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Original Research Article

FROM CONSOLIDATION TO CANCER: RARE CASE OF MUCINOUS ADENOCARCINOMA OF THE LUNG

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ABSTRACT

Background: Invasive mucinous adenocarcinoma (IMA) of the lung is a rare subtype of non-small cell lung cancer. It frequently presents with diffuse consolidations and bronchorrhea, mimicking infections such as tuberculosis and community-acquired pneumonia, contributing to delayed diagnosis.

Case Presentation: A 65-year-old male, chronic beedi smoker and farmer, presented with progressive exertional dyspnea, copious sputum production, loss of appetite, and significant weight loss for two months. Empirical antitubercular therapy was initiated at an outside facility for non-resolving consolidation, despite negative microbiological evaluation. At our center, CT imaging showed bilateral multifocal consolidation with cavitary areas and interlobular septal thickening. Bronchoscopy revealed purulent secretions without endobronchial growth. CT-guided lung biopsy demonstrated mucinous adenocarcinoma with IHC positive for CK7/CK20 and negative for CDX2, SATB2, TTF-1, and Napsin-A. The patient was initiated on Pemetrexed + Carboplatin chemotherapy. In TB-endemic regions, IMA may be misinterpreted as pulmonary tuberculosis or pneumonia. Persistent consolidation should prompt early biopsy to avoid treatment delays.

Keywords: Invasive mucinous adenocarcinoma, Lung cancer, Tuberculosis mimic, non-resolving consolidation, CT-guided biopsy

INTRODUCTION

Mucinous adenocarcinoma of the lung is a rare but distinct histopathological variant of pulmonary adenocarcinoma, accounting for approximately 2–10% of all primary lung adenocarcinomas (1). Previously classified as mucinous bronchioloalveolar carcinoma under the 2004 World Health Organization (WHO) guidelines, it is currently recognized as invasive mucinous adenocarcinoma (IMA) based on its aggressive behavior and unique clinical, radiological, and molecular profile (2). The defining feature of this subtype is the proliferation of mucin-producing tall columnar epithelial cells along alveolar structures, frequently resulting in mucus accumulation within distal airspaces. The lepidic growth pattern with variable stromal and vascular invasion contributes to heterogeneous disease manifestations ranging from solitary nodules to diffuse multilobar involvement (3). IMA stands apart from non-mucinous lung adenocarcinoma on genetic grounds as well. While EGFR mutations are prevalent in typical adenocarcinomas, they are uncommon in IMA. Instead, KRAS mutations predominate in nearly 75% of cases, with occasional NRG1 fusions reported, which have therapeutic implications (4). Due to the predominance of mucin within the tumor, fluorodeoxyglucose positron emission tomography (FDG-PET) may underestimate disease burden, further complicating staging and clinical assessment (5). One of the greatest diagnostic challenges posed by IMA is its radiological mimicry of infectious lung diseases. On high-resolution computed tomography (HRCT), IMA frequently manifests as consolidation, ground-glass opacities, air bronchograms, and sometimes cavitary changes (6). Lesions may be unilateral or bilateral, commonly affecting lower lobes. These findings are difficult to differentiate from pneumonia, organizing pneumonia, or pulmonary tuberculosis (TB). In TB-endemic regions, such as India, this resemblance increases the likelihood of misdiagnosis and delays in appropriate management (7). Non-resolving pneumonia, particularly with copious sputum production or bronchorrhea, should prompt clinicians to consider

neoplastic etiologies including IMA (8).

Clinically, patients often present with chronic productive cough, breathlessness, fatigue, and weight loss symptoms that are nonspecific and frequently attributed to infections. Bronchorrhea, when present, is a valuable yet under-recognized indicator of mucinous tumors (9). Recurrent hospital visits, empirical antibiotic therapy, and even inappropriate antitubercular treatment commonly precede the correct diagnosis. Bronchoscopy may reveal mucinous secretions but often lacks visible endobronchial tumor due to the peripheral nature of the disease. Ultimately, definitive diagnosis relies on histopathological analysis and immunohistochemistry (10). IMA typically demonstrates positive staining for CK7 and CK20, and negative or weak staining for TTF-1 and Napsin-A, aiding distinction from metastatic mucinous carcinomas of gastrointestinal origin (11).

Prognosis in invasive mucinous adenocarcinoma depends on disease distribution and the presence of spread through air spaces (STAS), which is associated with increased recurrence rates (12). Localized disease may be amenable to surgical resection; however, multifocal or bilateral disease generally requires systemic therapy. Unfortunately, due to the predominance of KRAS-driven biology, effective targeted therapies remain limited, and responses to immunotherapy are variable (13).

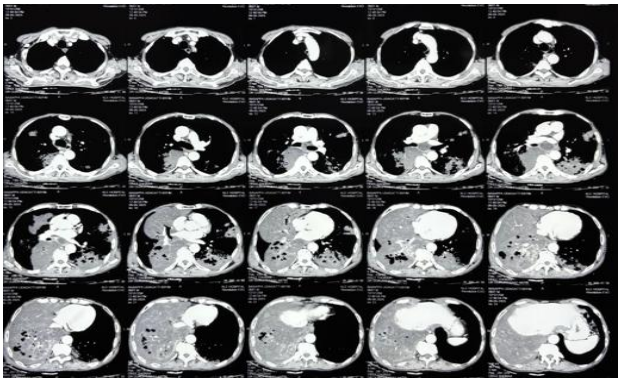
This case exemplifies the complexities of diagnosing IMA within a TB-endemic environment. Persistent radiological abnormalities unresponsive to standard medical therapy demand timely tissue sampling to avoid delays in identifying malignancy. Early recognition, multimodality assessment, and appropriate oncologic management are essential to improving outcomes in patients with this uncommon but aggressive lung cancer subtype.

CASE PRESENTATION

Clinical History: A 65-year-old male farmer with a significant history of chronic beedi smoking presented with a progressive onset of respiratory symptoms over two months. He experienced breathlessness on exertion, initially classified as MMRC Grade 2, which had worsened further over the preceding 15 days. The patient reported a chronic cough with copious whitish, serous expectoration measuring approximately 100 mL per day, accompanied by reduced appetite, unintentional weight loss of more than 5 kg, and generalized fatigue. There was no history of fever, chest pain, wheezing, hemoptysis, palpitations, gastrointestinal complaints, or exposure to individuals with tuberculosis. His past medical history was unremarkable with no known comorbidities and no prior use of inhaled medications. Initial Management and Referral: During multiple earlier consultations at local healthcare centers, he was hospitalized once and received symptomatic treatment. Based on radiological suspicion of pulmonary tuberculosis, and despite negative microbiological testing, empirical antitubercular therapy was initiated. His symptoms continued to progress without clinical or radiological improvement, prompting referral to our tertiary care institution for further evaluation.

Examination Findings: On admission, the patient appeared poorly built and poorly nourished. Vital signs revealed a pulse rate of 96 beats per minute, blood pressure of 100/70 mmHg, respiratory rate of 24 breaths per minute, and oxygen saturation of 86% on room air. Grade 2 digital clubbing was present, but there was no pedal edema or lymphadenopathy. Respiratory system examination demonstrated reduced chest movements on the right side along with the use of accessory muscles of respiration. Percussion revealed dullness over the right infra-axillary and infra-scapular areas, and auscultation revealed bilateral coarse crepitations with markedly decreased breath sounds over the right basal region.

Radiological Evaluation: An earlier high-resolution computed tomography (HRCT) scan performed outside showed segmental areas of consolidation and collapse of the right lower lobe with abrupt narrowing of the corresponding bronchus, accompanied by mild right pleural effusion. Additional subsegmental areas of consolidation were present in bilateral lung fields. A contrast-enhanced computed tomography (CECT) performed at our center later revealed consolidation with cavitary changes and adjacent ground-glass opacities, along with diffuse interlobular septal thickening and branching centrilobular nodules



involving multiple lobes. Necrotic mediastinal lymphadenopathy was also noted, raising suspicion of a non-infectious etiology.

Figure 1: CECT Thorax (Contrast-enhanced CT scan of the thorax showing heterogeneous soft-tissue attenuation and asymmetrical opacification within the upper thoracic region. Correlating with lower cuts demonstrated multifocal areas of consolidation with cavitary components and interlobular septal thickening

in both lungs, consistent with a pneumonic-consolidation pattern secondary to invasive mucinous adenocarcinoma. These findings, in conjunction with the patient's non-resolving respiratory symptoms, raised suspicion of a malignant etiology rather than infectious pathology)

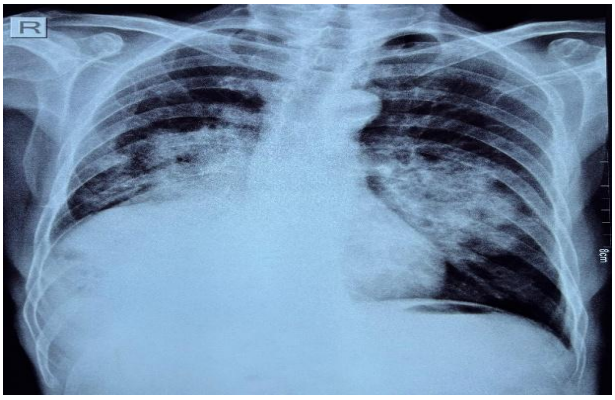


Figure 2: Chest Radiograph (Posteroanterior View) (The chest X-ray demonstrates non-homogeneous patchy opacities predominantly involving the right mid and lower lung zones, with partial silhouetting of the right hemidiaphragm along with non homogenous opacities involving the left mid and lower zones extending from the perihilar regions with sparing of costophrenic and cradiophrenic angles. There is loss of normal bronchovascular clarity and subtle volume loss suggestive of an underlying collapse–consolidation pattern. These imaging findings initially mimicked an infectious process, contributing to the provisional diagnosis of pulmonary tuberculosis; however, the subsequent non-resolving course raised suspicion for an underlying malignancy, later confirmed as invasive mucinous adenocarcinoma)

Bronchoscopy and Laboratory Findings: Bronchoscopy demonstrated thick purulent secretions in the right lower lobe but did not show any endobronchial narrowing or obstructive mass. Bronchoalveolar lavage tested negative for Mycobacterium tuberculosis by GeneXpert assay, and bacterial and fungal cultures did not yield pathogenic organisms. Further investigations including autoimmune screening were negative. A 2D echocardiogram revealed concentric left ventricular hypertrophy with preserved ejection fraction and mild pulmonary arterial hypertension, while abdominal ultrasound showed left renal calculi and basal lung consolidation correlating with thoracic imaging findings.

Histopathological Diagnosis: Due to persistent radiological abnormalities and lack of response to antimicrobial therapy, a CT-guided biopsy of the lung lesion was performed. Histopathology demonstrated lepidic and acinar proliferations of tall columnar mucin-secreting cells with abundant intracellular and extracellular mucin. Immunohistochemical staining was positive for CK7 and CK20 and negative for CDX2, SATB2, TTF-1, and Napsin-A, confirming the diagnosis of invasive mucinous adenocarcinoma of the lung.

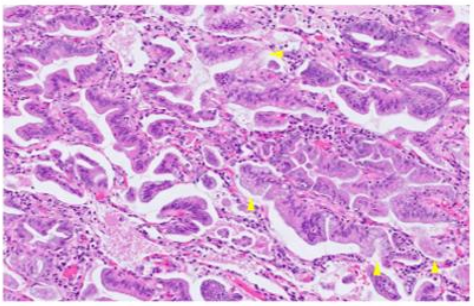


Figure 3: Histopathology of Lung Biopsy (H&E stain, high-power view) (This section shows invasive mucinous adenocarcinoma of the lung characterized by tall columnar tumor cells with basally located nuclei forming lepidic and acinar patterns. There is abundant intracellular and extracellular mucin (yellow arrowheads), producing a complex glandular architecture consistent with a mucin-secreting neoplasm.)

Hospital Course and Treatment: During his hospital stay, the patient received supportive treatment including intravenous piperacillin-tazobactam and linezolid along with supplemental oxygen. After the confirmation of malignancy and in view of multifocal, unresectable disease, systemic anticancer therapy was initiated with a combination regimen of pemetrexed and carboplatin. The patient showed gradual clinical improvement under multidisciplinary oncological care and continued therapy on follow-up.

DISCUSSION

Invasive mucinous adenocarcinoma (IMA) of the lung is a rare subtype of adenocarcinoma, exhibiting distinct histopathological and radiological characteristics that often lead to diagnostic challenges. Its presentation frequently mimics chronic pulmonary infections, particularly in tuberculosis (TB)-endemic regions, where persistent consolidations are readily attributed to infectious etiologies [14]. This case highlights the complexities involved in distinguishing IMA from pulmonary tuberculosis and other infectious processes, emphasizing the importance of timely tissue diagnosis.

The clinical manifestations of IMA are generally nonspecific, with chronic cough, dyspnea, fatigue, and weight loss as common early symptoms. Notably,

bronchorrhea is a more specific but under-recognized feature that results from excessive mucin production by neoplastic cells. The mucus accumulation within alveolar spaces leads to impaired ventilation and contributes to persistent radiographic opacities [9]. In our patient, persistent copious expectoration and non-resolving consolidation despite empirical antitubercular therapy served as crucial clinical clues suggesting an alternative diagnosis beyond infection. Radiologically, IMA often exhibits unilateral or bilateral consolidation, ground-glass opacities, air bronchograms, and occasionally cavitary lesions. These findings overlap substantially with bacterial pneumonia, organizing pneumonia, and pulmonary TB [15]. In endemic settings, the likelihood of a patient receiving empirical ATT is high, as occurred in this case. The multifocal and bilateral nature of changes seen on CECT thorax, combined with necrotic mediastinal lymphadenopathy, raised suspicion for malignancy rather than a purely infectious process. Importantly, the presence of diffuse interlobular septal thickening and branching centrilobular nodules further supported the need for histopathological confirmation [16].

Bronchoscopic evaluation in IMA frequently fails to reveal obstructive lesions due to the peripheral tumor distribution. The absence of endobronchial mass in our patient aligned with previously reported findings [17]. Microbiological investigations, including GeneXpert and cultures, were negative, reinforcing the need to pursue alternate diagnostics. Current guidelines recommend consideration of malignancy in any case of persistent consolidation unresponsive to 4–6 weeks of appropriate therapy, highlighting the importance of early biopsy intervention [18].

Pathologically, IMA is characterized by mucin-producing tall columnar epithelial cells demonstrating lepidic or acinar growth. The immunohistochemical profile plays an essential role in differentiating primary pulmonary lesions from metastatic mucinous adenocarcinomas originating from the gastrointestinal tract [14]. In our case, positivity for CK7 and CK20 with negativity for CDX2 and SATB2 confirmed primary lung origin and excluded gastrointestinal metastasis. TTF-1 and Napsin-A expression are typically weak or negative in IMA, which is another important distinction from non-mucinous adenocarcinoma.

From a molecular standpoint, IMA exhibits a unique driver mutation pattern, with KRAS mutations being the most prevalent and EGFR mutations relatively rare. This pattern influences therapeutic outcomes, as KRAS-driven tumors demonstrate limited benefit from EGFR-targeted therapies. In advanced or multifocal disease, as seen in our patient, systemic chemotherapy remains the primary treatment modality [19]. Pemetrexed-platinum–based regimens have shown modest benefit, while the role of immunotherapy remains under investigation owing to variable PD-L1 expression and reduced immunogenicity due to mucus barriers. Emerging targeted therapies for KRAS G12C mutations may reshape future treatment strategies but remain limited in availability [20].

Prognosis in IMA is influenced by disease stage, presence of spread through air spaces (STAS), and multifocal dissemination. Early-stage, localized tumors can be managed surgically, whereas diffuse or bilateral lesions often carry poorer outcomes. The diagnostic delay observed in many cases due to misinterpretation of radiographic patterns significantly affects patient survival. Therefore, high clinical vigilance is crucial in high TB-burden settings to ensure early detection [21].

This case underscores the importance of multidisciplinary collaboration and timely escalation of diagnostic strategies. Persistent lung opacities, particularly those associated with significant mucus production and lack of microbiological evidence, must prompt suspicion for invasive mucinous tumors. Early histopathological diagnosis and tailored oncologic management are vital to achieving improved outcomes.

CONCLUSION

Invasive mucinous adenocarcinoma of the lung poses a diagnostic dilemma due to its clinical and radiological resemblance to infectious diseases, especially pulmonary tuberculosis in endemic regions. This case illustrates how misclassification of persistent lung consolidation can result in delayed diagnosis and progression of a malignant process. A negative microbiological evaluation in a patient with non-resolving symptoms should prompt further investigation, including advanced imaging and tissue biopsy. Accurate histopathological and immunohistochemical evaluation is essential for distinguishing IMA from metastatic mucinous tumors and guiding appropriate therapy. Early recognition, timely referral, and multidisciplinary cancer management are crucial to prevent therapeutic delays and to optimize survival outcomes in this aggressive and uncommon lung cancer subtype.

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