ABSTRACT

In patients with central airway obstruction (CAO), clear definitions and classifications are relevant to determine treatment options, estimate prognosis and provide a common language for meaningful research. In Indonesia, one of most commonly found benign central airway obstruction is endobronchial tuberculosis. “All that wheezes is not asthma” (Mc Conkey). A patient with endobronchial tuberculosis complaining of wheeze.

Endobronchial tuberculosis (EBTB) is defined as tuberculous infection of the tracheobronchial tree with microbial and histopathological evidence. It is seen in 10-40% of patients with active pulmonary tuberculosis. More than 90% of the patients with EBTB have some degree of bronchial stenosis.

Five potential mechanisms have been suggested for the development of endobronchial infection due to M. (1) direct extension from adjacent parenchymal focus; (2) implantation of organisms from the infected sputum; (3) hematogenous dissemination; (4) lymph node erosion into the bronchus; and (5) through lymphatic drainage from parenchyma to the peribronchial region.

Ten to 20 percent have normal chest radiograph. Therefore, a clear chest radiograph does not exclude the diagnosis of EBTB. Bronchoscopic sampling has been the key to the diagnosis producing more than 90% yield on smear as well as on culture. Bronchoscopy and computed tomography are the methods of choice for accurate diagnosis of bronchial involvement and assessment for the surgical interventions. In patients with central airway obstruction caused by benign diseases treated by placement of airway stents using a flexible bronchoscope under sedation and local anesthesia, have been reported. However, notable complications including granulation tissue formation, stent fracture, and recurrent stent obstruction by the lumen were also reported. For patients with central airway obstruction caused respiratory distress, the primary goal of therapy is to relieve the obstruction in the central airway. Treatment options include laser ablation, photodynamic therapy, and cryotherapy. Cryotherapy, using flexible or rigid bronchoscopy, has a relatively long history of use, and quickly freezes endobronchial mass to -70°C prior to removal. Previous studies have mentioned that cryotherapy is useful to relieve symptoms of central airway obstruction in patients with malignant diseases. However, there is insufficient data of cryotherapy in patients with benign obstructive lesions.

Keywords: Central Airway Obstruction, Endobronchial tuberculosis
Introduction

In patients with central airway obstruction (CAO), clear definitions and classifications are relevant to determine treatment options, estimate prognosis and provide a common language for meaningful research. The syndrome of CAO generally is defined as occlusion of > 50% of the trachea, mainstem bronchi, bronchus intermedius, or a lobar bronchus. The first step in evaluating CAO is to classify the obstruction objectively on the basis of histologic findings, mechanism, and dynamic features. The extent and severity of airway narrowing and their impact on functional status should be assessed objectively. Parameters that impact decision-making process regarding bronchoscopic dilation, stent insertion, and surgical resection in patients with CAO are reviewed herein.1

Qualitative and Quantitative Criteria

Figure 1 – Quantitative and qualitative classification criteria for CAO. Histologic results are subclassified as benign or malignant; dynamic features, as fixed or variable (aka dynamic); and mechanism of obstruction, as exophytic endoluminal, strictures, extrinsic compression, and mixed obstruction. Quantitative criteria are based on objective assessments: severity of narrowing usually is defined as normal, mild (< 50% obstruction), moderate (51%-70%), or severe (71%-100%). Vertical extent, more pertinent to strictures requiring surgery or stent insertion, must be measured precisely. The airway morphology (ie, shape of the narrowing) must be documented objectively because it impacts flow, independent of the reduction in the cross-sectional area. CAO ¼ central airway obstruction.

Background

The prevalence of tuberculosis-induced tracheobronchial stenosis varies as a function of the prevalence of tuberculosis, and is estimated to be as high as 10% to 40% in patients with pulmonary tuberculosis.

Tracheobronchial tuberculosis (TBTB) is diagnosed on histopathological examination of bronchoscopically obtained specimens showing granulomatous inflammation with caseation necrosis and/or positive acid fast bacilli culture on the microbiological exam. Specimen for culture can also be obtained from sputum but it is less sensitive compared to bronchial washing, biopsy or bronchoalveolar lavage; as described by Qingliang et al.
in China where only 3/22 (13%) patients were sputum acid fast bacilli positive, and the remainder required bronchoscopic sampling for the diagnosis.\textsuperscript{2,3} The diagnosis of TBTB is often delayed due to its non-specific clinical symptoms. The course of endobronchial tuberculosis is highly variable and can range from complete resolution of the disease to fibrotic central airway obstruction.\textsuperscript{4}

About 68\% of the patients with TBTB develop some degree of bronchostenosis in the initial 4–6 months of the disease and up to 90\% of patients have some degree of stenosis beyond this initial time period.\textsuperscript{3,5,6} Among patients with active disease involving the pulmonary parenchyma, 10–39\% of patients are shown to have a component of TBTB.\textsuperscript{7} Initial treatment is a 4 drug regimen therapy as in pulmonary tuberculosis. However, due to a highly unpredictable disease progression when it involves the tracheobronchial tree, future interventions including bronchoscopic airway dilation or stent placement may be necessary.

**Phatogenesis**

Although the exact pathogenesis of TBTB is not well understood, at least four different pathways are proposed leading to infection of tracheobronchial mucosa by mycobacteria tuberculi. Anyone or combinations of these pathways may lead to infections. In 1951, Smart proposed different methods of infection which included:

I. Direct spread of tubercle bacilli from parenchymal tuberculosis or cavitary lesions containing abundant tubercle bacilli;\textsuperscript{8-11}

II. Dissemination of tubercle bacilli from peribronchial lymphatic channels draining pulmonary parenchymal tuberculosis. This is supported by the finding that endobronchial biopsy in this patient population shows intact mucosa but submucosal involvement is noted on biopsy;\textsuperscript{8}

III. Disease spread from contiguous mediastinal lymph nodes to the bronchial mucosa, occasionally resulting in Broncho nodal fistula. This mode of infection is particularly known to affect the pediatric population due to weaker airway walls and smaller airway diameter;\textsuperscript{12,13}

IV. Direct implantation of inhaled mycobacterium tuberculosis into the bronchial wall mucosa.\textsuperscript{14}

TBTB can be clinically divided into active disease (bronchoscopic findings of active caseating material, ulceration or granulation tissue formation or histologic findings of caseating necrosis or a positive tubercle bacilli on culture) and fibrotic diseases (fibrosis seen on bronchoscopic view or biopsy-confirmed fibrostenotic tuberculosis often found to be culture negative).\textsuperscript{8} During the healing phase of active endobronchial tuberculosis, cicatrization can cause mucosal ulceration, necrosis and fibrosis leading to stenosis.\textsuperscript{7}
Diagnosis

- Clinical symptoms: the prevalence of endobronchial tuberculosis is found to be twice as high in females as males. Lee and colleagues hypothesized that female patient population tend to expectorate less frequently due to social customs and norms causing endobronchial stasis of the secretions and subsequent infection.
- The diagnostic yield of sputum examination is very variable. Despite best efforts and appropriate collection techniques a highly variable diagnostic rate of 13.6–53% is reported in patients with TBTB. Ozkaya et al. reported on their experience with 23 patients with biopsy proven endobronchial tuberculosis all of whom were sputum smear negative. Such reports have ben indicative of a high false negative rate of negative sputum for acid fast bacilli in the diagnosis of TBTB;
- Tuberculin skin test was found to be positive in only 59.1% Its lack of sensitivity in immunocompromised patients and lack of specificity due to its cross reactivity with non-tuberculous mycobacterium makes it an ineffective test to rule in or rule out pulmonary tuberculosis
- Pulmonary function testing (PFT): The large airways contribute to approximately 50% of the total airway resistance. It is unclear what test most accurately quantifies the degree of upper airway obstruction. Spirometry typically shows limitation of maximal inspiratory and expiratory flows at high lung volumes.
- Chest imaging: chest imaging does not rule out endobronchial tuberculosis. Lee et al. in a retrospective study found that 10% of the patients have normal chest X-ray. Pulmonary infiltrate is the most common findings seen on chest X-ray. In a study from south Korea chest images of 121 patients with TBTB were reviewed. Seventy-one out of 121 patients (60%) had parenchymal infiltrate while 24% had loss of volume. 8% of patients had cavitating lesions while surprisingly, 8% of patients had completely clear lung fields.
- Bronchoscopic view: Chung et al. reported on their detailed bronchoscopic examination of patients with TBTB and classified the bronchoscopic view of endobronchial tuberculosis to seven subtypes: actively caseating, edematous-hyperemic, fibrostenotic, tumorous, granular, ulcerative and nonspecific bronchitic.

Treatment

Treatment of TBTB depends on the stage at which the diagnosis is made. In the active phase of the disease, the goal is to control the infection and prevent tracheobronchial stenosis. There is no clear evidence that any single mode of therapy can decrease the incidence of TBTB in this patient population. The following management strategies are proposed in the literature.

- Corticosteroids: corticosteroids have been used in children and adults without any benefit. As mentioned above, tracheobronchial stenosis is the most common long term complication despite adequate treatment.
- Medical therapy: medical treatment is of no benefit in the fibrotic stage. Restoring the airway patency and relieving the symptom is the key to the
treatment in fibrotic stage. Patients with TBTB caused by organisms known or presumed to be drug susceptible are treated in the same way as pulmonary tuberculosis.

- Bronchoscopic: in tracheobronchial stenosis, bronchoscopic intervention is not standardized and patients are treated on case by case basis depending on the symptoms, PFT, co-morbidity, chest imaging and bronchoscopic findings.  

![Algorithm for the endoscopic management of central airway obstruction.](image)

**Fig 2.** Algorithm for the endoscopic management of central airway obstruction.  

**Conclusions**

- Diagnosis TBTB should established early and aggressive treatments must be startet to favourably changer the course of the disease
- Therapy should be individualized according to the stage of the disease demonstrated by bronchoscopic examination. Close follow up and intervention therapy are essential, specifically tumourous variety to prevent consequences
- The ideal approach would be utilization of these various avalaible technologies along with focus on research to maximize the preventive, palliative, and therapeutic effect
References