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## Lung adenocarcinoma - a diagnostic challenge

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## **Abstract**

Cavitary lung nodules are produced by a variety of diseases ranging from benign to malignant disease. According to the Fleischner Society, the pulmonary cavity is characterized by a gas-filled space, seen as a lucency or low-attenuation area, within pulmonary consolidation, a mass, or a nodule. Though the number and thickness of the wall of the cavity may help to differentiate causes, arriving at a diagnosis is challenging. Even though radiological findings will help to differentiate benign from malignant etiology, histopathology is needed for confirmation of diagnosis. Here, we describe a metastatic lung adenocarcinoma case presenting as multiple cavitary nodules.

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## **Introduction**

Lung cancer is the leading cause of cancer deaths in both men and women. Adenocarcinoma is the most common subtype of lung cancer. It is classified under non-small cell lung cancer, and its occurrence is higher in smokers.<sup>1</sup> Patients present with varied symptoms like cough, chest pain, hemoptysis, dyspnea, and constitutional symptoms like loss of appetite and weight. During the early stage, it can be diagnosed as an incidental finding during routine screening, or may present with signs and symptoms of distant metastasis or paraneoplastic syndromes. Other unusual presentations are ground glass opacities and consolidation, which is a diffuse pneumonic type. On histology, it appears as lepidic growth with the filling of alveolar spaces with mucin and tumor cells. This type of carcinoma is slow-growing.<sup>2,3</sup> This poses a diagnostic challenge as this may be the manifestation of a wide range of acute and chronic benign conditions, like inflammation and infection of lung parenchyma. Here, we present a case of lung adenocarcinoma as chronic bilateral lung consolidation and cavitary nodules with rapidly progressing respiratory failure.

## **Case Report**

A 35-year-old female patient working in the ambulance as a nursing staff member, with no comorbidities, presented with a cough with whitish expectoration for 1 month and left-side

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pricking chest pain for 1 day, with a history of loss of appetite and loss of weight. She did not have any history of skin rash, joint pain, neck swelling, abdomen pain, or leg swelling. She did not have any history of pulmonary tuberculosis in the past. Pet exposure and nearby factory pollution were ruled out. Her menstrual history was insignificant. There was no similar family history. Baseline blood investigations were normal. Computed Tomography (CT) of the thorax suggested bilateral multi-lobar consolidation with cavities. The patient was started on Antituberculosis Therapy (ATT) based on radiological presentation. However, the patient did not have any improvement. In October 2021, the patient developed difficulty in breathing. The modified Medical Research Council (MRC) Scale for muscle strength was grade 2-3, and intermittent fever for 7 days, for which the patient was admitted and was managed with antibiotics, antifungal, antiviral, and ATT for non-resolving pneumonia. In view of persistent symptoms, the patient was referred to our hospital. On admission, the patient was moderately built and nourished. Vitals were blood pressure of 110/80 mmHg, pulse rate of 112/min, and oxygen saturation by pulse oximetry of 88% on room air. With 2-liter oxygen, she was maintaining a saturation of 97%. Respiratory rate was 22/min. Arterial Blood Gas (ABG) was suggestive of hypoxemic respiratory failure. Hence, the patient was put on oxygen by nasal prongs. Chest X-ray was suggestive of bilateral multi-lobar nodular opacities (Figure 1). Contrast-Enhanced Computed Tomography (CECT) of the chest showed lobar consolidation involving the left lower lobe, with multiple air-attenuating foci and air bronchograms within, suggestive of necrotizing consolidation. Consolidation was also noted in the

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inferior lingular segment, left upper lobe posterior segment, right middle lobe, right upper lobe and anterior basal segment of right lower lobe. Multiple randomly distributed nodules were noted in the rest of the bilateral lung parenchyma, many of them showing cavitation within. No significant mediastinal lymphadenopathy was noted (Figure 2). Sputum for fungal culture, pyogenic culture, acid-fast stains, and cytology were normal. Hence, a Bronchoalveolar Lavage (BAL) from the bilateral lung and a transbronchial biopsy from the left lung lower lobe were done. BAL fluid bacterial, gram stain, and CBNAAT were negative. Transbronchial biopsy was suggestive of acute interstitial inflammation; hence the patient was started on steroids and septran prophylaxis, but she did not improve clinically or radiologically. Further, serum angiotensin converting enzyme, serum calcium, and urine calcium were done to rule out sarcoidosis. The auto-immune panels, including Antinuclear Antibody (ANA) and Antineutrophil Cytoplasmic Antibodies (ANCA), were negative. Ultrasound-guided biopsy from the left lung lower lobe was done, which was inconclusive. A repeat CT-guided biopsy obtained from the left lower lobe was done, which was suggestive of adenocarcinoma with predominantly lepidic and focal acinar patterns. On immunohistochemistry, Thyroid Transcription Factor (TTF-1) was positive (Figure 3). By the time the diagnosis was made, the patient had worsened clinically, and the oxygen requirement also increased. A multi-disciplinary approach, including medical oncology, was considered, and it was decided to give palliative supportive care.

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## **Discussion**

According to the 2021 World Health Organization (WHO) lung carcinoma classification, lung cancer is classified into different types, namely adenocarcinoma, squamous cell carcinoma, adeno-squamous, large cell, and neuroendocrine carcinomas based on histopathology. Adenocarcinoma is the most common among all types, especially among non-smokers. Broncho-alveolar carcinoma, which was a subtype of adenocarcinoma, has now been included in the invasive adenocarcinoma type.<sup>4</sup>

Radiographically, atypical adenomatous hyperplasia, adenocarcinoma *in situ*, and broncho-alveolar carcinoma will appear as ground glass opacity or as solid lesions.<sup>4</sup> Pneumonic-Type Lung Adenocarcinoma (P-ADC) was defined as “adenocarcinoma presenting with pneumonia-like areas of infiltrates or consolidations involving a region of the lung”.<sup>3</sup> On histology, it is seen as lepidic growth, in which alveolar spaces are filled with mucin or tumor cells. Lung carcinoma presenting as cavitating nodules or consolidation poses great diagnostic difficulty in a wide range of diseases like infection and inflammation. Infectious causes include pulmonary abscess, septic emboli, mycobacterium tuberculosis, non-tuberculous mycobacteria, and aspergillosis. Systemic diseases like granulomatosis with polyangiitis, rheumatic nodules, and sarcoidosis can cause cavitating

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nodules. Malignancy that causes cavitating nodules is metastatic carcinoma from squamous cell carcinoma, and rarely from primary bronchogenic carcinoma, in which squamous cell carcinoma is more common if compared to other malignancies.<sup>5</sup> Multifocal involvement of adenocarcinoma is less compared to single lobe involvement and multifocal involvement will have different stage from preinvasive (ground glass opacity) to invasive malignancy (solid nodules).<sup>6</sup> In our case, primary lung adenocarcinoma presented as bilateral multi-lobar cavitory nodules with consolidation.

Cavities in malignancy are due to three main mechanisms. Bronchial obstruction due to the mass and infection and rupture of parenchyma distal to the obstruction is the most common cause. Other causes include breakdown by growth itself and spillover abscess. In primary lung cancer, multiple cavitating nodules are a rare event. However, multifocal bronchoalveolar carcinoma can be associated with multiple cavitating nodules coalescing with each other.<sup>7</sup>

Yield of carcinomatous cells in bronchoscopy procedures in bronchoalveolar carcinoma, such as 9.20% in BAL, 14.81% in bronchoscopy biopsy, and 40.70% in bronchial brushing.<sup>8</sup> Risk factors associated with malignancy are genetic and acquired, which include advanced age, smoking, and environmental and occupational exposure, but our patient did not have any risk factors. A bilateral multi-lobar consolidation form of lung tumor was described by Malassez.<sup>9</sup>

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## **Conclusions**

Lung adenocarcinoma has many varieties of presentation, and several presentations are identical to or nearly mimic non-malignant processes like infectious causes, mainly in non-smokers and younger age groups. Hence, suspicion of malignancy should be considered as a differential diagnosis in case of multiple cavitating nodules, even if the presentation mimics infectious etiology and gets a different histopathological report, mimicking non-malignant etiology.

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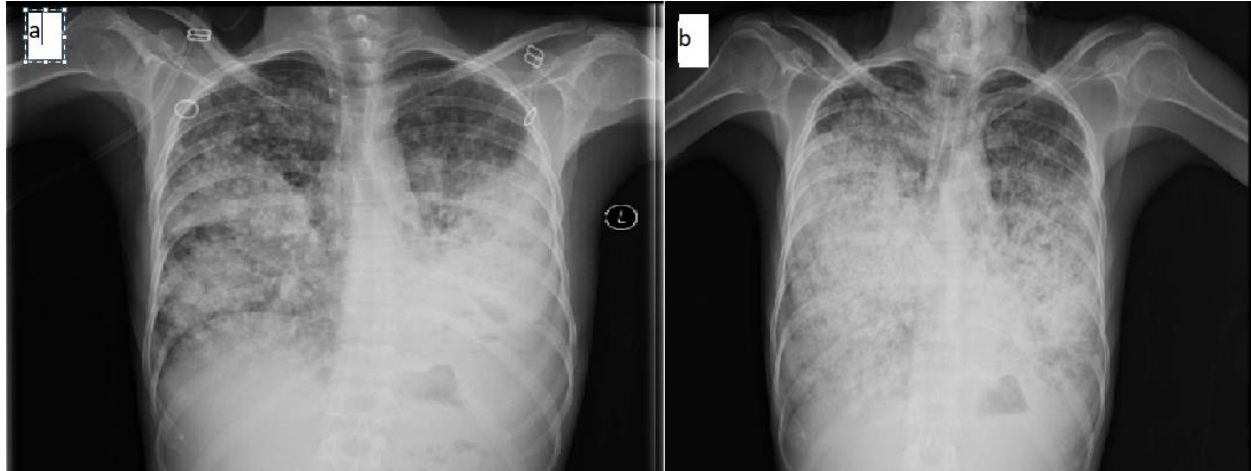
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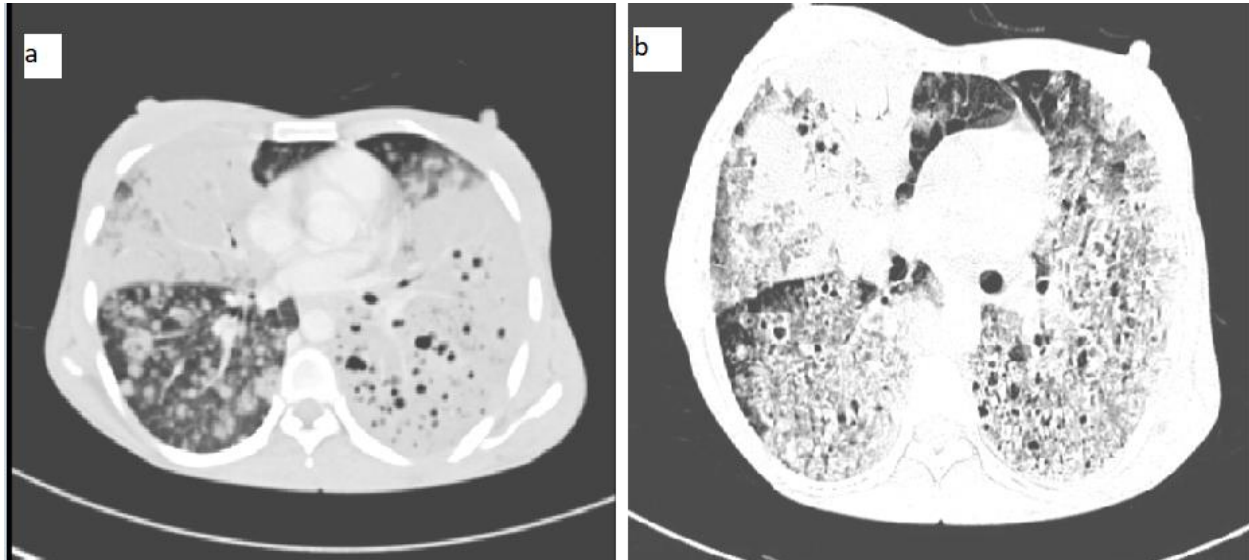


**Figure 1. a)** Chest X-ray Postero-Anterior (PA) view showed left side consolidation with right side mid and lower zone nodules. **b)** Bilateral midzone and lower zone non-homogenous opacity with nodules, which has progressed from initial admission.

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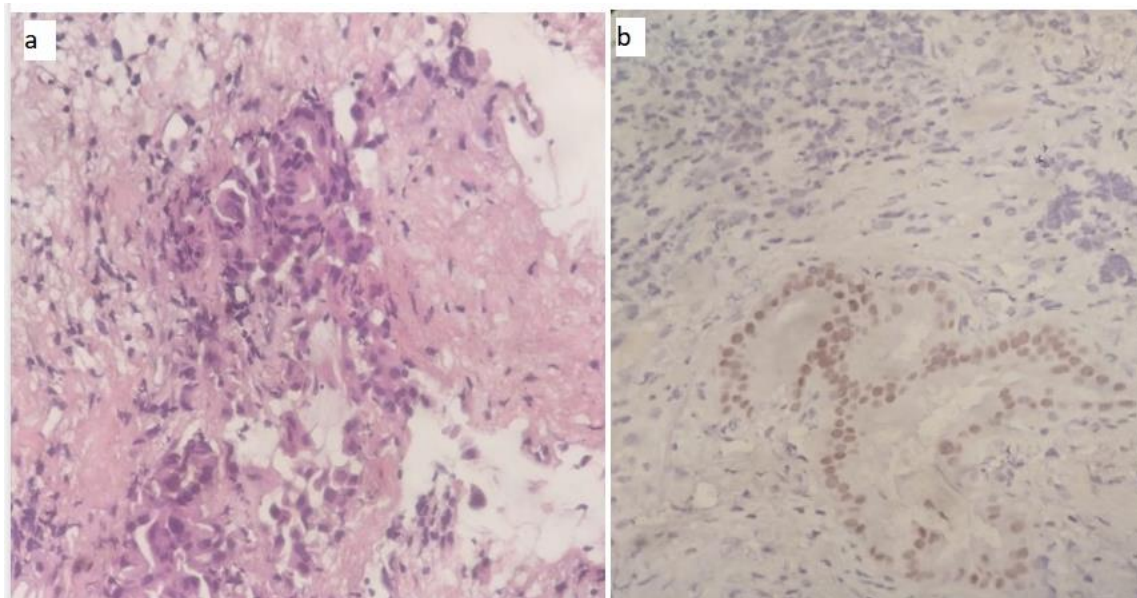


**Figure 2.** a) Contrast Enhanced Computed Tomography (CECT) of the chest showed right upper lobe and left lung necrotizing consolidation with right lung lower lobe cavitating nodules. b) Bilateral all lung lobes necrotizing consolidation, which has progressed from cavitating nodules to necrotizing consolidation.

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**Figure 3. a)** Lung biopsy histopathology image suggestive of adenocarcinoma (HE-400X). **b)** Immunohistochemistry showed Thyroid Transcription Factor (TTF-1) positivity.

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