



REACTIVATION OF TUBERCULOSIS COEXISTING WITH SMALL CELL CARCINOMA

Pulmonary Medicine

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ABSTRACT

Lung cancer is the leading cause of cancer related deaths and Tuberculosis is the leading infectious killer. The association between the two has been studied previously. The most common association has been found with squamous cell carcinoma followed by adenocarcinoma. The chances of this association were also found to increase in cases of reactivation of tuberculosis compared to new cases. However, only a few studies have reported the association between tuberculosis and small cell carcinoma in the past. We hereby report a case of small cell carcinoma, diagnosed in a patient with reactivation of pulmonary tuberculosis based on clinical and radiological suspicion and confirmed by histopathology. However, whether the carcinoma arose from the residual TB lesion could not be ascertained. Because of rare association of small cell carcinoma with tuberculosis especially in a treated patient of tuberculosis we report this case. It should prompt the clinicians to have a high degree of suspicion to rule out alternative or coexisting diagnosis in treated cases of tuberculosis and to not merely limit themselves to a single diagnosis for optimal patient care.

KEYWORDS

Reactivation, Tuberculosis, Small Cell Carcinoma, Coexistence

INTRODUCTION

Lung cancer has emerged from a rare disease to the 2nd leading cause of global cancer incidence after breast cancer : 2 million diagnosis and 1.8 million deaths. ^[1] However, it remains the leading cause of cancer related mortality. Small Cell Lung cancer comprises only 15% of lung cancer cases, but has high mortality and 5 year survival below 7%. ^[2]

Tuberculosis, one of the leading infectious killers accounted for an incidence of 10.6 million and 1.6 million deaths in 2021. Chronic inflammation with TB leads to release of cytokines like TNF alpha, interleukin 1,6,3,4 and ROS resulting in fibrosis causing DNA damage and activation of oncogenes. ^[3]

Onset of lung cancer in the area of healed pulmonary tuberculosis can stimulate reactivation of TB by lysis of old healed/calcified lesion. It can also be a result of immunosuppression and release of cytokines- TNF alpha, TGF beta, IFN gamma, interleukins 10 and 6.

The coexistence between lung cancer and TB was first studied by Bayle in 1810. ^[4] Most common association of TB is found with squamous cell or adenocarcinoma. We report a case of reactivation of pulmonary tuberculosis coexisting with small cell carcinoma because of its rarity.

CASE REPORT

A 54 year old male smoker, treated twice for pulmonary tuberculosis in 2015 and 2021, presented with history of cough, left sided chest pain and loss of weight for 1.5 months. He had no comorbidities. General physical examination was within normal limits except for grade 2 clubbing, tachycardia (PR- 105 bpm) and tachypnoea (RR-24). No lymphadenopathy. Signs of left sided pleural effusion were present. Scar of previous Eloesser flap procedure done in 2015 was present on left side of the chest.

Haematological investigations revealed mild anaemia (Hb -10.6) Leucocytosis (TLC – 14,240, Polymorphs 68, Lymphocytes 21), ESR (80). LFT and RFT were within normal limits.

Chest Xray showed left whiteout lung, left main bronchus cut off, left costophrenic angle not visualised and mild tracheal deviation to left. Right lung appeared hyperinflated, calcified lesions in the right upper zone and mild right costophrenic angle blunting.



Fig 1: Scar from Eloesser flap procedure



Fig 2: Image of Chest Xray

USG Abdomen and Thorax was suggestive of hepatomegaly with hypoechoic lesions in right lobe of the liver and moderate left sided pleural effusion with thick septations.

CECT chest revealed narrowing and cut off of left upper and left lower lobe bronchi with a soft tissue mass (heterogenous lobulated measuring 5.3 x 4.6 cm) in this region with mediastinal involvement and complete collapse /consolidation of distal left upper and lower lobes. Loculated left pleural effusion and mild right pleural effusion.

Fibrocalcific and cavitary lesions in the right lung . Multiple hypodense lesions in the visualised sections of the liver, upper abdominal lymph nodes, sub centimetric mediastinal lymph nodes and lytic lesions in the left 9th rib.

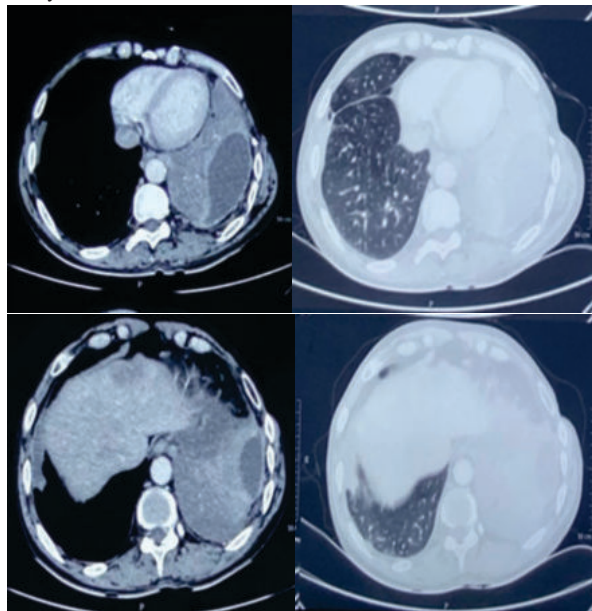


Fig 3,4,5,6 : Showing CECT Chest Cuts With The Above Mentioned Findings

Pleural Aspiration and Bronchoscopy were done. Pleural fluid findings: CBNAAT – MTB detected , Rifampicin Resistance not detected. No Malignant Cells, ADA 106.5, Lymphocytes 65, Neutrophils 35, Protein 3.91 g/dL, No organisms seen on gram stain , AFB negative, pH 8.

Bronchoscopy revealed an irregular growth partially occluding the left mainstem bronchus with mucous secretions. BAL, Cytobrush and Biopsy were taken from the growth.

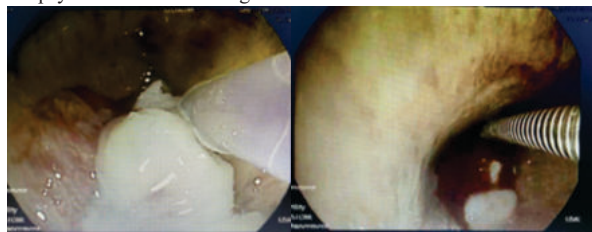


Fig 7 and 8: showing Cytobrush and Biopsy samples being taken from the growth in left main bronchus

Histopathology was suggestive of small cell carcinoma. BAL AFB was negative. MTB was not detected on BAL CBNAAT. Cultures grew no organism.

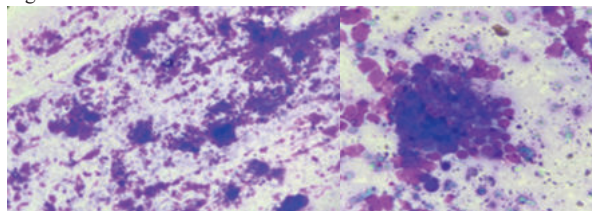


Fig 9 and 10: HPE showing Leishman and Giemsa stain at 10x and 40x magnification respectively

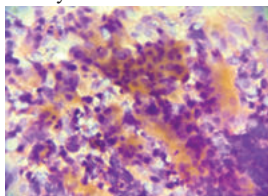


Fig 11: HPE showing Papanicolaou stain 40x magnification

The patient was started on ATT as per NTEP protocol. He had a performance status of ECOG score 3 and Karnofsky score 60. He was advised further palliation/management, however the patient refused any management for carcinomatous condition. On follow up, it was known that he had died of his condition 1.5 months after diagnosis.

DISCUSSION

Our patient, a smoker, suffered TB on two occasions with residual right sided fibrocalcific lesions and Eloesser flap scar for left sided pleural effusion. He could have developed small cell lung cancer since he fits into the profile of a middle aged smoker or as a result of scar carcinoma. Carcinoma could have led to immunosuppression or invaded old healed tuberculous lesion causing reactivation and left pleural effusion. Pleural fluid CBNAAT showed MTB detected with no rifampicin resistance. Small cell carcinoma is rapidly metastasising which possibly caused seedling of pleura leading to malignant pleural effusion. However, our patient's pleural fluid showed CBNAAT positivity but no malignant cells. But, rib erosion, hypodense liver lesion, enlarged abdominal and mediastinal lymph nodes pointed towards stage IV disease. Pleural biopsy, and confirmation of aetiology of rib and liver lesions was advised but the patient refused further evaluation. Hence in the present case it is evident that the patient had recurrence of TB because of immunosuppression due to small cell lung cancer but coexisting malignant aetiology or secondaries could not be confirmed. Development of carcinoma on residual tubercular lesion although possible, could not be established.

Meta-analysis by Liang *et al.* from 1966 to 2009, found significant association of coexistent TB with adenocarcinomas but not with the squamous and small cell type.^[5] Dacosta and Kinare's study estimated the prevalence of coexistence of TB and lung cancer at 13.1% Histology was: undifferentiated carcinoma (76%), adenocarcinoma (56%), epidermoid carcinoma (5.44%).^[6] A 5 year study by Vesna Cucik showed the most common histopathological type was planocellular carcinoma - 13 cases, followed by squamous cell carcinoma - 8, adenocarcinoma - 7 and small cell carcinoma - 6 cases (17.65%).^[7]

Studies by Hara *et al.*, Aoki and Tamura *et al.* all estimated incidence of active pulmonary TB in lung carcinoma patients to be 2.22% and 1-2% respectively, with squamous cell type being the most common.^[6]

Antonis *et al.* found prevalence of active TB was 8-10 times higher in lung cancer patients compared with the general population. Studies by Aoki *et al.* and Chen *et al.*, found active pulmonary TB was significantly higher among lung cancer patients with old TB lesions or a past history of TB than in lung cancer patients without such lesions or history (5.6% vs 0.52%).^[6] Also, an active TB diagnosis was associated with more advanced lung cancer stages. These findings can be reflected in our case.

In several studies like those by Vesna Cucik *et al.* and Antonis *et al.* male predominance was found with the median age of TB cases with lung cancer at 60±14.1 years, also seen in our case.^[6,7]

There have been conflicting studies based on the correlation of occurrence of lung cancer and site of old TB. Xie *et al.* suggested occurrence of lung cancer was highly correlated to the site of TB, Chen *et al.* reported that in most patients, lung cancer and TB lesions were ipsilateral. Tamura *et al.* deduced that the location of lung cancer and TB to be independent.^[6] Our case findings suggest but do not confirm that carcinoma arose from the residual TB lesion.

As in our patient with a history of Old Koch's once reactivation is confirmed clinicians might miss underlying malignancy. But in our case we further confirmed malignant aetiology. This emphasises the importance of ruling out alternative aetiological diagnosis as a part of holistic approach.

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