Review Article

Endobronchial Tuberculosis

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Abstract
Endobronchial tuberculosis refers to tuberculous infection of the tracheobronchial tree. Diagnosis requires a high index of suspicion since symptoms are attributed to co-existing pulmonary tuberculosis and airway lesions are not detectable on chest radiograph. While computed tomography and bronchoscopy are useful for the evaluation of tracheobronchial stenosis or obstruction, goals of treatment remain in the eradication of tubercle bacilli and prevention of airway stenosis. Corticosteroids may halt progression of active disease to fibro-stenotic stage, however if tracheobronchial stenosis causing post-obstructive pneumonia, atelectasis and dyspnea has occurred, airway patency must be restored mechanically by surgery or bronchoscopic techniques.

Keywords: pulmonary tuberculosis, endobronchial tuberculosis, bronchoscopy, surgery, airway stricture

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Introduction

Involvement of the trachea and major bronchi by tuberculosis was first described by Morton in 1698.[1] Endobronchial tuberculosis (EBTB) defined as tuberculous infection of the tracheobronchial tree is not uncommon. EBTB is found to account for 42% of 1000 autopsies of patients with tuberculosis,[2] and affects 10-38.8% of living patients undergoing rigid bronchoscopy.[3-5]

After the introduction of effective anti-tuberculous drugs, interest in pulmonary tuberculosis (PTB) eclipses the study of EBTB. However EBTB continues to be a major public health problem because its diagnosis is often delayed, and airway stenosis with its attendant complications of post-obstructive pneumonia, atelectasis, hemoptysis, wheezing and dyspnea can develop during the course of treatment.[6-8] Owing to HIV infection, poverty, ageing population, migration, multi-drug resistance, failure in health systems and rise in diabetes, a resurgence in tuberculosis is observed which accounts for 8.8 million new cases and 1.8 million TB related deaths each year.[9,10] It is also likely that HIV may be associated with a higher incidence of EBTB.[11,12]

The pathogenesis of EBTB is not fully understood and is thought to arise from direct implantation of the tubercle bacilli onto the tracheobronchial tree from adjacent pulmonary parenchymal lesion. This theory is supported by finding tuberculosis affecting the bronchus opposite to the airway that drains the tuberculous cavity. Another cause is direct airway infiltration by adjacent tuberculous mediastinal lymph node more commonly seen in children while lymphatic and hematogenous spread is rare.[13-15] The clinical course of EBTB can be variable and complex, dependent on the interaction of mycobacteria with host immunity and anti-tuberculous drugs.[16,17]

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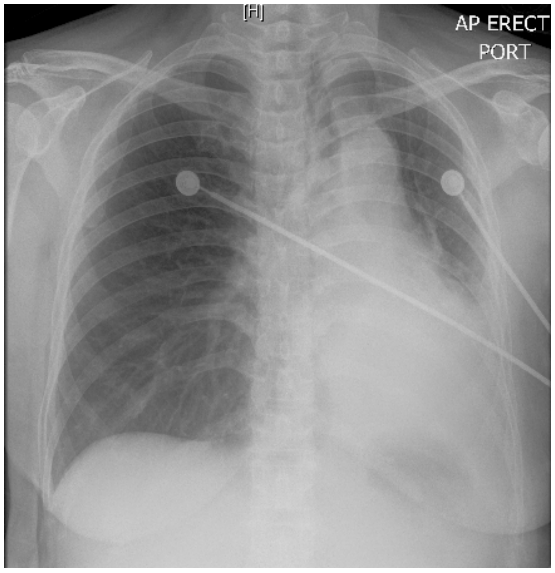

Figure 1. CXR showing left lower lobe collapse

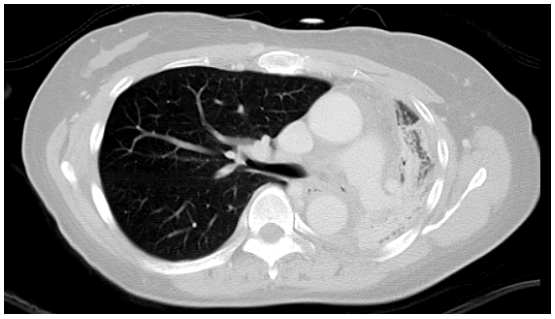

Figure 2a. CT scan of left main bronchial stricture, distal lingular and lower lobe collapse

Figure 2b. 3D CT reconstruction showing LMB stricture with left lung collapse

Clinical features and Radiology

EBTB appears to occur more frequently in women in their second and third decades of life even though they have a lower incidence of pulmonary TB.[6,13,16,17] One explanation is implantation of mycobacteria from infected sputum occurs more frequently in females as they do not expectorate sputum well due to socio-cultural circumstances. Clinical features depend on the type and stage of EBTB. Some are asymptomatic while most complain of productive cough, fever, hemoptysis, hoarseness, chest pain and generalised weakness.[6] Wheezing can be detected by auscultation in a third of patients erroneously managed as asthma with steroids, and decreased air-entry in a quarter.[8,18-20]

Diagnosis of EBTB is difficult based on symptoms since they can occur as part of pulmonary TB or other respiratory diseases. CXR can be normal as these lesions are not detectable unless airway obstruction has occurred causing distal atelectasis (Figure 1). Interestingly the lower or middle lung lobes are affected slightly more often than upper lobes which would favour the direct implantation theory of EBTB by gravity.[6,8,16,18] Pleural effusions and military tuberculosis may be observed.[14,21] CT is more useful in demonstrating bronchial wall irregularities and lymphadenopathy associated with bronchial lesion, and 3D CT reconstruction for degree and extent of tracheobronchial stenosis especially if surgery or bronchoscopic intervention is planned (Figure 2).[22,23]

Sputum smear for acid fast bacilli (AFB) is positive in 17% and increases to 79% when combined with bronchoscopic specimens.[6,18] This finding is unexpected as EBTB is presumed to yield higher sputum AFB smear positivity. However sputum expectoration may be difficult due to mucus entrapment by proximal granulation tissue, or mucosal ulceration may be necessary for positive AFB smear. PCR for mycobacteria tuberculosis is increasingly applied to improve the diagnosis of EBTB.[24,25]

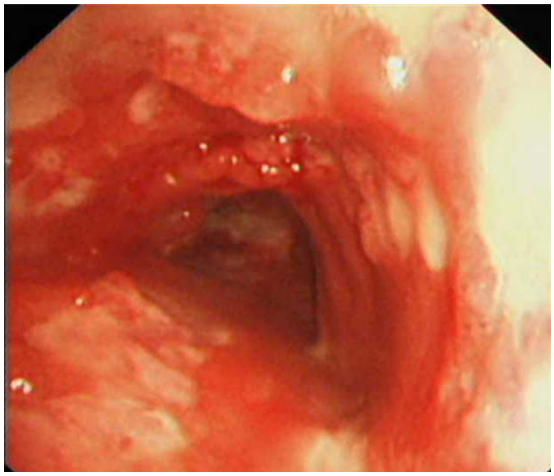

Figure 3a. Actively caseating EBTB of trachea and main carina

Figure 3b. Tumorous EBTB of right upper lobe

Bronchoscopy and Histopathology

EBTB affects the trachea, main bronchi and upper bronchi (Figure 3). Biopsy specimens are definitive for EBTB if caseating granulomas or AFBs are present, or if they show non-caseating granulomas and Langhan's giant cells for which sarcoidosis, fungal or granulomatous diseases are excluded. Chung and co-workers classified EBTB into 7 categories (% prevalence): non-specific bronchitis (8%), actively caseating (43%), granular (11%), edematous hyperemic (14%), ulcerative (3%), tumorous (10.5%), and fibrostenotic (10.5%). In this study, serial bronchoscopy was performed from the diagnosis of EBTB to completion of anti-tuberculous treatment and actively caseating, edematous-hyperemic, tumorous and fibrostenotic lesions demonstrated higher risk of progression to tracheobronchial stenosis, usually within 3 months.[6,26]

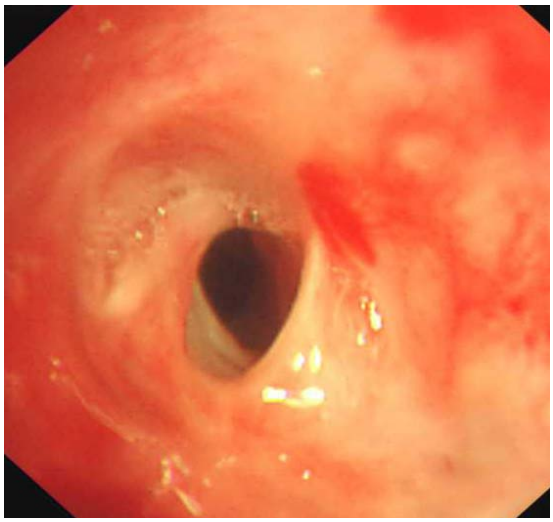

Figure 3c. Fibrostenotic EBTB of left main bronchus

The classification of EBTB can be explained pathologically by disease progression. The initial lesion is characterised by erythema and lymphocytic infiltration which corresponds to non-specific bronchitis. As the disease advances submucosal tubercles develop giving it a granular appearance (granular) while marked mucosal edema describes the edematous-hyperemic type. It can undergo caseous necrosis (actively caseating) or becomes ulcerative if the inflammation continues. The actively caseating or ulcerative lesion can either evolve to hyperplastic inflammatory polyp (tumorous type) or heal by fibrostenosis.[15,27,28] Associated intrathoracic tuberculous lymph node can erode and protrude into the airway akin to tumorous EBTB.[11,14,28] Rikimaru and co-workers further divided the ulcerative type into active (Stage A), healing (Stage H) and scarring (stage S). Only Stage A lesions were observed before anti-tuberculous treatment.

During 1 and 2 months of therapy 76% of ulcerative lesions were in Stage A or H, and thereafter 63% were in Stage S of which one-third of patients developed inflammatory polyps.[29]

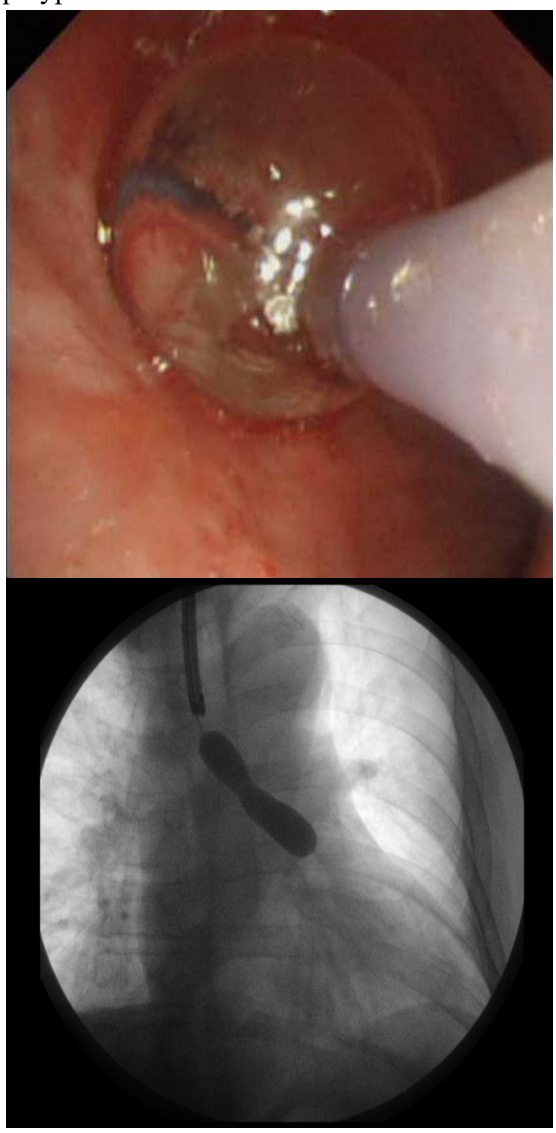

Figure 4. Balloon Bronchoplasty of left main bronchus with fluoroscopy

Treatment

Active and fibrous subtypes must be differentiated. Fibrous disease is considered inactive TB but it can lead to bronchial stenosis which can be a challenging sequel to manage during or after treatment of EBTB.

Active EBTB

In active EBTB, the most important goal of treatment is in the eradication of tubercle bacilli without selecting for drug-resistant mycobacteria. The second most important goal is in the prevention of tracheobronchial stenosis. Chemotherapy eradicates tubercle bacilli except for multi-drug resistant TB while the sequel of tracheobronchial stricture is atelectasis with dyspnea or obstructive pneumonia. Tracheobronchial strictures can develop despite prompt anti-tuberculous therapy,[6,8,16,26] and previously topical silver nitrate application has been attempted for ulcerative EBTB[30,31] and electrosurgery via rigid bronchoscopy for tumorous or polypoidal lesions.[32] A recent systematic review and meta-analysis concludes that steroids could be effective in reducing mortality for all forms of tuberculosis including PTB.[33] However, the role of corticosteroids in preventing fibrostenosis consequent to EBTB remains controversial. In 2 prospective, randomized, placebo-controlled studies of children with endobronchial obstruction from enlarged tuberculous hilar lymph nodes demonstrated significant improvement in the group treated with steroids.[34,35] There was only 1 randomized study in adults which did not show any difference in the rate of bronchial strictures between the steroid-treated and placebo groups. It was a small study, and timing of initiation of systemic steroids could contribute to the failure since there were other case reports which showed favourable response to both systemic and endoscopic injection of steroids.[36]

Shim recommends steroids for the edematous-hyperemic, actively caseating and tumorous types as these tend to progress to tracheobronchial stenoses. Prednisolone at 1mg/kg is prescribed for 4 to 6 weeks followed

by slow taper for the same duration.[37] In 1963 Nemir and colleagues observed that short course prednisone of less than 4 months was an effective adjunct to the anti-tuberculous therapy for EBTB.[38]

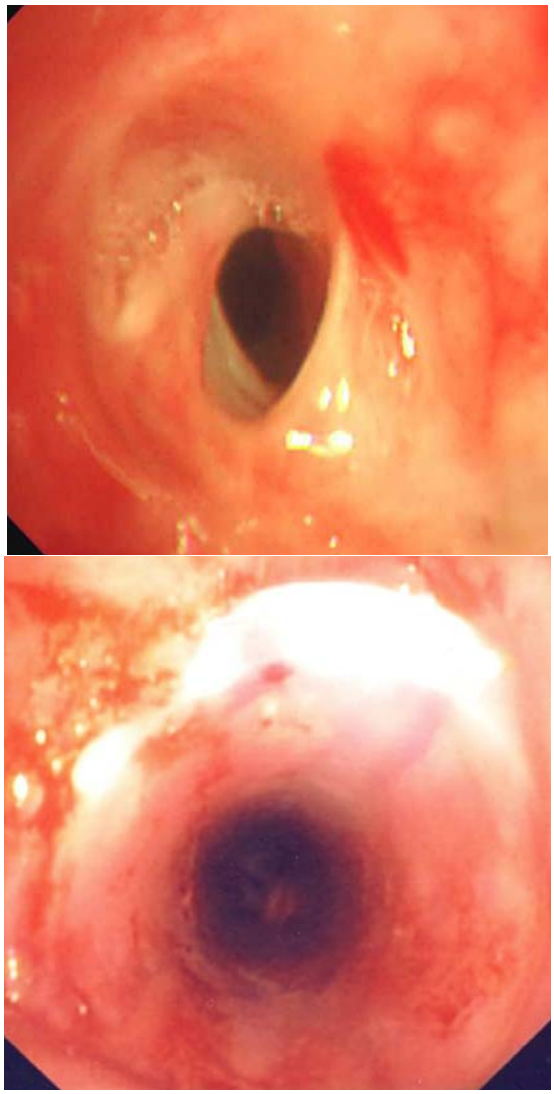

Figure 5. Fibro-stenotic left main stricture (a), radial cuts applied with electrosurgical knife, dilated with balloon bronchoplasty (not demonstrated), and silicon stent placement (b)

Song and co-workers also observed good response if steroids were initiated within 3 months of symptoms and concluded that steroids were beneficial in early phase EBTB but had no impact on bronchial stenosis.[39] Rikumaru and coworkers also observed that heal time for ulcerative EBTB was shorter, and bronchial stenosis less severe if patients were treated with twice daily aerosol therapy of streptomycin 100mg, dexamethasone 0.5mg and naphazoline 0.1mg in addition to anti-tuberculous therapy.[40] Um and co-workers found that age >45 years, fibrostenotic subtype and >90 days between symptom onset to the initiation of anti-tuberculosis chemotherapy were independent predictors of persistent airway stenosis, and oral corticosteroids (prednisolone equivalent ≥ 30 mg/d) did not reduce the frequency of airway stenosis.[41] It is therefore apparent that steroids do not affect regression of the fibro-stenotic lesions but can ameliorate inflammation and edema if administered in the early course of EBTB.

Fibrous EBTB

An important sequel of EBTB is bronchial stenosis which causes atelectasis and obstructive pneumonia. Patients present with dyspnea and wheezing. As steroids are unable to reverse tracheobronchial stenosis, airway patency must be restored by surgery or bronchoscopic intervention. Surgical resection of an atelectatic lung with stenotic main stem bronchus (pneumonectomy) has been normal practice but lung sparing surgery such as sleeve resection, carina resection and end-to-end anastomosis are increasingly performed.[42-44] Bronchoscopic techniques that include laser, electrosurgery, argon plasma coagulation, cryotherapy and balloon bronchoplasty (Figure 4) have been applied singly or in combination to restore airway patency.[45-54] Silicon stents are deployed following airway recanalization and dilatation as adjunct to the management of complex strictures (Figure 5)[55-57] while metallic stents should be avoided since they are difficult to remove due to

airway epithelization.[57,58] Complications consequent to dilatation techniques and stenting include airway perforation, stent migration and stent related obstructing granuloma, which can cause subcutaneous emphysema, pneumothorax, pneumomediastinum, mediastinitis, dyspnea, and hemoptysis.[58] We reported a patient who received silicon stent for post-TB complex stricture developed obstructing granuloma that was successfully treated with laser and topical mitomycin C application.[59]

It is indeed challenging to determine who would respond to interventional procedures or surgery. In fact Lee and coworkers reported that only 30% experienced successful re-expansion defined as recovery of lung volume > 80% of estimated original volume. These responders were younger with median age 22 years versus 34 years for non-responders. Presence of parenchymal calcification as well as bronchiectasis within the atelectasis showed higher tendency for failure whilst mucus plugging, extent of airway narrowing, volume loss on CT and endobronchial TB activity at the time of intervention did not affect lung re-expansion.[60]

Conclusion

Diagnosis of EBTB is often delayed as it is difficult to detect on CXR. Symptoms of hemoptysis, wheezing and dyspnea as well as CXR finding of atelectasis should alert the physician of EBTB. EBTB is divided into 7 categories based on bronchoscopic appearances, and actively caseating, edematous-hyperemic, tumorous and fibrostenotic lesions demonstrate higher risk of progression to tracheobronchial stenosis. Airway strictures occur in up to two thirds of EBTB and steroids when instituted early can prevent progression to tracheobronchial stenosis. Aerosol therapy comprising of streptomycin and corticosteroid is also an effective adjunct to anti-tuberculous treatment. 3D reconstruction CT is not only useful in the planning of bronchoscopic intervention or surgery it can also be a means to follow EBTB during therapy instead of serial bronchoscopy. Patients with airway strictures consequent to EBTB will require surgery or bronchoscopic procedures that may include a combination of tools such as laser, electrocautery, argon plasma coagulation or cryotherapy, balloon bronchoplasty or stent.

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