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Bronchiectasis: An Orphan Disease

ABSTRACT

Bronchiectasis is a common disease especially in India as a sequel are of Tuberculosis. It can vary from mild to severe and can result in recurrent exacerbations due to secondary infection and colonisation with gram negative bacteria resulting in respiratory failure. Appropriate management of recurrent infections and prevention of recurrent infections is also very important. In this article we are providing a concise review of current recommendations in diagnosis and management of bronchiectasis.

Key words: Bronchiectasis management, Cystic bronchiectasis, Radiology findings in bronchiectasis

INTRODUCTION

Bronchiectasis is defined as an abnormal and permanent dilatation of one or more bronchi, derived from Greek *broncos* meaning airways, and *ectasia* meaning stretching out.

It is a common respiratory disease worldwide, affecting up to 566/100,000 population in developed countries. The EMBARC and Respiratory Research Network of India Registry which published its results of 2195 patients across 31 centers in India in 2019 reported that patients with bronchiectasis in India showed significant differences from those previously reported in Europe and the USA. Indian patients were younger men and had more severe cystic bronchiectasis.[1] A large study, of 385 patients with tuberculosis (TB) in Malawi, found High resolution computed tomography (HRCT) revealed moderate-to-severe bronchiectasis in 44.2% of HRCT. If these findings are to be correlated to the Indian subcontinent, an estimate of 2.8 million cases of TB per year, the prevalence of bronchiectasis would be huge. Despite being a common disease in Indian patients it is often disregarded just as sequelae of prior infection and not treated as a disease itself. It, however depending on severity and colonization with gram-negative bacteria can have serious morbidity and mortality. Therefore, awareness about its newer management principles is important in everyday practice.

AETIOPATHOGENESIS

The vicious cycle hypothesis by cole is the most accepted mechanism causing Bronchiectasis. TB leading to lung destruction and bronchiectasis is commonly seen in our country and can be due to various mechanisms, endobronchial TB causing obstruction, wall destruction, post TB stenosis or due to obstruction by lymph nodes. EMBARC- India reported that TB and other severe infections as the commonest cause while idiopathic bronchiectasis was seen only in 21.4%.[1] Allergic broncho-pulmonary aspergillosis (ABPA) was also highly prevalent as a cause of bronchiectasis.

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PATHOLOGY

Bronchial deformities can be cylindrical or follicular or tubular dilatation, in severe cases will show saccular/cystic bronchiectasis. Surrounding lungs may show fibrosis, atelectasis. Hypoxemia will lead to the development of pulmonary hypertension and cor pulmonale.

CLINICAL FEATURES

Productive large volume cough is the commonest symptom with mucopurulent sputum with often diurnal variation and postural changes. In some patients with minimal secretions, it is called dry bronchiectasis (bronchiectasis sicca) and seen in upper lobe disease. Hemoptysis can occur and occasionally be large. Dyspnea occurs with extensive disease and destruction. Patients may have prior history of sinusitis, cold. The bronchiectasis severity score or BSI is a scoring system using age, body mass index, FEV1, previous hospitalization, exacerbation frequency, colonization status, and radiological appearances. It is helpful to predict future exacerbations and hospitalizations, health status, and death over 4 years. Indian data shows 33.2% with mild, 30.7% with moderate, and 36.1% with severe bronchiectasis. Indian patients tend to have a high burden of symptoms and higher hospital admission for exacerbations due to chronic infection with *Pseudomonas aeruginosa*.[1] Prior TB was also a risk factor for exacerbations. Classical findings are early and mid-inspiratory

crackles or crepitations more at the bases. Clubbing may be seen in long-standing moderate-to-severe disease. In advanced disease signs of collapse or corpulmonale may be present.

DIAGNOSIS

Diagnosis involves identifying bronchiectasis and the etiology as this will determine further management. Chest radiography in bronchiectasis is unreliable and can be normal in 50%. HRCT has become the investigation of choice in bronchiectasis and has replaced bronchography Table 1. Thin section HRCT with 1–2 mm cuts at 10 mm intervals has a sensitivity of 82–97% in diagnosis may also give clues as to the diagnosis based on extent, location of bronchiectasis, and presence of mucous plugging Table 2 and Figure 1. Aetiological workup should be in detail. Table 3.[2] Indian patients have a relatively equal distribution between bronchiectasis affecting the upper, middle, and lower lobes with cystic dilatation being the most common radiological pattern.[1]

FUNCTIONAL ASSESSMENT

Functional impairment is related to severity of bronchiectasis. Data from India has shown that airflow obstruction was the predominant spirometric abnormality affecting 34.8% of patients and significant number have no post-bronchodilator reversibility. Low FVC had a strong association with post-TB bronchiectasis. DLCO is also reduced in bronchiectasis as seen in previous series. Lung functions do not help in diagnosis, however, response to bronchodilators may allow changes in treatment.

Table 1: Radiologic features of bronchiectasis

Chest radiograph
Thickened bronchi with tram track appearance
Ring shadows/cystic – dilated end on bronchi sometimes with air-fluid levels
Tubular opacities looking such as toothpaste column, if branching produce gloved finger shadows
Nodular opacities due to mucous plugging
Volume loss due to atelectasis or fibrosis
Consolidation due to secondary infection
Dextrocardia in kartegener's syndrome
HRCT
Direct signs
Broncho-arterial ratio>1 (internal airway lumen vs. adjacent pulmonary artery) signet ring appearance
Lack of tapering of bronchi at periphery
Airway visibility within 1 cm of costal pleural surface or touching mediastinal pleura
Other changes such as cylindrical, cystic, or varicose (beaded)
Indirect signs
Mucus impaction
Air fluid levels
Bronchial wall thickening, centrilobular nodules
Mosaic perfusion/air trapping on expiratory CT
Atelectasis or volume loss

HRCT: High resolution computed tomography

MANAGEMENT

The main aims of the management of bronchiectasis are to reduce symptoms, exacerbations, and improve quality of life.

MEDICAL TREATMENT

Medical treatment is targeted to control infection with antibiotics, removal of secretions with physiotherapy and postural drainage, and bronchodilators when needed Figure 2.

Antibiotics

During exacerbation, treatment should be guided based on sputum cultures. Empirical antibiotic choice while awaiting cultures should be amoxicillin-clavulanate combination or

Table 2: Patterns on HRCT to suggest underlying etiology

Finding	Possible Disease
Upper lobe predominance	TB, cystic fibrosis, ABPA, traction bronchiectasis, associated with conditions like pneumoconiosis, sarcoidosis, and silicosis
Middle lobe/lingual predominance	Brock's syndrome, ciliary dyskinesia, mycobacterium avium disease
Lower lobe predominance	Aspiration, COPD, alfa 1 antritrysin deficiency, hypogammaglobineamia syndromes
Focal	Endobronchial tumors, strictures, foreign body, or due to external compression by lymphadenopathy
Central bronchiectasis	ABPA, Mounier- Kuhn syndrome
Calcified lymphadenopathy and volume loss	Post TB
Mucous plugging	Cystic fibrosis
Hyper attenuated mucous	ABPA
Large trachea and main bronchi	Mounier- Kuhn syndrome
Oesophageal dilatation	Aspiration syndromes
Emphysema	COPD, alfa 1 antritrysin deficiency
Situs invertus, dextrocardia	Kartegener's syndrome
Bilateral patchy distribution	Childhood viral infection, bronchopneumonia
Consolidation, airfluid level	Suggest active secondary infection

ABPA: Allergic broncho-pulmonary aspergillosis, HRCT: High resolution computed tomography, COPD: Chronic obstructive pulmonary disease

Table 3: Recommended Evaluation in newly diagnosed adult bronchiectasis

Recommendation (adapted from BTS guidelines)	Disease	Strength of recommendation
History and clinical findings for prior LRTI, TB	Post infectious, TB	C
CBC, serum total IgE (>500) and positive specific IgE or skin prick test to *A. fumigatus*	ABPA	D
Serum IgG, IgA and IgM	hypogammaglobinaemia	A
Screening by sweat chloride and mutation in upto 40 years of age	Cystic fibrosis	D
Saccharine test and or exhaled FeNO only if infertility or recurrent URTI	Immotile cilia syndrome	D
Sputum for bacterial and mycobacterial culture	Suspected TB	D
RF, anti CCP, ANA and ANCA in patients with coexisting clinical features of arthritis, CTD and/or systemic vasculitis	Connective tissue disease (CTD	C
Testing for A1AT deficiency in patients with coexisting basal panacinar emphysema.	Alfa 1 Antitrypsin deficiency	D
Bronchoscopy in localized disease	Tumor, foreign body	D
Investigations for reflux and aspiration	Aspiration syndromes	D

ABPA; Allergic broncho-pulmonary aspergillosis

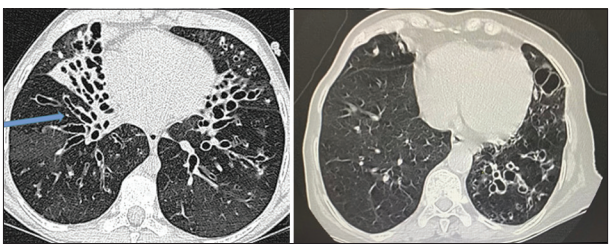

Figure 1: HRCT pattern showing bilateral extensive cystic and cylindrical pattern on the left image. In the image on right unilateral involvement with cystic pattern of varying sizes

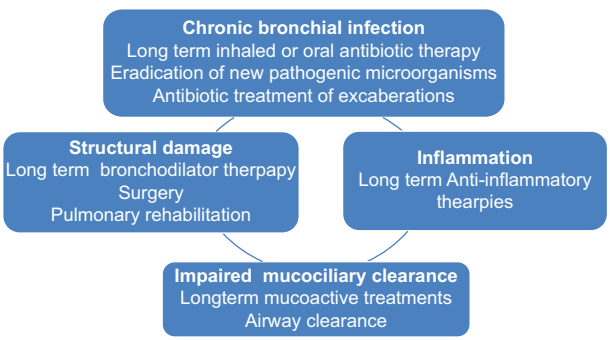

Figure 2: Treatments for bronchiectasis

ciprofloxacin. However, in India due to high burden of TB quinolones should be avoided unless absolutely necessary to prevent resistance. In severe exacerbation, an antibiotic that covers gram-negative and pseudomonas should be given. Duration should be 2 weeks in pseudomonas infection. Indian registry has shown most frequent isolated organism was *P. aeruginosa* in 13.7% patients, followed by Enterobacteriaceae species 9·8% such as *Escherichia* and *Klebsiella pneumoniae*. *Acinetobacter* spp. was isolated in 1% of patients. *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, and non-tuberculous mycobacteria were less commonly seen.[1]

Long-term antibiotics are recommended in patients with bronchiectasis who experience 3 or more exacerbations per year (Figure 3) as evidence suggests long-term antibiotic use reduces the number of exacerbations, time to first exacerbation, sputum purulence, and breathlessness in adults.[3] Pseudomonas predisposes to poor quality of life hence eradication of pseudomonas is recommended Figure 4. Sputum cultures for bacteria, mycobacteria (if macrolide to be used then NTM culture as well), and fungi before and after long-term antibiotics are essential to decide choice of antibiotic and identify emerging resistance. Colonization is identified by persistent isolation of same organism in 2–3 consecutive samples during the stable state.[2,3]

Drug toxicity monitoring is also required, especially with macrolides and inhaled aminoglycosides. The use of inhaled antibiotics is associated with a 10–32% risk of bronchospasm. Prior inhalation of a short-acting bronchodilator is advisable. Monitoring of QTCon macrolides is recommended. Use aminogylcosides with caution if the patient has significant hearing loss or balance issues.

Physiotherapy and postural drainage

Airway clearance techniques and postural drainage has been regarded as mainstay of treatment. These techniques help in loosening the secretions for patients to expectorate them. HRCT is integral to understanding which area to target. Patients should be offered active cycle of breathing techniques or oscillating positive expiratory pressure as recommend by the BTS and devices such as flutter, acapella is useful.

Nutrition and hydration

Hydration is important to prevent drying up of secretions. In cystic bronchiectasis and severe disease adequate high protein diet is recommended.

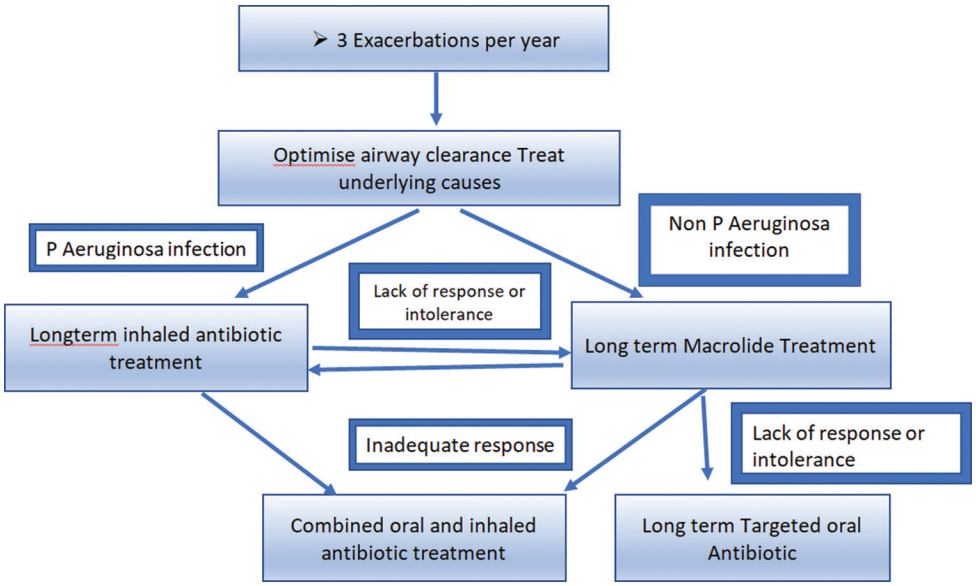

Figure 3: Recommendation for long term antibiotic in bronchiectasis

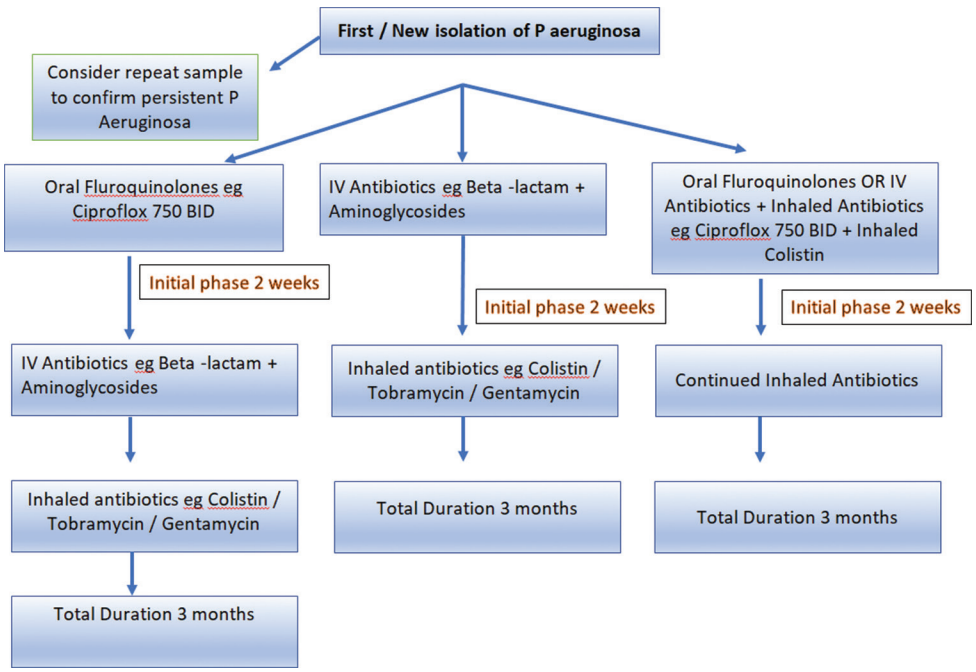

Figure 4: Possible eradication pathways for Pseudomonas aeruginosa

Other treatments

Inhaled bronchodilators (beta 2 agonist or antimuscarinic) are recommended when lung function show obstructive defect. Inhaled corticosteroids should only be advised to patients with concomitant conditions such as ABPA, chronic asthma, severe Chronic obstructive pulmonary disease. Oral steroids are indicated in proven ABPA as per the recommended doses and duration. No role of theophylline. Vaccination for influenza and pneumococcal pneumonia prevention is recommended.

SURGICAL TREATMENT

Common indication for surgery is recurrent infections with chronic symptoms such as cough, copious purulent sputum that is uncontrolled despite appropriate medical management

in localized disease. Recurrent large and life-threatening hemoptysis refractory to bronchial artery embolization is an indication for surgery. Video-assisted thoracoscopic surgery is preferred modality for surgery. Overall, surgical interventions seem to be beneficial only in carefully selected patients and this decision should be in conjunction with pulmonologist opinion. ELF/EMBARC patient advisory group suggests that patients choose surgery only if there was no effective medical option for treatment.[3]

COMPLICATIONS

Infective exacerbations and pneumonia are common complications. Massive hemoptysis is rare but may be life-threatening requiring BAE. Pulmonary hypertension and chronic respiratory failure complicate end-stage bronchiectasis. Frequent sinusitis has been observed.

PROGNOSIS

Chronic colonization with Pseudomonas is a risk factor for recurrent severe exacerbations and decline in lung function. Poor nutritional status, lack of regularised care, and vaccination are also risk factors for exacerbations. Extensive cystic Bronchiectasis on HRCT and severe disease with the need for long-term oxygen therapy are poor prognostic indicators.

FUTURE ADVANCES

Brensocatib (formerly known as INS1007) has been given breakthrough therapy designation by U.S. FDA to treat adult patients with non-cystic fibrosis bronchiectasis for reducing exacerbations. Brensocatib may decrease the damaging effects of inflammation by prohibiting DPP1 and its activation of neutrophil serine proteases. An upcoming Phase III clinical trial will provide further information.

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