



Respiratory Medicine

A RARE CASE PRESENTATION OF EXTRAPULMONARY TUBERCULOSIS WITH NEUROENDOCRINE TUMOR - CASE REPORT.

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ABSTRACT Tuberculosis associated with lung malignancy is a rare condition that can coexist, and there clinical presentations are indistinguishable; leading to delay in diagnosis and treatment of lung malignancy. A 54-year-old male patient presented with breathlessness on exertion, chest pain and dry cough for 15 days. Chest X-ray-PA and USG Thorax were suggestive of left-sided pleural effusion. Pleural fluid investigations revealed tubercular pleural effusion. HRCT Thorax was suggestive of soft tissue attenuation lesion and loculated pleural effusion of the left side. As it was identified that the pleural fluid is tubercular, the patient was started on FDC4ATT-3 tabs/day. CT-guided biopsy was done which was suggestive of a Neuroendocrine tumour (WHO grade 1) and the final diagnosis was confirmed by immunohistochemical analysis.

KEYWORDS : Extrapulmonary Tuberculosis, Pleural effusion, Neuroendocrine tumor

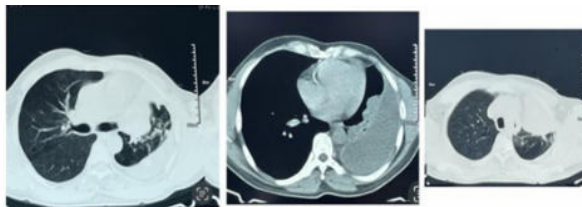
INTRODUCTION:

Tubercular pleural effusion and lung malignancy are two pathological conditions that can rarely be present together, there coexistence is relatively uncommon, occurring in less than 5% of cases and as they have similar signs and symptoms, it may lead to delay in diagnosis and treatment. So being aware of this condition can help improve prognosis by making diagnosis earlier and starting treatment early.

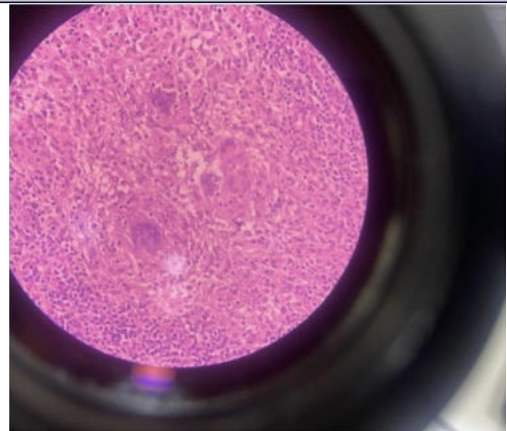
Case History: 54 year old male patient presented with symptoms of breathlessness on exertion initially MMRC grade II, later increased to MMRC grade III since 15 days, left-sided chest pain since 15 days and dry cough since 8 days. No history of hemoptysis, fever, weight loss or loss of appetite. There was no history of pulmonary tuberculosis in past. The patient has occasionally been alcoholic for 10-15 years with no significant family history.

Clinical Findings: The general survey revealed no abnormality. His temperature was 97.2F, PR-84/min, RR-22/min and BP-120/80mmHg. Examination of the respiratory system revealed diminished movement of the chest wall on the left side, apical impulse in the left 5th intercostal space, 1.5cm lateral to left midclavicular line, stony dull percussion over the left chest wall, on auscultation absent vesicular breath sounds on the left side, suggestive of left-sided pleural effusion. Examination of other systems revealed no abnormality.

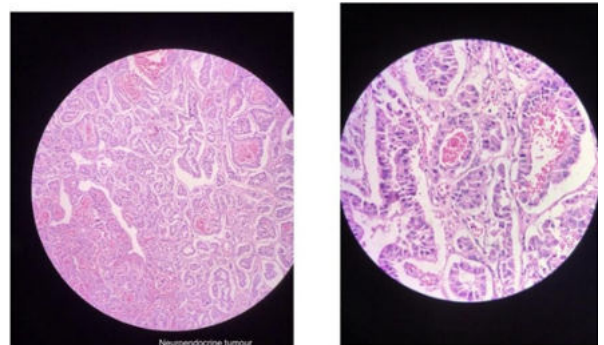
Diagnostic Assessment: Complete hemogram was within normal limits. Chest X-ray-PA revealed left-sided pleural effusion as shown in figure 1. USG Thorax was suggestive of moderate left-sided pleural effusion as shown in figure 2. Pleural fluid was sent for investigations- Lights criteria-0.86 that is suggestive of exudative fluid, cytology-mixed inflammation and CBNAAT was suggestive of Mycobacterium Tuberculosis detected, Rif resistance not detected. Pleural fluid cytology was suggestive of mixed inflammation. HRCT Thorax was done as shown in figure 3 which was suggestive of soft tissue attenuation lesion in the left upper lung lobe with abrupt bronchial cut-off likely suggestive of Neoplastic aetiology- Carcinoma Lung and loculated pleural effusion on the left side.



HRCT showing-(1) Soft tissue attenuation lesion in the left upper lung lobe with abrupt bronchial cut off likely suggestive of Neoplastic etiology- Carcinoma lung.
(2) Loculated pleural effusion on left side.



Photograph of histopathology of pleural biopsy tissue showing central caseous necrosis, Langhans giant cells, epithelioid cells, surrounded by lymphocytes suggestive of tuberculosis



Photograph of Histopathology of pleural biopsy tissue showing Neuroendocrine tumor WHO grade -1

Therapeutic Intervention: USG guided therapeutic tap was done and 100ml of thick yellow coloured fluid was aspirated. USG guided pigtail insertion was done on 28/11/22 and around 500ml fluid was drained. CT guided biopsy of the left lung mass was done and biopsy sample was sent for histopathological examination which was suggestive of well differentiated Neuroendocrine tumor (Carcinoid) WHO Grade I. Immunohistochemistry was done suggestive of PCK, synaptophysin and chromogranin positive, TTF 1 negative. The proliferation marker protein Ki-67 labeling index was positive (2%). These results were consistent with neuroendocrine tumour, grade I.



Tubercular pleural effusion was diagnosed, so patient was registered under NTEP-DOTS and initiated on Fixed Drug Combination ATT according to weight band. As patient's weight was 47kg he was started on Intensive phase of ATT- Isoniazid 225mg, Rifampicin 450mg, Pyrazinamide 1200mg, Ethambutol 825mg once daily for 2months followed by Continuation phase Isoniazid 225mg, Rifampicin 450mg, Pyrazinamide 1200mg, Ethambutol 825mg once daily for 4 months. Left lung lobe Lobectomy was planned.

DISCUSSION:

India is tuberculosis endemic zone and most common cause of pleural effusion is tuberculosis. Tubercular pleural effusion is exudative and is lymphocyte predominant. Tubercular pleural effusion is suspected when pleural effusion ADA (Adenosine deaminase) levels are more than 40U/L. As in our case ADA levels were more than 40U/L, pleural fluid was tubercular in origin. However CECT thorax, pleural fluid cytology, thorascopic biopsy and immunohistochemistry are must to confirm the diagnosis and rule out malignancy.

Diffuse malignant mesothelioma is the most common primary malignant tumor of pleural tissue¹. Most common neoplastic lesions of pleura is metastatic carcinoma of pleura². Malignant pleural tumors present with pleural nodules or pleural effusion.

But clinical features of inflammatory lesions of pleura, metastasis, Benign tumors and primary malignant tumor of pleura are indistinguishable. Therefore, cytological and biochemical analysis of pleural fluid, histopathology of pleural biopsy tissue and Immunohistochemistry of pleural tissue are essential to establish exact cause of pleural pathology.

Neuroendocrine tumors account for about 0.5% of all newly diagnosed malignancies.³ Pulmonary neuroendocrine tumors are rare, accounting for 1-2% of all invasive lung malignancies and involve about 20-25% of primary lung malignancies.^{5,9} Their prevalence has increased by 6% per year over the past 30 years. They originate from hormone producing cells of neuroendocrine system and are most commonly seen in gastrointestinal tract, brain, and lungs^{3,4}.

Neuroendocrine tumors of lung arise from Kulchitzky cells of bronchopulmonary mucosa⁵. Neuroendocrine differentiation is considered if at least one among following features is present: 1. demonstration of numerous dense core membrane bound granules by electron microscopy or 2. Argrophilia the demonstration of neuron-specific enolase or 3. Other neuropeptides like synaptophysin or chromogranin A by immunohistochemistry⁶. The carcinoid syndrome presentation includes flushing, wheezing, anxiety, vomiting and hypotension due to production of 5-hydroxytryptamine, bradykinin, prostaglandin, etc. This syndrome always reflects metastasis of carcinoid tumor, usually to liver. Other rare manifestations includes Zollinger-ellison syndrome, hyperinsulinemia and associated with MEN-I⁷. None of these above mentioned features were present in our patient who presented with non specific symptoms such as cough, chest pain and breathlessness which lead to delay in the diagnosis and treatment. Occurrence of pulmonary carcinoid tumor and tuberculosis is very unusual. Although all histological types of lung cancer can coexist with tuberculosis, only few coexisting cases of neuroendocrine tumor and tubercular pleural effusion have been reported in the literature, possibly because the pulmonary carcinoid tumors are rare tumors. In our case diagnosis was confirmed by immuno histochemistry which showed positive for synaptophysin and chromogranin and occasionally for Ki-67 but negative for TTF-1⁷. Therefore, the tumour was malignant and of neuroendocrine origin- as synaptophysin-positive round to oval cells present.

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