Mediastinal Adenopathy in India: Through the Eyes of Endobronchial Ultrasound

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Abstract
Objectives: Aetiology of mediastinal adenopathy is likely to vary with geographic location and socioeconomic status of a population. Whilst most of adenopathy in the West could be attributed to malignant disorders, causes of the same in a developing country like India has not been extensively studied earlier due to lack of less invasive tools to sample these nodes for cytological and microbiological analysis. Endobronchial ultrasound (EBUS) helps us reach these nodes as a minimally invasive procedure to take aspirations under real-time ultrasound guidance. The aim of the present study is to study the aetiology of mediastinal adenopathy in our population with the help of EBUS.

Methods: This was a retrospective analysis of all EBUS procedures done by the authors and the diagnosis thus obtained at Sir Ganga Ram Hospital, New Delhi, India between April 2010 and December 2011.

Results: A total of 300 patients underwent EBUS in the above period. Most common aetiology encountered in our population was a granulomatous disorder (53% cases) like tuberculosis and sarcoidosis whilst malignancy was third in order of diagnosis (17% cases). Lymph node enlargement due to anthracosis was another uncommon aetiology encountered in the study (5% cases).

Conclusions: Benign granulomatous disorders like tuberculosis and sarcoidosis are the most common causes of mediastinal adenopathy in our population. EBUS is proving its worth for diagnosing mediastinal adenopathy.

Introduction

Mediastinal lymphadenopathy is a common problem for which a pulmonologist’s opinion is sought and the need for this has increased since the use of advanced imaging modalities like CT and PET scans.

The location of mediastinal nodes and masses made them relatively difficult to sample and till very recently, needed complex surgical procedures like mediastinoscopy or thoracotomy¹ to obtain adequate tissue for evaluation. CT guided transthoracic needle aspiration² also could access only limited stations of lymph nodes and was also fraught with a small but definite risk of pneumothorax. Blind bronchoscopic transbronchial needle aspirations (TBNA)³ as an alternative, though popular with some, was however associated with variable sensitivity and specificity and access with this procedure was largely limited to sampling the subcarinal (Station 7) and right paratracheal (Station 4R) nodes. However, with the development of convex probe endobronchial ultrasound (EBUS) scope which incorporates a small ultrasound probe with a Doppler mode attached to the tip of the bronchoscope and a dedicated TBNA needle being passed through its working channel, TBNAs could be performed under real-time guidance thus making it much more accurate and safe.⁴

EBUS has proven its utility in diagnosing and staging the mediastinum for malignant lesions.⁵,⁶ It has now become the preferred method to sample mediastinal lymph nodes with sensitivity and specificity

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comparable to mediastinoscopy, which is the gold standard.7 However, the role of EBUS in non-malignant mediastinal involvement has not been studied extensively.

The aetiology of mediastinal adenopathy is likely to vary according to geographical location, and between various ethnic and socio-economic groups. Whilst malignant aetiologies have been highlighted in most such studies from the West, the few studies enrolling small number of patients from our country suggest that we are much more likely to encounter benign causes of mediastinal adenopathy in our population.8,9

Material and Methods

Patients

The present study was a retrospective analysis of data of all the cases of EBUS FNAC procedures performed by the authors between April 2010 and December 2011 conducted at Sir Ganga Ram Hospital, New Delhi, India, a 650 bedded super-speciality hospital. Clinical details of patients, the location of nodes sampled, and the final diagnosis achieved after cytopathological and microbiological examination of the aspirated material was recorded. Patients in whom a diagnosis of tuberculosis was made without microbiological confirmation were followed up by phone interview or physician visits for clinical and radiological improvement on treatment with antitubercular drugs. Patients who were diagnosed with sarcoidosis were followed up similarly to assess their improvement on medication and any change in their diagnosis on follow up.

Procedure

EBUS TBNA was carried out as out-patients / in-patients under local anaesthesia with sedation. Procedures were performed with an endobronchial ultrasound bronchoscope (BF-UC180F), Processor-EU ME1, Light source-CV 150, Olympus, Japan. Air-dried and alcohol-fixed smears were prepared and sent to cytopathology laboratory. Rapid on-site cytology was not used. The smears were stained using May Grunwald Giemsa (MGG) and Papanicolaou stains. One of the MGG stained smear with representative material was destained and used for Ziehl Neelsen stain for AFB. Needle contents from one dedicated pass were submitted in saline for microbiological analysis. All specimens were subjected to direct fluorescent staining using auramine and rhodamine stains (AR stain) and culture by Bact/Alert 3D (Biomerieux Durham, North Carolina, USA) or Lowenstein Jensen media. Positive growths in either media were identified using Accuprobe molecular identification system.

Results

Most common indications for EBUS at our institute were undiagnosed mediastinal adenopathy; diagnosing and staging of Ca lung; suspected tuberculous or sarcoid nodes; and to take samples to test for mycobacterial drug sensitivity in suspected multidrug resistant cases.

A total of three hundred patients underwent EBUS FNAC in the period mentioned above. Of this, 178 were male and 122 were female patients. Age ranged from 11 – 88 years.

A total of 574 sites (mediastinal nodes and parabronchial masses) were sampled in 300 patients, Subcarinal LN being the most common (223 patients). (Figure 1 for various sites). Forty-six paratracheal / parabronchial masses were also samples and two paratracheal cysts were punctured.

Out of a total of 300 patients, material was reported as unsatisfactory for opinion on cytopathological examination in 36 patients (12%). Adequate material was thus obtained with 88% success rate.

Out of the 264 adequate samples in which adequate tissue was identified by cytopathologists, 33 LN aspirates were reported as reactive adenitis. In 231 cases, a definitive diagnosis could be made using EBUS FNAC (Figure 2).

Eighty-four patients had well defined epithelioid cell granulomas with no necrosis and on the basis of clinicoradiological features and other investigations like a negative Mantoux test and positive serum ACE (angiotensin converting enzyme), a diagnosis of sarcoidosis was made. These patients were followed up by phone interview to assess clinical improvement and to confirm if any alternative diagnosis was entertained later in follow up.

A final diagnosis of tuberculosis was made in 75 patients. Out of these 75, 32 (43%) patients had
a positive staining for acid fast bacilli. Mycobacterial culture was positive in 23 (30%) cases. 21 of these were *M. tuberculosis*, one *M. avium intracellulare* and one *M. abscessus*. Thus, 41 (55%) patients had a definitive microbiological diagnosis of tuberculosis on the basis of positive AFB stain or culture. Other patients who were diagnosed with tuberculosis had granulomas with necrosis or only granulomas on cytopathology with clinicoradiological features suggestive of tuberculosis or good response to antitubercular drugs on follow up.

Diagnosis of a malignant disorder was made in 52 cases. Amongst these, 46 cases were diagnosed by sampling masses which were adjacent to a major airway and the needle was advanced into the mass directly under ultrasound guidance using EBUS. Mediastinal nodes, if any, in these cases were also sampled in the same sitting to stage the disease. Six cases were diagnosed by sampling mediastinal lymph nodes only. If we are able to sample the mass lesion directly, the accuracy of EBUS in achieving a diagnosis is close to 100 percent. Most common thoracic malignancy diagnosed in our population was adenocarcinoma (20 cases) followed by squamous cell carcinoma (12 cases), small cell carcinoma (9 cases), and poorly differentiated carcinoma (4 cases). We were able to diagnose two cases of non-Hodgkin’s lymphoma. Other malignancies diagnosed were metastases from non-thoracic primaries.

**Seventeen patients had cytopathological features suggestive of anthracosis.** Of these, two patients had positive mycobacterial culture from the aspirate and hence were diagnosed as tuberculosis. The other 15 cases were stain and culture negative for *Mycobacterium tuberculosis*, showed endobronchial deposition of black anthracotic pigment on the airways and had features of anthracostenosis and anthracofibrosis on bronchoscopy. The lymph node aspirate usually had black particulate matter and in a couple of cases even black tarry thick liquid could be aspirated from the lymph node.

Two lesions reported on CT scan as lymph nodes turned out to be cysts and in one case, we were able to demonstrate fungal elements resembling mucormycosis from a right lower lobe mass.

Since it was an observational study, no attempt was made to compare EBUS with other diagnostic modalities like bronchoscopic lung biopsy, mediastinoscopy or thoracosopic procedures that were used in some negative cases to confirm the diagnosis.

### Discussion

To the best of our knowledge, this is the first study from India regarding the use of endobronchial ultrasound for diagnosis of mediastinal adenopathy and the largest study of its kind which gives us an idea about the aetiology of intrathoracic adenopathy which we are likely to see in our population. As a granulomatous pathology was demonstrated in more than 50% of our cases, our initial experience suggests that CP EBUS will be very helpful in diagnosing benign mediastinal disorders which are much more prevalent in the developing world as opposed to malignant disorders.

Sarcoidosis is a multisystem disorder of unknown aetiology and the diagnosis requires clinical and radiological features along with histopathological demonstration of non-caseating epithelioid cell granulomas after excluding other infectious causes for the same. The most common organ involved being the lung and the mediastinal lymph nodes; they are the most frequent sites for biopsy. Earlier bronchoscopic techniques utilized were broncho-alveolar lavage, transbronchial needle aspiration and endobronchial and transbronchial biopsies. Recently, there has been interest in utilizing CP EBUS guided FNACs as the diagnostic modality for patients suspected with sarcoidosis. A transbronchial lung biopsy is diagnostic in 65% (40-90) patients with sarcoidosis but also carries a risk of pneumothorax and pulmonary haemorrhage. Blind TBNAs have been shown to have a diagnostic yield of 42–76%. CP EBUS-guided FNACs have been shown to have a diagnostic yield of around 90% in various studies. Combined EBUS FNA and TBLB are likely to pick up 94% cases of sarcoidosis. Our data suggests that sarcoidosis is more common cause of mediastinal adenopathy in our population than tuberculosis. However, this may not be correct because of the referral bias to a tertiary care hospital like ours. Many more patients with mediastinal adenopathy with necrosis and Mantoux positivity would have been treated for tuberculosis and not subjected to any further evaluation which would be a confounding factor.

Tuberculosis has always been endemic in our country and poses a diagnostic dilemma when it presents with mediastinal adenopathy. The differentiation between sarcoidosis and tuberculosis presenting as mediastinal adenopathy can be very difficult. A few of the radiological differences being in the distribution of adenopathy, presence of necrosis in the glands as assessed by CT scan and peripheral rim enhancement would suggest tuberculosis as the likely diagnosis. The most definitive diagnosis comes from the detection of *Mycobacterium tuberculosis* either in the stain or grown in culture. Another distinguishing feature on cytopathology is the presence of necrosis in the granulomas which would favour a diagnosis of tuberculosis. Our study demonstrates that aspirate samples taken by EBUS FNA are adequate
for microbiological assessment for mycobacterial diseases. Final diagnosis of tuberculosis was entertained in 75 of our patients on the basis of clinical and radiological features, presence of necrosis in the aspirate and good response to ATT on further follow up. Out of 75, 41 cases (55%) were bacteriologically confirmed on staining or culture. We were also successful in growing non-tubercular mycobacterium in two of these cases. Out of the culture positive cases, five cases proved to be multidrug-resistant. The implication of this finding is important in the diagnosis and treatment of extrapulmonary multi-drug-resistant tuberculosis. Very few studies have evaluated the drug-resistant tuberculosis. Very important in the diagnosis and treatment of extrapulmonary multi-drug-resistant tuberculosis. Very few studies have evaluated the use of EBUS FNAC for diagnosing tubercular mediastinal adenopathy and the results suggest that it is a very useful tool for the same. 37

A positive diagnosis of malignancy was made in 52 cases and lymphoma was diagnosed in two cases. As we see, the number of cases with malignant disease of the mediastinal nodes in our country is significantly less, 52 (17%) patients out of 300 as compared to Western experience where majority of patient would have a malignancy associated adenopathy.

Another uncommon aetiology which we stumbled upon in this journey with EBUS is anthracosis. Anthracosis is a lesser known cause of mediastinal adenopathy. It is often mistaken for tuberculosis because of radiological similarities between the two disorders and most of the patients would have been treated with antitubercular therapy before a definitive diagnosis is reached. EBUS helps in differentiating between the two pathologies and thus avoids unnecessary therapy. Few limitations of our study should be noted. It is a retrospective, single centre study done from a tertiary care hospital in Delhi. Data from other places in our country with a different subset of population might vary in their distribution of diseases. Patients who were diagnosed with reactive adenopathy and those in whom EBUS sample was reported as inadequate were not followed up.

Our results suggest that benign disorders like tuberculosis and sarcoidosis are the most common causes of mediastinal adenopathy in Indian population followed by malignancy, benign hyperplasia and anthracosis. Endobronchial ultrasound gives us an excellent, minimally invasive tool to ascertain the diagnosis. With the increasing availability of EBUS at newer centres and the felt-need for definitive diagnosis before starting treatment for mediastinal adenopathy, we are likely to see much more data on the subject coming out in the near future.

References


