International Journal of Pulmonary and Respiratory Sciences

ISSN Print: 2664-8504
ISSN Online: 2664-8512
Impact Factor: RJIF 5.42
IJPRS 2025; 7(1): 06-08
www.pulmonologyjournals.com
Received: 12-10-2024
Accepted: 17-11-2024

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Diffuse pulmonary nodules and diagnostic dilemmas: Lung adenocarcinoma masquerading as miliary tuberculosis

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DOI: https://doi.org/10.33545/26648504.2025.v7.i1a.29

Abstract
Lung adenocarcinoma is the most common subtype of lung cancer, often presenting with nonspecific symptoms. It is rare for adenocarcinoma to mimic miliary tuberculosis, creating a diagnostic challenge. This case report details a 40-year-old male with a 9-month history of dry cough and shortness of breath. Initial chest X-ray demonstrated a miliary pattern of nodular shadows in both lungs and a homogeneous opacity in the middle zone of the left lung. Contrast-enhanced computed tomography (CECT) of the thorax revealed a mass lesion involving the lingular segment of the left upper lobe and diffuse interstitial coarse reticulations with tiny cysts involving both lung parenchyma. A biopsy taken from the left upper lobe lung lesion confirmed the diagnosis of lung adenocarcinoma.

Keywords: Lung adenocarcinoma, miliary tuberculosis, pulmonary nodules

Introduction
Lung adenocarcinoma, the most common subtype of non-small cell lung cancer (NSCLC), accounts for nearly 40-50% of lung cancer cases worldwide. It often presents with nonspecific clinical symptoms, including cough, dyspnoea, chest discomfort, and sometimes haemoptysis. These symptoms overlap significantly with other pulmonary conditions, such as infections and inflammatory diseases, complicating the diagnostic process.
Miliary tuberculosis, a form of disseminated tuberculosis, is characterised by a hematogenous spread of *Mycobacterium tuberculosis*, resulting in numerous tiny nodules visible throughout the lungs on imaging. This pattern is Laboratory associated with systemic symptoms such as fever, weight loss, and night sweats. However, a radiological miliary pattern is not pathognomonic and may be seen in other conditions, including metastatic cancers, fungal infections, and sarcoidosis.
The coexistence of lung cancer with tuberculosis has been well-documented, especially in regions where tuberculosis is endemic. However, cases where lung cancer mimics miliary tuberculosis are exceedingly rare. This overlap poses a significant diagnostic challenge, as tuberculosis is often the primary suspected diagnosis due to its prevalence and treatability. Misdiagnosis or delayed identification of the underlying malignancy can lead to poor outcomes, underscoring the importance of thorough evaluation in atypical presentations.
In this report, we discuss a rare case of lung adenocarcinoma in a 40-year-old male, initially presenting with radiological findings consistent with miliary tuberculosis and confirmed adenocarcinoma by lung biopsy.

Case report
A 40-year-old nonsmoker male presented with an 8–9-month history of progressive shortness of breath and dry cough. His symptoms were associated with weight loss and loss of appetite, but he had no significant past medical history.
Upon admission, the patient was hemodynamically stable, with a pulse rate of 86 beats/minute, a respiratory rate of 18 breaths/minute, and oxygen saturation of 98% on room air. Physical examination revealed diminished percussion and breath sounds over the left mammary, infraaxillary, and infrascapular areas, with rhonchi heard diffusely.

Laboratory findings were unremarkable except for mild leucocytosis with a total leukocyte count of 13,370/mm³. A haemoglobin concentration of 16.5 g/dL was well within the typical range and renal and liver function tests were normal. Pleural fluid analysis revealed an exudative, lymphocytic fluid with low adenosine deaminase (ADA) levels. Sputum and bronchoalveolar lavage (BAL) were negative for acid-fast bacilli (AFB), and cartridge-based nucleic acid amplification testing (CBNAAT) for TB was also negative. Chest X-ray (Fig**.** 1A) showed Bilateral miliary nodular shadows and a homogeneous opacity in the middle zone of the left lung. Contrast-Enhanced CT Thorax (Fig. 1C) showed A mass lesion in the lingular segment of the left upper lobe causing bronchial cutoff. Diffuse nodular thickening of the left pleura—confluent consolidation with air bronchograms in the superior and basal segments of the left lung. Diffuse coarse interstitial reticulations with tiny cysts in both lungs. Mild right-sided pleural effusion with paraaortic and paratracheal mediastinal lymphadenopathy. Multiple miliary nodular opacities in both lungs. CT-guided biopsy of the left lung mass was performed, revealing invasive adenocarcinoma with a lepidic growth pattern. Immunohistochemical staining was positive for TTF1, Napsin A, and CK7, confirming the diagnosis of primary lung adenocarcinoma.

Discussion

Lung cancer is a significant global health issue, ranking among the most commonly diagnosed cancers and the leading cause of cancer-related mortality worldwide [1]. Non-small cell lung cancer (NSCLC) comprises the majority of cases, with adenocarcinoma being the most prevalent subtype, accounting for approximately 50% of diagnoses. Adenocarcinoma of the lung exhibits an unusual epidemiological trend, being more commonly diagnosed in nonsmokers than smokers and showing a higher incidence in females than males [2]. Unlike squamous cell carcinoma and small cell lung cancer, which typically present as central lesions, adenocarcinoma often appears as peripheral masses or nodules, frequently involving the pleura [3]. Lung adenocarcinoma can occasionally mimic infectious diseases by presenting with diffuse pulmonary nodules. This pattern may arise from mechanisms such as hematogenous spread or lepidic growth, where tumour cells proliferate along alveolar walls. Lung cancer commonly presents with respiratory symptoms, systemic "B symptoms" like unexplained weight loss, fever, and night sweats, as well as manifestations caused by obstruction of the airway or surrounding structures [4].

Diagnosing lung adenocarcinoma can be particularly challenging in regions where tuberculosis (TB) is endemic. The clinical and radiological features of adenocarcinoma, such as diffuse pulmonary nodules, weight loss, and respiratory symptoms, closely resemble those of miliary TB. Consequently, patients presenting with these findings are often initially managed for TB, especially when the region's prevalence and clinical suspicion of infection are high. This case underscores the necessity of expanding the differential diagnosis to include malignancies, particularly when TB investigations yield negative results.

The patient described in this report exhibited a miliary pattern on chest imaging, pleural thickening, and a lung mass—features that strongly suggested miliary TB. Despite this, diagnostic tests for TB, including sputum microscopy, bronchoalveolar lavage (BAL) analysis for acid-fast bacilli (AFB), and PCR testing, were all negative. Further evaluation, including pleural fluid analysis revealing an exudative lymphocytic profile with low adenosine deaminase (ADA) levels, led to the ultimate diagnosis of lung adenocarcinoma. This case highlights the importance of tissue sampling and histopathological examination in accurately identifying the underlying pathology when initial diagnostic investigations are inconclusive. Primary lung cancer rarely presents as miliary nodules, with such a presentation observed in less than 5% of cases. This pattern typically signifies an unusual metastatic spread of the tumor or an advanced disease state [5].

The differential diagnosis for miliary nodules extends beyond TB. It includes a range of conditions such as fungal infections (e.g., histoplasmosis, coccidioidomycosis), inflammatory diseases (e.g., sarcoidosis), occupational lung diseases (e.g., silicosis), and metastatic malignancies originating from the thyroid, breast, prostate, or kidney [6]. In TB-endemic regions, however, the overwhelming focus on infection often delays the recognition of alternative diagnoses, such as metastatic lung cancer, until later stages.

When lung adenocarcinoma presents with miliary metastasis, it often signifies advanced disease with a poor prognosis [7]. This diffuse dissemination limits therapeutic options and highlights the urgency of an accurate and timely diagnosis. Current advancements in treatment, such as targeted therapies and immunotherapy, may offer some hope for patients with specific genetic mutations, although their efficacy in cases of widespread metastases remains limited.

This case underscores the value of a comprehensive and methodical diagnostic approach. Clinicians must integrate imaging, laboratory findings, and histopathological data to distinguish between infectious and malignant aetiologies. While TB remains the predominant cause of miliary nodules in endemic areas, the possibility of malignancy should not be overlooked, particularly when conventional diagnostic tests for infection are negative. Early recognition of lung adenocarcinoma, even in its atypical presentations, is critical to ensuring prompt and appropriate management.

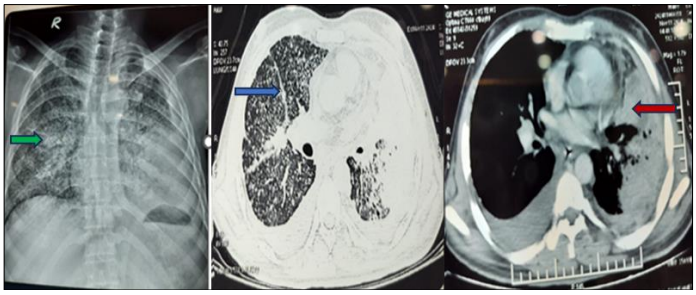

Fig 1A: Chest Xray showing multiple miliary nodules (green arrow): 1B- CT Thorax- Perilymphatic nodules suggestive of lymphangitis carcinomatosis (blue arrow): 1C-CT showing left upper lobe mass (red arrow)

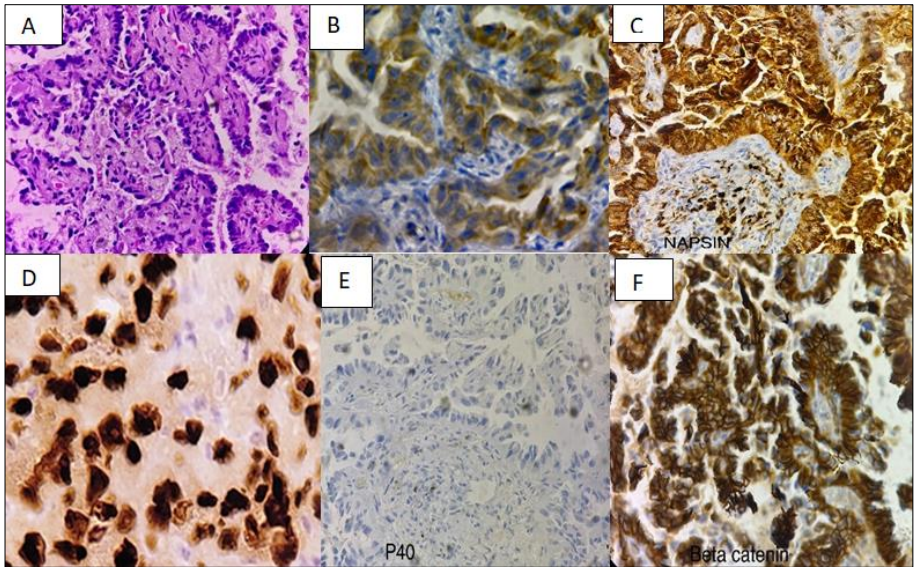

Fig 2: Histopathology: A: H and E stain, B: IHC-CK7 (positive), C: IHC-Napsin A (positive), D: IHC-TTF1 (positive), E: IHC P40 (negative), F: IHC -Beta-catenin (negative)

Conclusion

This case highlights the importance of a systematic diagnostic approach in evaluating patients with diffuse pulmonary nodules. In endemic areas, TB is a common consideration, but clinicians should remain vigilant for malignancies, particularly in patients with atypical presentations or negative TB investigations. Early biopsy and histopathological confirmation are crucial for accurate diagnosis and prompt initiation of appropriate therapy.

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