LETTER TO THE EDITOR

Unmasking Lepidic Adenocarcinoma in a COPD Patient: Overlapping Features with Inflammatory Etiologies

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Dear Editor,

Lepidic adenocarcinoma is a distinct histological subtype of lung adenocarcinoma characterized by neoplastic proliferation along intact alveolar septa with minimal stromal invasion. Although it is generally associated with an indolent clinical course, its presentation often overlaps with infectious and inflammatory pulmonary diseases, posing a significant diagnostic challenge.[1,2] This challenge is particularly pronounced in patients with chronic obstructive pulmonary disease (COPD), in whom worsening respiratory symptoms and pulmonary infiltrates are frequently attributed to infective exacerbations. We report a case of lepidic adenocarcinoma in a patient with COPD that initially masqueraded as an inflammatory pulmonary condition, emphasizing the importance of considering malignancy in patients with persistent or non-resolving respiratory symptoms despite appropriate treatment.

A 61-year-old male, a chronic smoker and known case of COPD, presented to the pulmonary medicine outpatient department with complaints of intermittent low-grade fever, worsening breathlessness, and cough with scanty blood-tinged sputum for 1 week. He also complained of fatigue, generalized weakness, and loss of appetite. There was no history of chest pain, purulent expectoration, or significant weight loss. On examination, grade II clubbing was noted without pallor, icterus, pedal edema, or peripheral lymphadenopathy. His oxygen saturation was 94% on room air, and his temperature was 99.8°F. Respiratory examination revealed bilateral wheezing and basal crepitations. Chest radiography demonstrated multiple bilateral patchy non-homogeneous opacities suggestive of an infective or inflammatory process (Fig. 1).

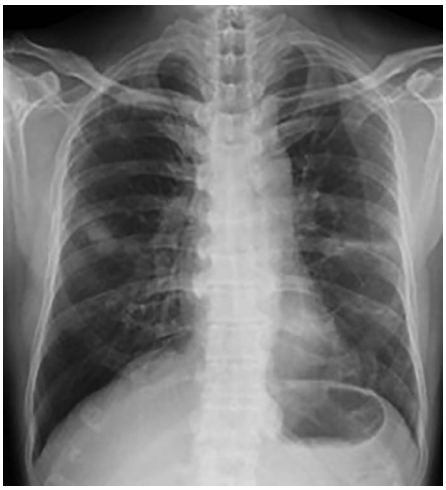

Fig. 1: Chest X-ray PA view showing bilateral patchy nonhomogeneous opacities and bilateral emphysema

Initial laboratory investigations showed elevated C-reactive protein (32 mg/dL), leukocytosis (16.4 × 10^9/L) with neutrophilic predominance (85%), while the remaining routine investigations were within normal limits. Sputum samples were sent for bacterial culture and sensitivity, acid-fast bacilli (AFB) smear, and cartridge-based nucleic acid amplification test (CBNAAT). Considering the clinical presentation and inflammatory markers, the patient was managed as an infective exacerbation of COPD with intravenous ceftriaxone, azithromycin, nebulized bronchodilators, corticosteroids, and supportive care. However, sputum culture revealed only normal respiratory flora, while AFB smear and CBNAAT were negative. Truenat testing for influenza and COVID-19 was also negative, making an infectious etiology less likely.

In view of the atypical presentation and negative microbiological investigations, contrast-enhanced computed tomography (CECT) of the thorax was performed. It revealed multiple irregular soft-tissue nodules with spiculated margins and surrounding ground-glass opacities involving both lungs, along with a few enlarged enhancing mediastinal lymph nodes. The lesion also appeared to involve the parietal pleura, favoring a malignant etiology with radiological staging of T3N1M0 (Fig. 2). The combination of multifocal nodules and surrounding ground-glass opacities broadened the differential diagnosis to include atypical infection, organizing pneumonia, inflammatory lung disease, and primary lung malignancy.[3,4]

Flexible bronchoscopy did not reveal any endobronchial abnormality. Bronchoalveolar lavage (BAL) samples were obtained for microbiological analysis and cytological examination. BAL culture remained sterile, CBNAAT was negative, and cytology was inconclusive. Since the radiological findings continued to raise

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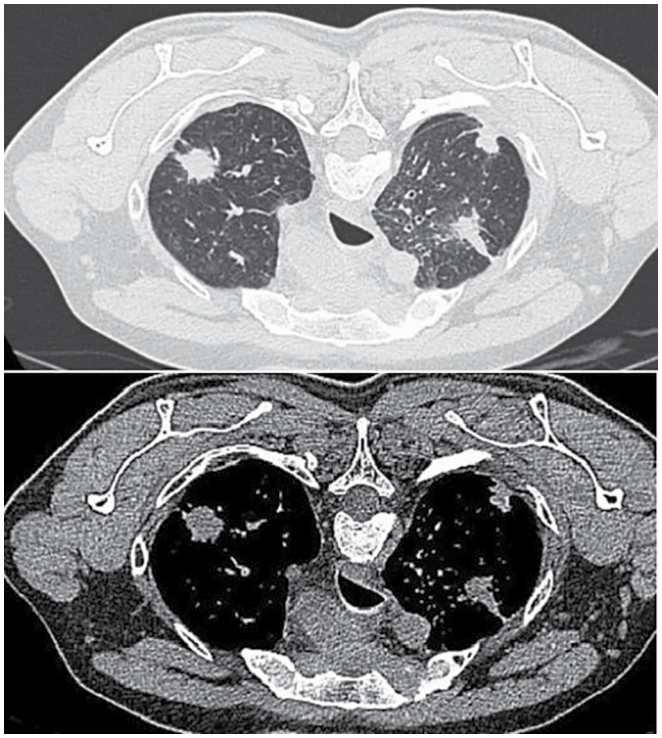

Fig. 2: Contrast-enhanced CT thorax images showing multiple irregular soft tissue nodules with spiculated margins and surrounding ground-glass opacities in bilateral lung fields

suspicion for malignancy despite nondiagnostic bronchoscopic investigations, CT-guided transthoracic biopsy of a right lung lesion was performed. The procedure was complicated by an iatrogenic pneumothorax that was successfully managed with an intercostal drain, following which complete lung expansion was achieved.

Histopathological examination demonstrated atypical cuboidal-to-columnar epithelial cells with hyperchromatic nuclei and eosinophilic cytoplasm arranged in a lepidic growth pattern with focal glandular formation. Areas of desmoplasia and focal necrosis were present, while tumor cells lined intact alveolar septa without significant destruction of the underlying lung architecture, consistent with lepidic adenocarcinoma (Fig. 3).[1,2,4] Immunohistochemistry showed diffuse positivity for cytokeratin-7 (CK-7), thyroid transcription factor-1 (TTF-1), and Napsin-A, confirming primary pulmonary adenocarcinoma with a lepidic growth pattern. The patient was subsequently referred to the Medical Oncology department of a tertiary cancer center for further management.

Patient Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying clinical images.

Acknowledgment

Nil.

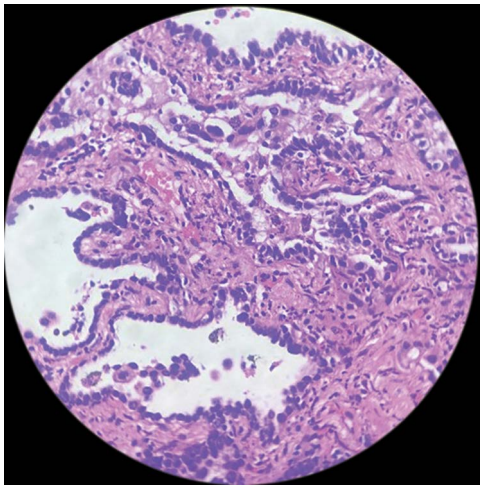

Fig. 3: Microscopic image of lung biopsy specimen showing atypical cuboidal to columnar cells with hyperchromatic nuclei and eosinophilic cytoplasm, arranged in a lepidic pattern with focal glandular formation

Authors' Contributions

Supriya Adiody: Conceptualization, literature review, clinical data collection, manuscript preparation, manuscript review, and critical revision of the manuscript.

Vishnu Narayanan: Clinical management, data collection, literature review, manuscript preparation, manuscript review, and critical revision of the manuscript.

Both authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

AI Declaration

Artificial intelligence tools were not used for the generation, analysis, or interpretation of the scientific content of this manuscript. The authors take full responsibility for the content of the manuscript.

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