

The Masked Masquerader - Lung Malignancy Disguised as Fungal Pneumonia

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ABSTRACT

An elderly male without comorbidities presented with complaints of cough with expectoration for 6 months and breathlessness on exertion for 15 days. He had history of weight loss of 5 kilograms in 6 months. Chest X-Ray (CXR) showed bilateral fluffy opacities with areas of consolidation and diffuse nodules. He underwent treatment at an outside clinic in view of suspected *Pneumocystis jirovecii* pneumonia (PJP) after which he showed transient improvement but worsened again. He delayed going to a hospital by 3-4 months and presented to our OPD with worsening symptoms. He underwent routine investigations and was started on antibiotics. Fungal pneumonia was suspected and he was started on anti-fungal therapy. Due to non-improvement of general condition, a contrast-enhanced computerised tomography (CECT) thorax was done, which showed "Multiple bilateral diffuse centrilobular and peripheral enhancing patchy opacities and nodular lesions are noted in segmental and lobar distribution. The lesions show air bronchogram and enhancing pulmonary vessels within" which was consistent with infection and a differential diagnosis of fungal pneumonia or malignancy was suspected. A CT-guided fine needle aspiration cytology (FNAC) of the lesion was done which showed 'non-small cell carcinoma (NSCC) favouring adenosquamous carcinoma'. Patient required further

testing in the form of immunohistochemistry (IHC) but was unwilling for the same and requested discharge against medical advice (DAMA). On follow up with the patient party, it was found that the patient expired 8 days following discharge from the hospital.

BACKGROUND

Bronchoalveolar carcinoma (BAC), a subtype of lung adenocarcinoma, is a relatively rare form of lung cancer, accounting for approximately 2.6-4.3% of all lung cancers. It typically arises in the lung periphery and proliferates along the alveolar walls without causing significant damage to the lung parenchyma. This growth pattern often results in multicentric occurrences, sometimes originating from previously stable scars^[1].

The diagnosis of lung malignancies, including BAC, has evolved with the advent of various cytological techniques. Early and accurate diagnosis is crucial in reducing lung cancer mortality. Bronchoalveolar lavage (BAL), bronchial brushing, and fine needle aspiration cytology (FNAC) are key cytological methods employed. These techniques not only complement tissue biopsies but also offer comparable diagnostic yields. Among these, CT-guided FNAC has been reported to have the highest diagnostic yield, emphasizing its crucial role in diagnosing lung malignancies, including BAC^[2].

The management of BAC differs from other types of lung cancers, primarily due to its unique histological characteristics and disease spectrum, which ranges from histologically pure BAC to adenocarcinoma. Treatment approaches are still evolving, with ongoing clinical trials aiming to provide further insights, particularly regarding the role of limited resection. The use of epidermal growth factor receptor tyrosine kinase inhibitors has shown promise, particularly in patients with advanced or recurrent BAC who have not responded to conventional cytotoxic chemotherapy^[3].

Bronchoalveolar carcinoma has a multicentric appearance and spreads within the lung itself, hence also termed adenocarcinoma in-situ. The radiological challenge is that it may have a similar appearance to that of infectious pneumonias. This case report outlines an elderly man who had chronic cough who was treated as PJP pneumonia outside, treated for fungal pneumonia in-hospital with no improvement and eventually diagnosed as non-small cell lung carcinoma (bronchoalveolar carcinoma)^[4].

CASE PRESENTATION

An elderly male with no known comorbidities presented to the Pulmonary Medicine Department with history of cough for 2 months, insidious in onset, continuous, aggravated on lying down on the right side, not relieved with any medication, associated with expectoration, which was mucoid in consistency, white, copious amount, non-foul smelling,

non-blood tinged. Complaints of breathlessness on exertion for 15 days (modified medical research council (MMRC) Grade I), acute in onset, not aggravated by change in position, no associated factors. Complaints of wheezing was present, on and off with no variation. The patient also gave history of loss of weight, about 5kg over 6 months. No history of fever with chills, chest pain, hemoptysis. No significant family or habitual history^[5]. On examination, the patient was conscious, oriented to time, place and person, was mildly tachypnoeic with use of accessory respiratory muscles, tachycardia with hypoxia maintaining saturation with oxygen therapy via nasal prongs. Grade II clubbing was also seen. On respiratory system examination, the patient had bilateral supraclavicular hollowing, infraclavicular flattening, intercostal muscle retraction, palpation and percussion was normal. On auscultation, bilateral harsh vesicular breath sounds with bilateral rhonchi and coarse crepitations was heard. Investigations done showed increasing trend of total counts. Bacterial and fungal cultures of sputum were negative. CXR done showed 'multiple patchy opacities predominantly in the middle and lower zones of bilateral lung fields with mild deviation of mediastinum to the right side. Bilateral hila could not be detected (Figure 1)^[6].

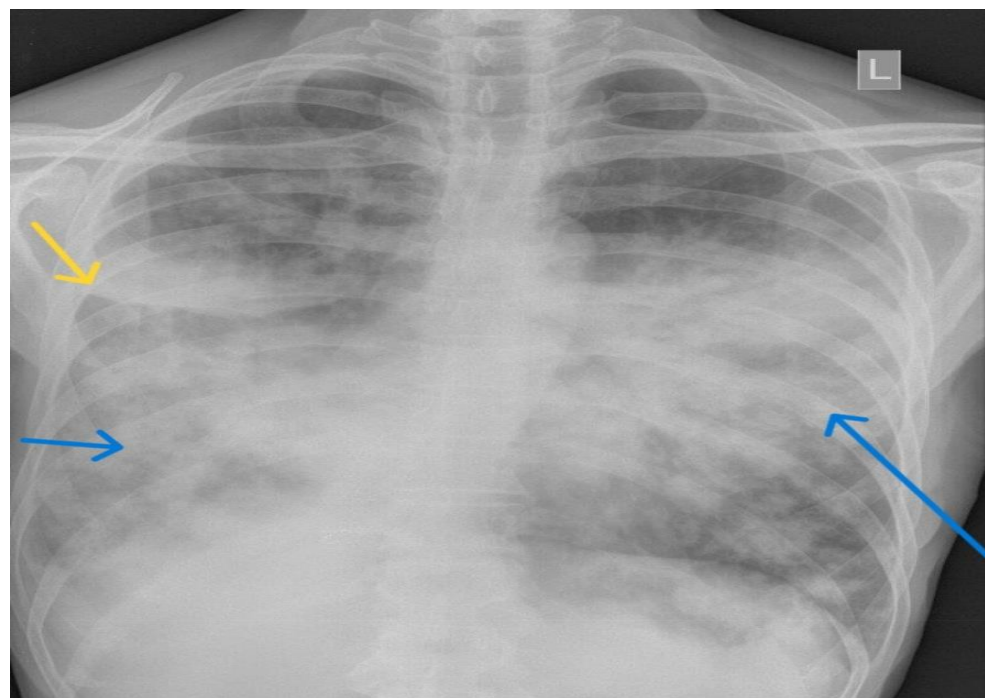


Figure 1: CXR showing fluffy opacities over bilateral chest fields with bulging of right fissure

Serial CXR's during the period over a week showed worsening of opacities. CECT Thorax done showed 'Multiple bilateral enhancing lesions of lung with likely perilesional hematoma with enlarged infra-carinal lymph nodes and loculated right pleural effusion with enhancing pleura (Figure 2,3)^[7].

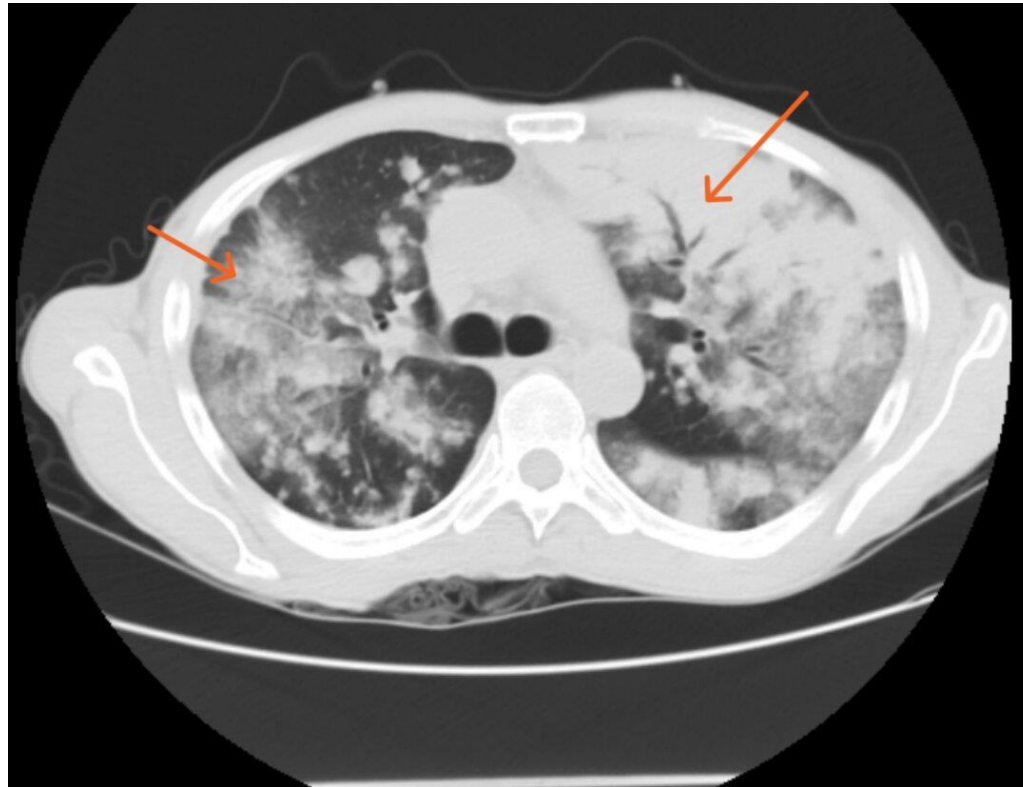


Figure 2: CT Thorax in the lung window showing bilateral fluffy opacities with air-bronchograms, suggestive of fungal pneumonia

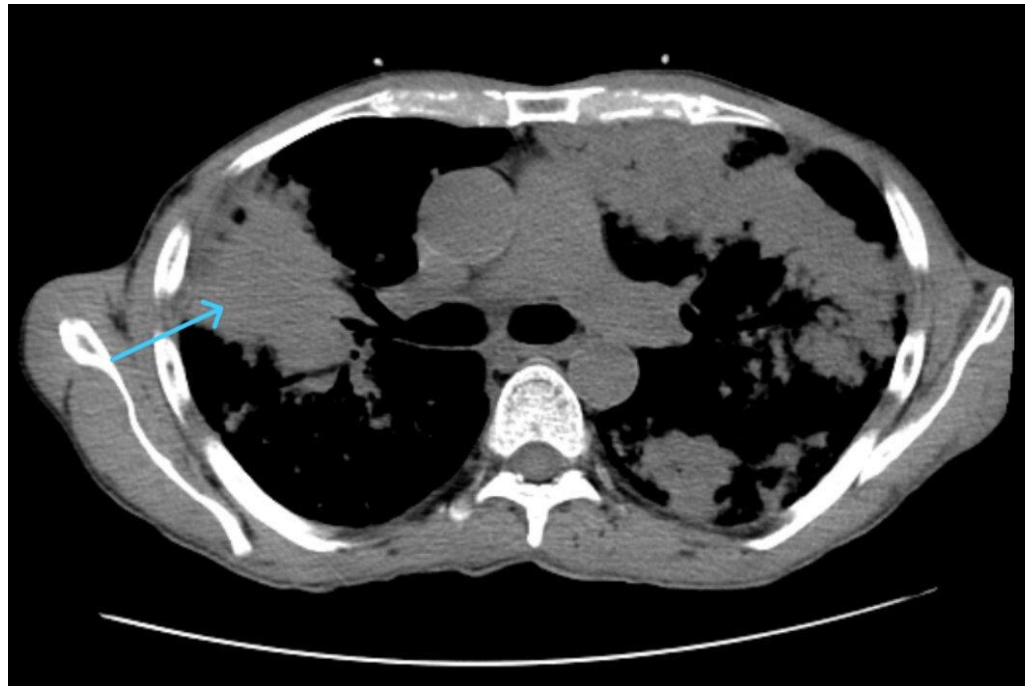


Figure 3: CT Thorax in the mediastinal window showing a mass-like lesion in the right upper lobe from where CT guided FNAC sample was taken.

The CECT was suggestive of Malignant or infective (fungal) etiology following which CT guided FNAC was done which was suggestive of non-small cell lung carcinoma favoring adenosquamous carcinoma (Figures 4,5).

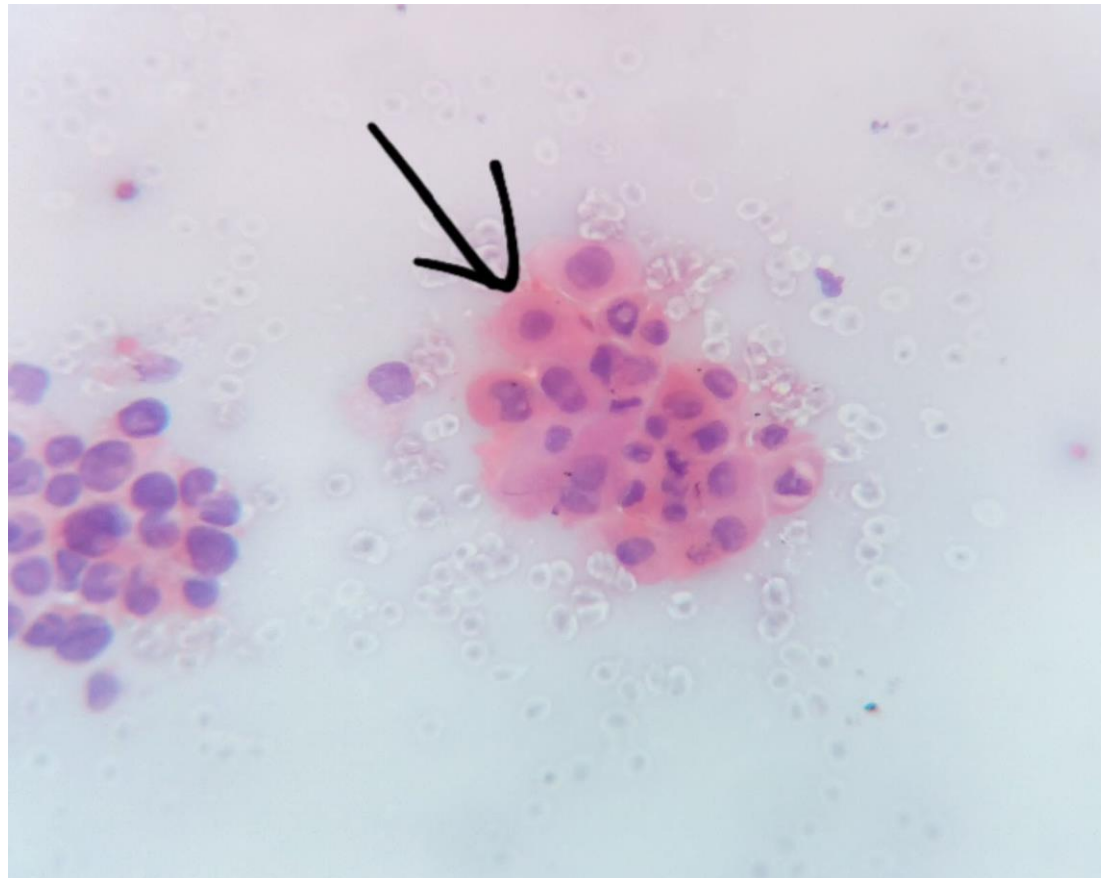


Figure 4: Cytopathology microphotograph showing the squamous cell carcinoma component in adenosquamous carcinoma displaying pleomorphic tumor cells with individual cell keratinisation (PAP stain X 45x magnified)

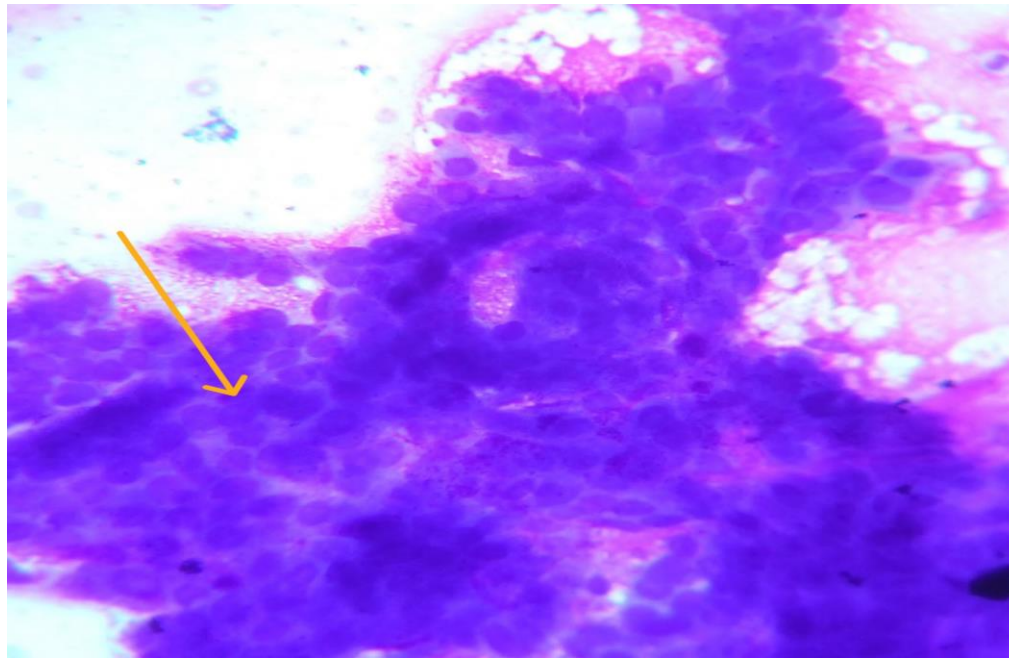


Figure 5: Cytopathology microphotograph showing the adenocarcinoma component in Aden squamous carcinoma displaying tumor cells arranged in cribriform pattern with rounded cytoplasmic margins (MGG Stain X 45x magnified)

Magnetic resonance imaging (MRI) of the brain showed some gliotic changes in the left parieto-occipital lobe without any intracranial metastasis. The patient was prescribed antibiotics and empirically started on antifungal therapy. However, the patient continued to have worsening symptoms which required ICU management. The patient was advised further evaluation in the form of IHC but the patient was not willing for further evaluation and treatment and requested DAMA. It was later found that the patient succumbed to his condition 8 days following discharge

INVESTIGATIONS

CECT Thorax done showed 'Multiple bilateral enhancing lesions of lung with likely perilesional hematoma with enlarged infracarinal lymph nodes and loculated right pleural effusion with enhancing pleura (Figure 2,3).

FNAC done was suggestive of non-small cell lung carcinoma favoring adenosquamous carcinoma (Figure 4,5).

DIFFERENTIAL DIAGNOSIS

Possibility of fungal infection was considered in view of patchy cloudy opacities on CXR (Figure 1). CECT Thorax done was also suggestive of fungal Infection/malignancy (Figure 2,3). Fungal cultures and KOH mount were negative. The patient showed no improvement clinically and radiologically after commencing antifungal therapy which excluded the possibility of fungal infection

TREATMENT

The patient was initially suspected to have PJP pneumonia in an outside hospital for which he was treated with COTRIMOXAZOLE (15mg/kg/day for 21 days) without any signs of improvement. On admission he was treated with IV PIPERACILLIN/TAZOBACTAM 4.5gram every 6th hourly and AMOXICILLIN/CLAVULANIC ACID 1.2gram every 8th hourly and later with IV FLUCONAZOLE 200mg every 24th hourly and other symptomatic treatment. If the patient had not taken DAMA, he would have undergone further evaluation with IHC and then started on treatment from an Oncologist

OUTCOME AND FOLLOW-UP

The patient's condition deteriorated by the time he reported to our hospital. He was advised IHC for further evaluation. He was advised to be shifted to the intensive care unit (ICU) but the patient and attenders refused and requested DAMA. On follow up of the patient, it was found that he had expired 8 days following discharge from the hospital

DISCUSSION

The clinical and radiological picture of fungal infection and pulmonary malignancies have similar characteristics making it indistinguishable. Considering the difference in treatment, it is important to make an accurate diagnosis before commencing treatment.

Radiographically, fungal infections generally present as unilateral or bilateral consolidation, cavities with nodules "air crescent" (target meniscus), fungal ball, homogeneous well demarcated round nodules in the hilar region with calcification with or without hilar lymphadenopathy. The radiological imaging of Bronchoalveolar carcinoma initially presents as a single non solid / ground glass opacity, part solid nodules or as a diffuse consolidation unilaterally or bilaterally.

There have been multiple case reports of infections mimicking pulmonary infections, however it is significantly rare to find malignancy disguised as a pulmonary infection. This case report establishes the fact that malignancy can mimic pneumonia and that care should be taken to establish a solid diagnosis before considering empirical treatment. One case report showed an elderly patient, who was empirically started on treatment with antibiotics for 10 days without any improvement in clinical condition. Since the patient had no investigations suggestive of any active infection, a diagnosis of BAC was suspected and the patient was subjected to a transbronchial biopsy. A diagnosis of malignancy was established following which the patient underwent pneumonectomy and was cancer free for 10 months, which recurred and eventually died^[1].

A case study in early 2022 showed a patient admitted with skin lesions. CT chest done showed multiple nodules with cavities suggesting infective etiology following which the patient was treated for pulmonary fungal infection. The patient's clinical and imaging parameters worsened following which biopsy of the skin and lung lesion was done and sent for histopathology (HPE) which indicated malignant melanoma^[2].

A study at Stanford University Medical Centre showed the occurrence of invasive pulmonary fungal infections, namely aspergillosis, cryptococcosis and mucormycosis in patients with current or previously diagnosed non-small cell lung cancer (NSCLC). The similar radiological patterns seen made it difficult to distinguish if the findings were a recurrence of malignancy, progression of the disease or a super-added opportunistic infective pathology^[3].

A case report of a middle-aged woman with pulmonary symptoms suggestive of infective etiology, who underwent antimicrobial therapy and was later suspected to have Pulmonary tuberculosis and treated with Antitubercular treatment (ATT) without any response to treatment. On evaluation CT Thorax and Positron emission tomography (PET) CT showed a cystic mass with mediastinal lymphadenopathy. The patient was subjected to FNAC and mediastinoscopy on suspicion of malignancy but showed no malignancy. On exploratory thoracotomy, a mass lesion was located and tissue was sent for analysis which was reported as adenocarcinoma. The patient went through surgical resection of and lymph node dissection^[4].

A case series of four infective pulmonary cases mistaken for malignancy was reported. An elderly male with CT finding of a mass lesion who was later diagnosed with Actinomycosis with CT-guided biopsy, An elderly female with signs and symptoms suggesting a pancoast tumour was later diagnosed as mucormycosis. Another elderly male with radiographic imaging showing ill-defined cavitating solitary mass lesion in the left lower zone with loculated pneumothorax adjacent to the lesion suggestive of peripheral bronchogenic carcinoma. A CT-guided biopsy done revealed granulomas suggestive of pulmonary tuberculosis. A middle-aged female with radiographic findings of consolidation with effusion in right lower zone with a well-defined mass in the region of the right lower lobe bronchus suggesting a diagnosis of central bronchogenic carcinoma.

Bronchoscopic biopsy confirmed growth of nocardiosis. In all the above case reports, the patient presented with non-specific pulmonary symptoms and radiological imaging which raised suspicion of malignancy. However, biopsy done has confirmed diagnosis of an infective etiology^[5].

Our case report establishes the need for confirmation of the diagnosis when suspicion of malignancy is present to distinguish between malignancy or a chronic infective etiology.

LEARNING POINTS/TAKE HOME MESSAGES

- This case report shows that lung malignancies can present mimicking fungal pneumonia.
- Suspecting malignancy is important if an aged patient reports with chronic persistent symptoms.
- It is important to keep clinical suspicion for malignancy especially if patient has no previous comorbidities which could predispose to fungal pneumonia.
- The diagnosis of lung pathology should not be established based only on radiological diagnosis.
- When a long-standing presumed condition, such as pneumonia does not have any evidence leading to a definitive diagnosis and does not respond to appropriate treatment (antibiotics, antifungals), cytopathology or histopathology should be considered to rule out malignancy or establish a diagnosis

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