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Case Report

Lung adenocarcinoma presenting as miliary lung metastasis on imaging ^{☆,☆☆}

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ABSTRACT

Intrapulmonary miliary metastasis is a rare presentation of adenocarcinoma of the lung, characterized by the dissemination of cancer cells throughout the lung parenchyma in different patterns. This case report highlights an unusual presentation of adenocarcinoma of the lung with intrapulmonary miliary metastasis, emphasizing the diagnostic challenges and management considerations. Here, we report a case of a 51-year-old female who presented to the emergency department (ED) with a 2-month history of dry cough, which started after a flu illness and was associated with mild shortness of breath, left-sided chest pain, and miliary nodules on chest imaging. During bronchoscopy, a transbronchial biopsy was taken for further pathological assessment. The results showed histopathological evidence of lung adenocarcinoma.

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Introduction

Lung adenocarcinoma, a subtype of non-small cell lung cancer, is particularly common among nonsmokers and women. According to the Global Cancer Statistics report from 2020, lung cancer remained the most common type of cancer death worldwide, with approximately 1.8 million deaths [1].

The 2 types of lung cancer that can occur are small-cell lung cancer (SCLC) and nonsmall cell lung cancer (non-SCLC). Non-small cell lung cancer is classified into 3 subtypes: squamous cell carcinoma, large cell carcinoma, and lung adenocarcinoma [2].

Lung adenocarcinoma is considered to be the most common type of lung cancer, and both women and nonsmokers are more likely to develop it.

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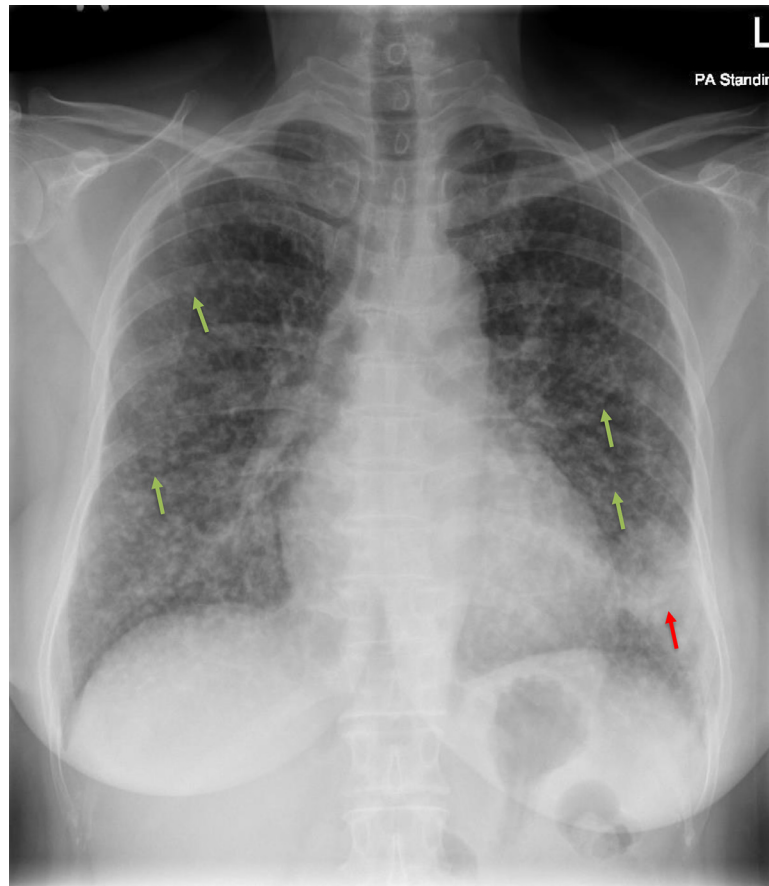


Fig. 1 – Innumerable, small miliary pulmonary nodules (green arrows) scattered throughout the lungs. Focal patchy lung lesion (red arrow) seen at left lower zone. Measure about (6.4 × 3.8) cm, posterior located. No plural effusion.

Smoking, family history of lung cancer, occupational exposure, and genetic mutations are well-known risk factors that are associated with this condition [3].

Lung adenocarcinoma typically occurs at the lung's periphery. Chest computed tomography (CT) scans of lung adenocarcinomas rarely show a miliary pattern and instead show ground glass, part-solid, or solid nodules. On chest radiography, miliary mottling is defined as many pulmonary opacities less than 3 mm in size dispersed across the lungs [4].

Here we're reporting a case of a 51-year-old nonsmoking woman with intrapulmonary miliary metastases of lung adenocarcinoma who presented with a chronic dry cough and miliary nodules on chest imaging.

Case presentation

A 51-year-old nonsmoking woman presented to the emergency department (ED) with a 2 months history of dry cough, which started after a flu illness and was associated with mild shortness of breath and left-sided chest pain. She had no history of fever, night sweats, or hemoptysis. She has a past medical history of diabetes mellitus, for which she takes metformin. The patient denied any history of recent travel, but she had a history of close contact with tuberculosis (TB) in her family. The patient is a housewife. A review of other systems was unremarkable. In the ED, her vitals were within normal

limits. Her temperature was 36.7°C (oral), her heart rate was 102 beats per minute, her respiratory rate was 20 breaths per minute, her blood pressure was 117/82 mmHg, and her oxygen saturation (SpO₂) was 93% in room air. Chest auscultation showed normal heart sounds and clear lungs. Examination of other systems was unremarkable.

Initial laboratory investigations revealed mild leukocytosis ($12.9 \times 10^3/\mu\text{L}$), anemia (hemoglobin level of 10.6 g/dL), thrombocytosis (platelet count of $508 \times 10^3/\mu\text{L}$), and elevated alkaline phosphatase (150 u/L). For further investigations, the Quantiferon-TB Gold test, sputum acid-fast bacilli smear (2 samples), TB polymerase chain reaction (PCR), and fungal cultures were sent, and the results came back negative (Table 1).

A chest X-ray was done, and it showed bilateral multiple miliary nodules scattered throughout the lung zone (Fig. 1). Results of the CT scan showed diffuse, innumerable miliary nodules randomly distributed throughout both lungs that appeared close to each other in size (Figs. 2 and 3).

The patient was admitted for further evaluation using bronchoscopy. During bronchoscopy, a trans bronchial biopsy was taken for further pathological assessment. The results showed histopathological evidence of lung adenocarcinoma, an acinar subtype that was negative for anaplastic lymphoma kinase (ALK 5A4) and programmed death-ligand (PD-L1) biomarkers. The patient's results following a positron emission tomography (PET) scan showed metastatic involve-

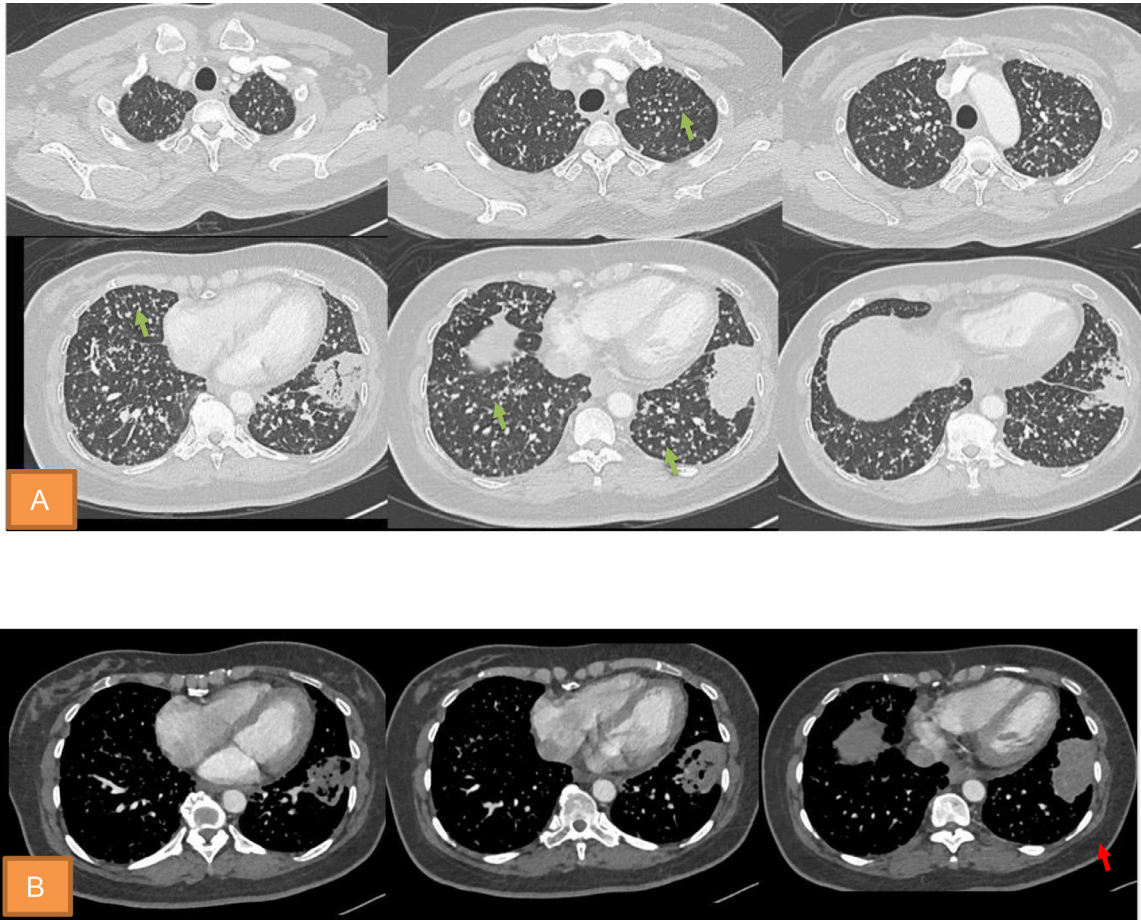


Fig. 2 – CT chest with intravenous contrast lung window [axial sections (A series) and soft tissue window [axial sections (B series)]. Showing Diffuse innumerable miliary nodules randomly distributed throughout both lungs that appear close to each other in size (green arrows). There is left lower lobe, lateral segment an irregular out lines mass measure (5.5 x 3.6 x 4.5) cm with central necrosis (red arrows).

Table 1 – Lab results.

General Hematology	At admission
WBC (x10 ⁹ /L)	12.9
RBC (x10 ⁶ /L)	5.3
Hgb (g/dL)	10.6
Platelet (x10 ⁹ /L)	508
Blood chemistry	At admission
Urea (mmol/L)	3.4
Creatinine (umol/L)	53
Sodium (mmol/L)	136
Potassium (mmol/L)	4.4
Alk (U/L)	150

Table 2 – Diagnostic markers associated with lung adenocarcinoma.

Test	Results
TTF1 Thyroid transcription factor 1	Positive
Napsin	Positive
ALK5A4	Negative
PD-L1	Negative
EGFR mutation L858R	Positive

ment in the lungs, pleura, mediastinal lymph nodes, and bones (Fig. 4). Mutations in the epidermal growth factor receptor gene (EGFR) were also detected through next-generation genetic sequencing tests (Table 2).

After a multidisciplinary team meeting, the patient was diagnosed with stage IV lung adenocarcinoma that metastasized to the lung, pleura, lymph nodes, and bones. The patient was prescribed vitamin B12 and folic acid and was referred to

the oncology department to start chemotherapy with carboplatin and pemetrexed.

Discussion

Lung carcinoma, also known as bronchogenic carcinoma, is one of the leading causes of cancer-related mortality. It's a malignant neoplasm of the lung that arises from the respiratory epithelium of the bronchus, or bronchiole [5]. The symp-

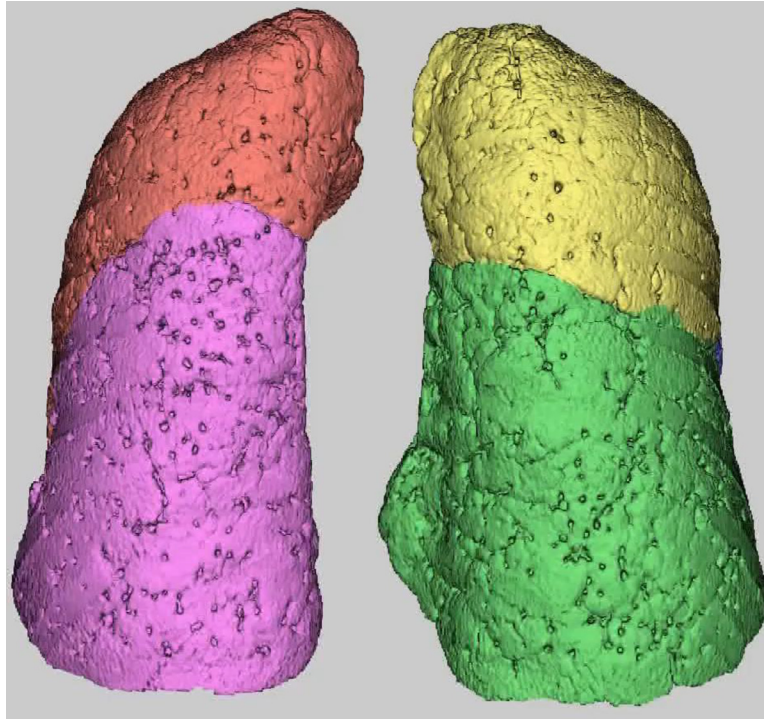


Fig. 3 – CT chest 3D format. Showing diffuse innumerable miliary nodules randomly distributed throughout both lungs that appear close to each other in size (yellow arrows). There is left lower lobe, lateral segment an irregular out lines mass (red arrows).

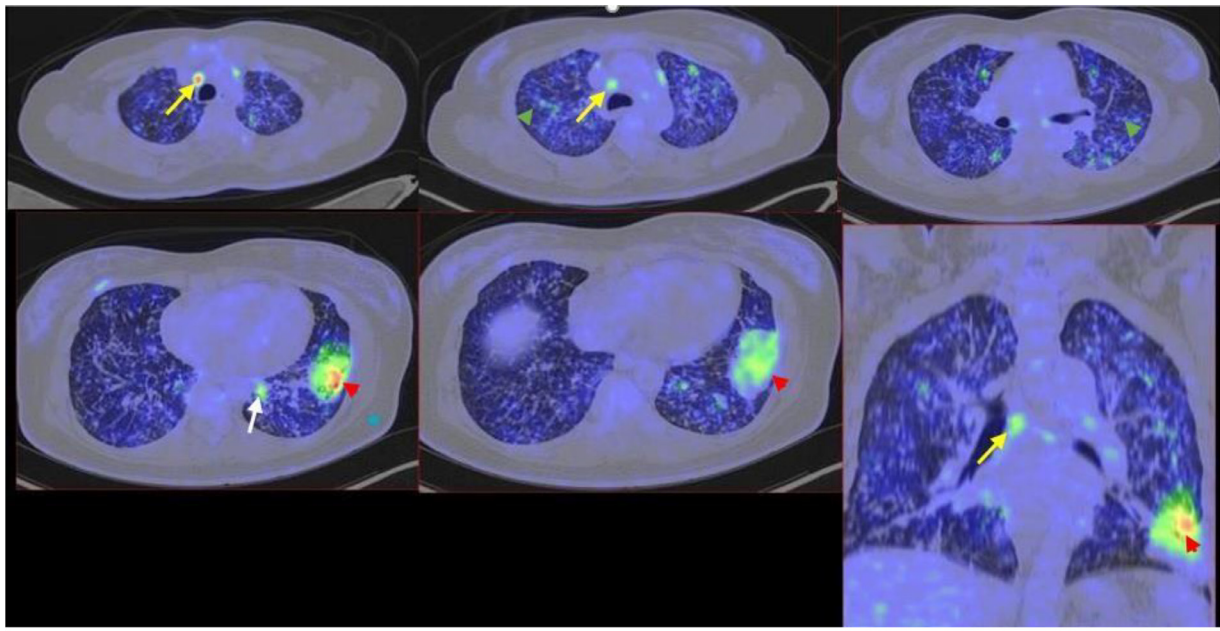


Fig. 4 – axial and coronal sections There are innumerable diffuse FDG avid reticular nodules seen in both lungs (green arrows head) . There is a large consolidation with cavitation seen in the left lower lobe, lateral segment with intense FDG uptake, measuring about (5.5 × 3.6 × 4.5) cm with SUV max of 8. (red head arrows) There is another lesion noted in the left medial aspect of the lower lobe (white arrow). There are multiple hyper metabolic lymph nodes seen in the bilateral perivascular, sub carina, and right hilar stations. (yellow arrows).

toms include general B symptoms, respiratory symptoms, and symptoms related to obstruction and invasion of local structures [6].

Adenocarcinoma of the lung is a subtype of nonsmall cell lung carcinoma and is the commonest type of primary lung cancer, accounting for 50% of lung cancers. It's more prevalent among nonsmokers than smokers and more prevalent in females than males [7]. In our case, the presence of the EGFR L858R mutation corroborates this association, highlighting the need for genetic testing in similar presentations [8].

A comprehensive review of the literature revealed 15 cases of lung cancer presenting with intrapulmonary miliary metastases [9]. In our case, our patient was a 51-year-old female who was never known to be a smoker and was found to have a mutation in the EGFR gene. Radiologically, adenocarcinoma of the lung usually presents as ground-glass, part-solid, or solid nodules [10]. It's very rare for primary lung cancer to present in a miliary pattern [11]. Miliary patterns can be described as multiple small nodules with sharp margins scattered throughout the lung, usually less than 3 mm in size [12].

The miliary pattern can represent a wide variety of pathologies, including but not limited to TB, histoplasmosis, coccidioidomycosis, sarcoidosis, silicosis, malignancies (thyroid, renal, prostate, and breast cancer), etc. In endemic areas, TB is a major cause of miliary nodules [13]. In our case, TB investigations came back negative, a chest X-ray showed bilateral multiple miliary nodules scattered throughout the lung with a focal patchy lung lesion seen at the left lower zone, and a CT scan confirmed the diagnosis of miliary nodules. There is a left lower lobe, lateral segment, and an irregular outlining mass with central necrosis.

As the presence of miliary patterns on radiological images is not specific, the final diagnosis cannot be established without a tissue biopsy. Histopathologically, the tumor can show acinar, papillary, micropapillary, solid growth, or lepidic features [14].

Our patient's histopathological analysis following bronchoscopy revealed features of lung adenocarcinoma, acinar subtype.

Our patient underwent a PET scan to evaluate for possible metastatic spread to other organs, and the results showed an increase in radiotracer uptake in the lungs, pleura, mediastinal lymph nodes, and bones. According to a study, lung adenocarcinoma is typically the most common type of lung cancer to metastasize to the bones [15]. Bone involvement has been associated with a poor prognosis [16].

To provide appropriate management, the patient's condition was discussed in multidisciplinary team meetings. The patient was then referred to the oncology department as a case of stage IV lung adenocarcinoma for chemotherapeutic management.

Conclusion

This case highlights a unique radiological presentation of lung adenocarcinoma as miliary nodules. It's crucial for clinicians to consider lung adenocarcinoma in the differential diagnosis of patients presenting with miliary patterns on chest imaging,

particularly when initial investigations for infectious etiologies are negative. Early identification and genetic testing for mutations like EGFR can significantly influence management and prognosis.

Patient consent

Informed consent for publication of this case was obtained from the patient.

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