient used to follow with a rheumatologist in the past for suspicion of moderate arthritis.

Plan at that time was to repeat chest computed tomography (CT) scan and pulmonary function tests (PFTs) as an outpatient after 6 weeks post-recovery. The patient then followed up in the pulmonologist clinic after around a month due to worsening shortness of breath post-discharge along with continued blood-streaked sputum when she was found to have a worsening O_2 requirement with ambulation, up to 4 l along with severe reduction in diffusion capacity on PFTs. She was then advised to be admitted to the hospital to consider bronchoscopy with biopsy for further evaluation. On presentation, patient was afebrile with no leucocytosis, on examination decreased bilateral breath sounds with fine crackles in the bibasilar region. Chest X-ray with bilateral opacities with slight worsening in the right lower lobe *(Fig. 2)*. The patient was admitted with the provisional diagnosis of ILD with the plan for bronchoscopy with biopsies. She saturated in 4 l via nasal cannula (goal SpO_2 88-90%) and continued to report dyspnoea and blood-streaked sputum. She reported that her dyspnoea worsened since she was diagnosed with coronavirus disease 5 months ago. She



Figure 1. Computed tomography angiography scan of the chest, a month prior, showing diffusely scattered cysts and ground-glass densities.



Figure 2. Chest X-ray during current admission showing worsening bilateral interstitial infiltrates 03/11/2025.

worked as a hairdresser and reported occasional exposure to fumes and hair dyes. She also reported that she has 3 cats and 1 dog, along with 2 parakeet birds. She underwent fluoroscopy-guided bronchoscopy along with BAL of the right-middle lobe (RML) and the left-upper lobe (LUL) and transbronchial biopsy of the RML *(Fig. 3)*. BAL samples were tested for cell counts which was predominantly 75% macrophages, bacterial/fungal/ acid-fast bacillus cultures with no growth, along with aspergillosis which was negative. Cytology showed no evidence of malignant cells, however the biopsy showed proliferation of atypical mucinous tall columnar cells predominantly in a lipidic growth pattern with focal papillary architecture, with immunohistochemical stains diffusely positive for CK7 and focal stating for CK20 and negative for TTF-1, Napsin A and CDX2, findings most consistent with invasive mucinous adenocarcinoma. Adenocarcinoma usually presents as a peripheral nodule and rarely presents as interstitial growth, which is the case here.

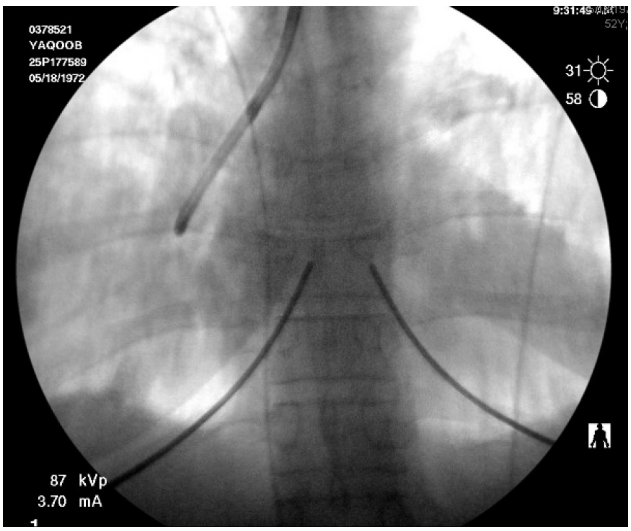


Figure 3. Transbronchial bronchoscopy 03/12/2025.

DISCUSSION

Lung adenocarcinoma is a prevalent subtype of NSCLC, which accounts for approximately 40% of all lung cancers[1]. Lung adenocarcinoma's clinical presentation is highly variable often mimicking benign or inflammatory lung conditions which can result in delayed diagnosis and treatment[2]. Our case exemplifies the diagnostic challenge posed by IMA which is a rare subtype that, unlike the more typical solid or acinar variants, frequently exhibits diffuse, interstitial-like involvement rather than forming discrete tumours. Our case emphasizes the need for early tissue sampling in patients with atypical ILD patterns among the population with significant smoking history or worsening oxygen requirements. The initial imaging findings in our patient, scattered cystic changes, ground-glass opacities, and interstitial thickening which strongly suggested ILD, can lead to an autoimmune workup that ultimately returned negative. This scenario is not uncommon as IMA frequently presents as multifocal consolidations, reticular opacities, or ground-glass densities that closely resemble cryptogenic organizing pneumonia or nonspecific interstitial pneumonia[3]. Diagnostic overlap results in inappropriate early management with corticosteroids or immunosuppressants, as seen in our case, which may transiently alleviate symptoms while allowing tumour progression. Fluoroscopy-guided bronchoscopy with BAL and transbronchial biopsy was performed due to the patient's worsening hypoxia and persistent blood-streaked sputum. BAL cytology failed to identify malignant cells as a well-documented limitation in mucinous adenocarcinoma[4,5]. This is due to the lepidic (non-invasive) growth pattern of IMA which results in malignant cells being widely dispersed within the alveoli rather than forming compact tumour masses. Previous studies indicate BAL cytology yields a false-negative rate of up to 30% in cases of mucinous adenocarcinoma, which may require histopathological confirmation through biopsy. Histological examination revealed proliferation of atypical mucinous columnar cells with a lepidic growth pattern and focal papillary architecture. Immunohistochemical staining shows strong positivity for CK7 and PAS, while focal CK20 staining and negative results for TTF-1 and Napsin A-features characteristic of IMA[6]. Absence of TTF-1, a marker typically positive in conventional lung adenocarcinoma, which means a distinct molecular phenotype that differs from classical NSCLC subtypes. Given the aggressive nature and poor response to targeted therapies, early differentiation from other adenocarcinoma variants can help in its prognosis and management[7].

IMA is marked by the overproduction of mucin, which contributes to disease development. Tumour cells that secrete mucin can clog alveoli while causing gas exchange failure and progressive respiratory failure. In addition, the aerogenous dissemination of tumour cells over the alveolar surfaces adds to the diffuse, infiltrative character of the disease, complicating surgical resection[8]. The mucinous component of the tumour impacts not only imaging features but also a response to treatment, as mucin-containing tumours are resistant to conventional chemotherapy and epidermal growth factor receptor (EGFR)-targeted inhibitors. The patient's history of 30-pack-year smoking was a significant risk factor, as tobacco exposure is involved in the pathogenesis of lung adenocarcinoma through genetic and epigenetic changes. Smoking-related adenocarcinomas frequently contain KRAS mutations which are seen in about 50% of IMA cases[9]. KRAS mutations are linked with poor outcomes and poor response to standard treatments.

The progression of symptoms after COVID-19 infection in our patient prompts significant concerns regarding the relationship between viral illness and lung malignancy. Persistent inflammation and fibrosis caused by COVID-19 infection have the potential to stimulate accelerated tumour growth or worsen pre-existing lung pathology. Several recent studies have observed increased numbers of lung cancers being diagnosed following COVID-19 infection, suggesting the possibility of increased surveillance, but also conceivably a result of virus-mediated changes within

the lung microenvironment that foster tumorigenesis. Our patient had occupational exposure to fumes from chemicals as a hairdresser as well, and this has potentially contributed to her illness. Some epidemiologic research has correlated chronic exposure to hair dyes and other volatile substances with elevated risks of respiratory malignancies. Her exposure to numerous pets did bring up the potential for hypersensitivity pneumonitis as a consideration, but this was later excluded on biopsy. The multifactorial nature of interplaying environmental and occupational risk factors identifies the necessity of a multidisciplinary diagnostic approach in the atypical presentations of lung disease. The prognosis of IMA continues to be unfavourable among other adenocarcinoma types owing to its widespread dissemination and fewer treatment options. Five-year survival rates for stage IV IMA are less than 12-15%, and even in early-stage cases, recurrence rates remain much higher because of aerogenous dissemination. Systemic chemotherapy is the current treatment modality with minimal success. Immunotherapy with PD-L1 inhibitors has been promising in a few instances, but response rates are still unpredictable. Clinical trials investigating new mucin-targeted therapies and KRAS inhibitors hold promise for better outcomes in the future[10].

REFERENCES

1. Hutchinson BD, Shroff GS, Truong MT, Ko JP. Spectrum of Lung Adenocarcinoma. *Semin Ultrasound CT MR* 2019Jun;**40**:255-264. doi: 10.1053/j.sult.2018.11.009
2. Lantuejoul S, Colby TV, Ferretti GR, Brichon PY, Brambilla C, Brambilla E. Adenocarcinoma of the lung mimicking inflammatory lung disease with honeycombing. *Eur Respir J* 2004;**24**:502-505. doi: 10.1183/09031936.04.00124703
3. Hata A, Hino T, Yanagawa M, Nishino M, Hida T, Hunninghake GM, et al. Interstitial Lung Abnormalities at CT: Subtypes, Clinical Significance, and Associations with Lung Cancer. *Radiographics* 2022;**42**:1925-1939. doi: 10.1148/rg.220073
4. Khera R, Sharma RK, Kaushal M, Talwar D. Sticking to basics pays even today: Diagnosis of adenocarcinoma lung on sputum examination in patient reluctant to undergo biopsy - Providing opportunity for targeted therapy for palliation if not early detection. *Lung India* 2019;**36**:84-85. doi: 10.4103/lungindia.lungindia_337_18
5. Xiong J, Polsdofer E, Jing J. Common practice issues in pulmonary cytology/small biopsy: Diagnostic pitfalls and appropriate use of immunohistochemical stains. *Hum Pathol Rep* 2024;**36**:300735. doi: 10.4103/lungindia.lungindia_337_18
6. Gurda GT, Zhang L, Wang Y, Chen L, Geddes S, Cho WC, et al. Utility of five commonly used immunohistochemical markers TTF-1, Napsin A, CK7, CK5/6 and P63 in primary and metastatic adenocarcinoma and squamous cell carcinoma of the lung: a retrospective study of 246 fine needle aspiration cases. *Clin Transl Med* 2015;**4**:16. doi: 10.1186/s40169-015-0057-2
7. Yatabe Y, Mitsudomi T, Takahashi T. TTF-1 expression in pulmonary adenocarcinomas. *Am J Surg Pathol* 2002;**26**:767-773. doi: 10.1097/00000478-200206000-00010
8. Ge L, Wang L, Pei D. Pulmonary mucinous adenocarcinoma: An overview of pathophysiology and advancements in treatment. *Heliyon* 2024;**10**:e28881. doi: 10.1016/j.heliyon.2024.e28881
9. Marks JL, Broderick S, Zhou Q, Chitale D, Li AR, Zakowski MF, et al. Prognostic and therapeutic implications of EGFR and KRAS mutations in resected lung adenocarcinoma. *J Thorac Oncol* 2008;**3**:111-116. doi: 10.1097/JTO.0b013e318160c607
10. Chiner-Vives E, Cordovilla-Pérez R, de la Rosa-Carrillo D, García-Clemente M, Izquierdo-Alonso JL, Otero-Candelera R, et al. Short and Long-Term Impact of COVID-19 Infection on Previous Respiratory Diseases. *Arch Bronconeumol* 2022;**58**:39-50. doi: 10.1016/j.arbres.2022.03.011