CASE REPORT

# Mediastinal Lymphadenopathy in Malignancy: Metastatic or Granulomatous?

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**Abstract**

Mediastinal lymphadenopathy in patients with malignancy may not be always metastatic disease. We present three patients with proven thoracic or extra thoracic malignancies with mediastinal lymphadenopathy which were subsequently proven as granulomatous lymphadenitis by endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA). The objective of the current report is to emphasise that granulomatous lymphadenitis should be considered as an important differential diagnosis in such patients especially in tuberculosis endemic countries like India.

**Key Messages:** Granulomatous lymphadenitis should be considered as an important differential diagnosis in patients with coexistent intra or extra thoracic cancer, more so in tuberculosis endemic countries.

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**Introduction**

Lymph node enlargement in newly diagnosed or treated malignancies is often thought as metastatic lymph nodes. There are few case reports and studies in the literature showing coexistence of benign conditions such as tuberculosis causing cervical or axillary lymphadenopathy in patient with proven head and neck, lung or breast malignancies respectively.1,2 It might be a similar case for mediastinal lymphadenopathy in patients with thoracic or extra thoracic malignancies. Mediastinal lymph node sampling is warranted to avoid misdiagnosis. We present three patients having thoracic or extra thoracic malignancies with mediastinal lymphadenopathy subjected to endobronchial ultrasound guided transbronchial needle aspiration and found to have granulomatous lymphadenitis on histopathology.

**Case 1**

A 65 year old female was admitted with history of recurrent haemoptysis for two months. She had low grade fever and weight loss of 5 kilograms over 2 months and history of treated pulmonary tuberculosis 10 years prior to current admission. Haemoglobin was 7.8 gm/dl. Sputum smears were negative for acid fast bacilli. Computed tomography (CT) thorax revealed fibrotic lesions in right upper lobe with mediastinal lymphadenopathy. Whole body positron emission tomography (PET) CT showed FDG uptake in pretracheal, paratracheal and subcarinal lymph nodes. Flexible bronchoscopy showed irregular mucosa and narrowing of right upper lobe bronchus. Endobronchial ultrasound – transbronchial needle aspiration (EBUS-TBNA) from mediastinal lymph nodes was performed. BAL revealed atypical cells and were negative for acid fast bacilli. Transbronchial biopsy from right upper lobe showed poorly differentiated adenocarcinoma. Mediastinal lymph node aspirate showed granulomatous inflammation without any malignant cells. Tuberculosis PCR was positive in lymph node aspirate. This case turned out to be malignancy with co-existing tuberculosis.
Case 2

41 year old female who had undergone modified radical mastectomy and received adjuvant chemotherapy for carcinoma left breast one year ago presented with dry cough, chest pain and weight loss for one month, without any fever, breathlessness or haemoptysis. There was no history of tuberculosis in the past. Her clinical evaluation including vitals and systemic examination were unremarkable. CT scan of the chest showed left paratracheal and subcarinal lymphadenopathy. She underwent EBUS-TBNA for assessment of the mediastinal lymphadenopathy. TBNA cytology showed necrotising granulomas and aspirate was positive for TB-PCR. Patient was started on anti-tuberculosis treatment and showed good clinical response on follow-up.

Case 3

A 50 year old female who has completed three cycles of chemotherapy for advanced carcinoma of ovary recently, presented with dry cough and exertional breathlessness for one month. She had no history of fever, haemoptysis, and weight loss. Clinical examination and routine haematological parameters were normal. Chest X-ray revealed mediastinal widening and subsequent CT thorax showed subcarinal and right paratracheal lymphadenopathy. Patient had metastatic pelvic, retroperitoneal and mediastinal lymphadenopathy on PET CT (Figure 1). After three cycles of chemotherapy tumour markers were normal but pelvic and mediastinal lymph nodes were still positive on PET CT (Figure 2). Endobronchial ultrasound – transbronchial needle aspiration was performed and the cytology revealed necrotising granulomas suggestive of tubercular aetiology. No malignant cells were noted on cytology and PCR for tuberculosis was positive in the lymph node aspirate. Patient was started on anti tuberculosis treatment.

Discussion

Mediastinal lymphadenopathy is always a diagnostic dilemma especially in a clinical background that influences the diagnosis. In a recently conducted...
study which prospectively analysed mediastinal and hilar lymphadenopathy, 63 out of 101 patients (65%) were found to have malignancy and remaining 35% of patients had benign diseases including 4% of patients having tuberculosis. Co-existence of a malignant disease may increase the possibility of an enlarged mediastinal lymph node to be metastatic but it may not be true for all patients. In a recent analysis evaluating mediastinal lymphadenopathy in patients with extra thoracic malignancies, only in 40 out of 59 (66%) patients, lymphnodes were proven to be of malignant aetiology. Therefore in a case of mediastinal lymphadenopathy in a clinical background of a malignancy, differential diagnosis should include both benign and malignant diseases. PET CT can also be positive in tuberculous lymphadenitis. Hence, tuberculosis is an important differential in tuberculosis endemic country. Mediastinal lymph node sampling using mediastinal ultrasound can be helpful to differentiate metastatic from benign condition like tuberculosis.

Tuberculous mediastinal lymphadenitis either may be associated with pulmonary tuberculosis or may be a primary disease of lymph node. A study has shown that incidence of lymph node tuberculosis without pulmonary involvement was 5.1%, of which 1.3% of patients had isolated mediastinal lymphadenopathy. Mediastinal tuberculous lymphadenitis may manifest with dysphagia, stridor, cough, breathlessness and chest pain. It has been estimated that incidence of mycobacterial infection in cancer patients was three to five times higher than the general population in an institutional study. Malignancy and anticancer chemotherapy are risk factors for development of tuberculosis and poor prognostic factors in tuberculosis patients. Impairment of host defense mechanisms, poor nutrition, debility and immune suppression by chemotherapeutic agents have been proposed as attributing factors for the higher incidence of tuberculosis in patients with malignancy in tuberculosis endemic areas.

Various techniques are available for sampling mediastinal or hilar lymphadenopathy like mediastinoscopy, CT-guided percutaneous needle aspiration, conventional bronchoscopic transbronchial needle aspiration (TBNA), CT-guided TBNA, transoesophageal ultrasonograph guided needle aspiration. Real time endobronchial ultrasound guided TBNA (EBUS-TBNA) is safe and has a good diagnostic yield.

The findings of our reports highlight that in a tuberculosis endemic country, tuberculosis could be the diagnosis one year after malignancy, concomitantly during the diagnosis of malignancy and also during treatment of malignancy with chemotherapy.

Conclusion

In a scenario of newly diagnosed or prior cancer, with mediastinal lymphadenopathy, benign conditions like tuberculosis can be considered in differential diagnosis more so in TB endemic countries. Incidence of tuberculosis is higher in patients with malignancy receiving anticancer chemotherapy. Early suspicion and diagnosis of tuberculosis in these patients by novel techniques like EBUS-TBNA may improve the clinical outcome.

References