

FROM MIMIC TO DIAGNOSIS: PRIMARY LUNG ADENOCARCINOMA PRESENTING AS PERIPHERAL AIRSPACE OPACITIES MIMICKING ORGANIZING PNEUMONIA



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ABSTRACT

Lung adenocarcinoma may occasionally present with radiographic features resembling organizing pneumonia (OP), resulting in diagnostic uncertainty, delayed recognition, and potential inappropriate management. We present a case of a 77-year-old man with diabetes mellitus, hypertension, and ischemic heart disease who developed bilateral pulmonary infiltrates. Initial radiological findings suggested OP; for which an empirical course of antibiotics was started. However, due to the lack of clinical improvement and persistent symptoms, a tissue biopsy was subsequently performed. Histopathological examination revealed a moderately differentiated mucinous adenocarcinoma favoring a primary lung tumor. This case underscores a significant diagnostic pitfall and highlights the necessity of histological confirmation when encountering atypical radiologic features.

Keywords: Lung Adenocarcinoma, Invasive Mucinous Adenocarcinoma, Organizing Pneumonia, OP-like Pattern, Radiologic–Pathologic Correlation, Diagnostic Pitfall

Patient Consent

A consent waiver was requested from IRB, for publication of this case report and the accompanying images.

1. INTRODUCTION

Lung adenocarcinoma constitutes the most prevalent histologic subtype of non-small-cell lung cancer (NSCLC). It is characterized by a broad spectrum of radiologic presentations that often complicate timely and accurate diagnosis [1,2]. Although the prototypical manifestation involves a solitary pulmonary nodule or mass, an increasing number of cases demonstrate atypical imaging findings—including diffuse consolidations, ground-glass opacities, and reticulonodular infiltrates—particularly with the advent and widespread use of high-resolution imaging modalities [2,3]. Among these atypical presentations, organizing pneumonia (OP)-like patterns are relatively rare but of significant clinical relevance. Such presentations may lead to diagnostic ambiguity and result in inappropriate therapeutic interventions, notably the empirical use of corticosteroids under the presumption of a benign inflammatory etiology [3,4].

A particularly challenging diagnostic entity within this spectrum is invasive mucinous adenocarcinoma (IMA), a distinct histopathologic subtype of lung adenocarcinoma defined by mucin production and the propensity for aerogenous dissemination [5,6]. Radiologically, IMA frequently presents with features that mimic infectious processes or OP, including bilateral and multifocal consolidative opacities. These radiographic patterns closely resemble those seen in cryptogenic organizing pneumonia (COP) and various interstitial lung diseases, further compounding diagnostic uncertainty [6,9]. This radiologic mimicry constitutes a critical diagnostic pitfall, as transient or absent clinical response to antibiotics or corticosteroids may obscure the underlying malignancy, thereby delaying histologic evaluation and definitive management [9,10]. Even advanced functional imaging, such as fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT), lacks sufficient specificity to distinguish neoplastic from inflammatory processes in this clinical context [10].

Timely recognition of these atypical imaging features is imperative for both radiologists and pulmonologists. Definitive diagnosis continues to rely on histopathologic confirmation, with immunohistochemical analysis—including cytokeratin 7 (CK7), thyroid transcription factor-1 (TTF-1), and Napsin A serving as critical tools for differentiating primary pulmonary adenocarcinoma from

metastatic mucinous adenocarcinomas of gastrointestinal origin [6,8]. The presented case exemplifies the diagnostic complexity posed by IMA with OP-like radiologic patterns and underscores the importance of a multidisciplinary diagnostic approach integrating clinical, radiologic, and histopathologic data to guide appropriate management.

2. CASE PRESENTATION

2.1 History

A 77-year-old man with a past medical history of diabetes mellitus, hypertension, and ischemic heart disease (status post two coronary stents, with an ejection fraction of 40%) presented with symptoms that began in March 2025, including a dry cough, unintentional weight loss, and loss of appetite. He also reported shortness of breath, classified as New York Heart Association (NYHA) functional class II, with no chest pain or hemoptysis. He had no history of smoking. Family history is significant for gastrointestinal malignancies in both his sister and brother.

2.2 Initial Workup

At an outside general hospital, chest imaging demonstrated bilateral pulmonary consolidations. An empiric course of antibiotic therapy was initiated; however, there was no clinical or radiologic improvement. This lack of response raised suspicion for an alternative etiology, such as malignancy. Subsequently, an external lung biopsy was performed, revealing adenocarcinoma favoring pancreaticobiliary origin; however, no definite primary site was identified. Tumor marker CA 19-9 was elevated at 90 U/mL. CT of the abdomen and pelvis, as well as MRCP, were unremarkable.

2.3 Imaging Findings

On presentation to our institution on May 5, 2025, a chest CT performed on 8th of May 2025, demonstrated bilateral peripheral and subpleural consolidations involving the upper, middle and lower lobes with additional perilobular and peribronchial distribution. Scattered areas of airway dilatation were also seen (Figures 1 and 2). The Differential diagnoses at that stage included organizing pneumonia, eosinophilic pneumonia, and sarcoidosis.

A CT scan of the abdomen and pelvis revealed no pancreatic or biliary mass, and MRCP findings were unremarkable. Despite an elevated serum CA 19-9 level (90 U/mL), the absence of pancreaticobiliary pathology on imaging prompted reconsideration of the differential diagnoses in light of the pulmonary findings and previous histopathology results. Given this discordance, a repeat biopsy was

performed, deliberately targeting a different pulmonary lesion. Histopathology confirmed moderately differentiated mucinous adenocarcinoma, most likely consistent with primary pulmonary origin.



Figure 1: Axial non-enhanced chest CT images (A, B, C) show bilateral peripheral and subpleural consolidations in the upper, middle, and lower lobes, with perilobular (arrowheads) and peribronchial (white arrows) distribution and scattered airway dilatation (red arrows).



Figure 2: Coronal non-enhanced chest CT image shows bilateral peripheral and subpleural consolidations involving the upper, middle, and lower lobes, with perilobular (arrowheads) and peribronchial (white arrows) distribution.

2.4 Histopathology

The initial biopsy demonstrated adenocarcinoma positive for CK7, CK19, CDX-2, CK20, and focal thyroid transcription factor-1 (TTF-1), but negative for Napsin-A. These findings made the distinction between primary lung adenocarcinoma and metastatic gastrointestinal adenocarcinoma inconclusive.

Further investigations, including colonoscopy and esophagogastroduodenoscopy (EGD) performed on May 21, 2025, were unremarkable.

A repeat CT-guided lung biopsy was successfully performed on June 5, 2025. Histopathology revealed moderately differentiated adenocarcinoma with positive staining for CKAE1/3, CDX-2, CK7, CK19, and focal TTF-1, while negative for Napsin-A and epidermal growth factor receptor (EGFR) (Figure 3).

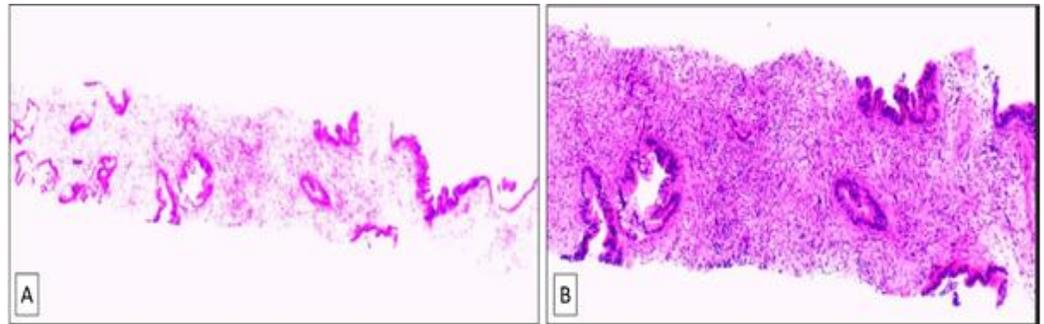


Figure 3: Images (A and B) show moderately differentiated adenocarcinoma

2.5 Hospital Course

The patient developed post-biopsy small pneumothorax, which was conservatively managed. Following multidisciplinary review with pulmonology, radiology, and oncology teams, the final diagnosis of metastatic adenocarcinoma of pulmonary origin was established. The patient was referred to the oncology department for further management.

3. DISCUSSION

Lung adenocarcinoma represents the predominant histologic subtype of non-small-cell lung cancer (NSCLC) and is notable for its diverse morphologic and radiologic manifestations [2,4]. While the majority of cases present as discrete pulmonary nodules or masses, a subset demonstrates diffuse or patchy alveolar involvement, often resulting in imaging patterns mimicking infectious or inflammatory processes, such as organizing pneumonia (OP) [3,5]. In particular, invasive mucinous adenocarcinoma (IMA) is characterized by mucin production and a propensity for aerogenous spread, leading to bilateral, multilobar airspace

opacities. This “pneumonic-type” presentation can closely resemble cryptogenic organizing pneumonia (COP) or eosinophilic pneumonia, creating significant diagnostic challenges [6, 9, and 10]. Such overlap may be especially misleading when patients exhibit transient or partial improvement after empirical antibiotic or corticosteroid therapy, potentially delaying further diagnostic evaluation.

Numerous case reports and series have described instances in which mucinous or EGFR-mutated adenocarcinomas were initially misdiagnosed as organizing pneumonia or community-acquired pneumonia, with correct identification only achieved upon subsequent histopathological analysis [4,5 and 10]. Delayed recognition in such cases can contribute to disease progression, upstaging, and reduced treatment options [10]. Therefore, persistent or progressive airspace opacities that do not resolve with appropriate medical therapy should raise suspicion for an underlying malignancy. In such scenarios, prompt tissue sampling is critical, particularly when radiographic findings are atypical, non-resolving, or inconsistent with the patient’s clinical trajectory.

Immunohistochemical (IHC) profiling remains an essential component of the diagnostic algorithm in suspected primary pulmonary adenocarcinoma. Most tumors demonstrate positivity for cytokeratin 7 (CK7) and thyroid transcription factor-1 (TTF-1), with Napsin A providing additional specificity in confirming a pulmonary origin [6, 8]. However, expression of gastrointestinal lineage markers such as caudal-type homeobox transcription factor 2 (CDX2) may be observed in mucinous or enteric variants, occasionally leading to diagnostic ambiguity [7]. In these cases, clinicopathologic correlation is vital, and further exclusion of a gastrointestinal primary through dedicated imaging or endoscopic evaluation is warranted. In the present case, focal TTF-1 expression, combined with the absence of evidence for gastrointestinal malignancy, strongly supported a primary pulmonary origin.

This case underscores the critical importance of a multidisciplinary diagnostic approach, incorporating the expertise of radiologists, pulmonologists, pathologists, and oncologists. Recognition of atypical or OP-like presentations of mucinous adenocarcinoma is essential to avoid misclassification and delays in appropriate oncologic management. Ultimately, non-resolving or atypical organizing pneumonia patterns, particularly those unresponsive to standard therapy, should prompt consideration of an underlying neoplastic process.

3.1 Teaching points

Two important points arise from this case:

1. Diagnostic pitfall: Lung adenocarcinoma may mimic OP on imaging, necessitating tissue confirmation in atypical or unresolved pulmonary consolidations.
2. Multidisciplinary approach: Collaboration among radiology, pathology, pulmonary, and oncology is vital to establish the correct diagnosis and guide management.

4. CONCLUSION

Lung adenocarcinoma may rarely present with radiological features mimicking organizing pneumonia, posing a diagnostic challenge. This case highlights the essential role of histopathology in confirming the diagnosis and emphasizes the importance of a multidisciplinary approach to ensure appropriate and timely management.

5. CONFLICT OF INTEREST

No commercial or financial declaration.

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8. DECLARATION OF GENERATIVE AI

During the preparation of this work the authors used GPT-4 (OpenAI, San Francisco, USA) to improve the readability of some of the sections, assure homogeneity of the passages and reduce redundancies in writing. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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