Review paper on Bronchiectasis

Sudhir Lohani[a]

[a]*Consultant Respiratory Physician, Darent Valley Hospital, Dartford, UK.*

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ABSTRACT

Bronchiectasis is characterized by dilatation of bronchi, airflow limitation and chronic infection/inflammation. The aetiology, pathology and management are discussed in this review. It is vital that we distinguish bronchiectasis from other obstructive airways disease like Asthma and Chronic obstructive airways disease as management strategies are different.

INTRODUCTION

Bronchiectasis is a condition where destruction and damage of bronchioles lead to chronic airflow obstruction and typically copious expectoration. It is characterized by permanent dilation of bronchi and bronchioles caused by destruction of the muscle and elastic tissue, resulting from or associated with chronic necrotizing infection.[1] This was first described by Laennec in 1819 and identified tuberculosis and pertussis as the most likely causes.[2]

It is difficult to be sure of the true prevalence of bronchiectasis. Various epidemiological studies have suggested prevalence of 1.3 per thousand to 17.8 per thousand.[3-6] The prevalence rises with increasing age. Studies from USA suggested prevalence of 4.2 per thousand in ages 18-34 , rising to 271.8 per thousand in people aged over 75.[6]

Bronchiectasis has traditionally been described as one of the obstructive airways disease along with Chronic obstructive airways disease and Asthma. However it is a distinct entity from pathological viewpoint. The destruction of wall of bronchioles which is seen in bronchiectasis is possibly an end product of repeated infection caused by some defect in immune system or some local defect caused by structural abnormality. This leads to chronic inflammation and excessive mucus production which are typical of bronchiectasis.

AETIOLOGY

There are a wide ranges of conditions that can cause bronchiectasis. An approach based on pathological process appears to be logical and is described in the table 1.[7]

CLINICAL PRESENTATION

Cough productive of sputum is the most common symptom associated with bronchiectasis.[8-12] Typically sputum is copious in amount and expectoration could be positional. Other symptoms are haemoptysis, breathlessness, chest pain and fever. Crackles associated with some wheeze are the most common clinical findings. Finger clubbing is said to be a feature associated with bronchiectasis and is usually associated with severe disease.

HISTOPATHOLOGY

Histopathologically bronchiectatic airways appear dilated and on examination have a cross sectional area that is much larger than accompanying pulmonary artery.[13] The airway lumen is filled with a mucopurulent exudates with neutrophils and macrophages. The bronchial wall is often destroyed due to loss of fibromuscular tissues and the elasic framework, and may show erosion and loss

***Corresponding author**
Consultant Respiratory Physician, Darent Valley Hospital, Dartford, UK.
Email address - sdlohani@aol.com

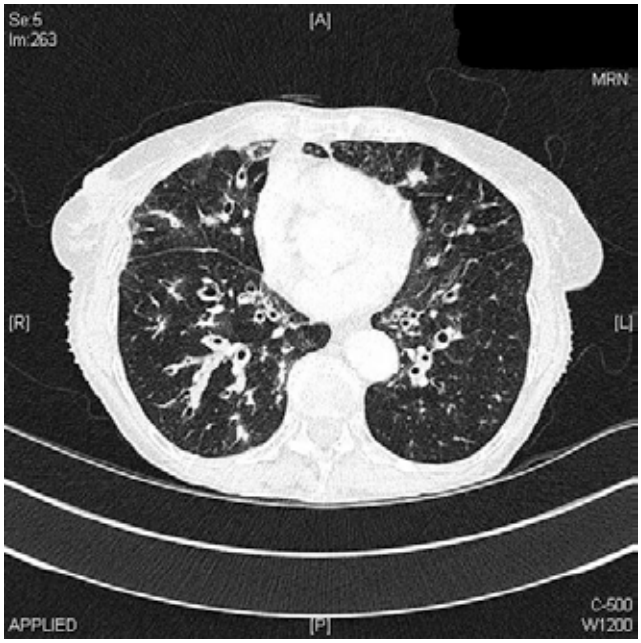

Figure 1. **High resolution CT scan showing features of bronchiectasis.**

of cartilage.[14] There is an associated chronic inflammatory cell infiltrate within the wall, predominantly lymphocytes and plasma cells, and in some cases lymphoid follicles with germinal centres may be prominent.[15] The airways are supplied by the bronchial arteries and the inflammatory destruction and healing processes result in the formation of broncho-pulmonary anastomoses.[12] Ulceration of the airways could lead to haemorrhage and haemoptysis.

The pathogenesis is complex and many different factors act together to set up a cycle of inflammation and destruction that leads to damage and destruction of the bronchial walls.[16] In the early stage of bronchiectasis, the most common bacterial isolate is Haemophilus influenza which has the capacity to damage the airway epithelium and induce the production of inflammatory mediators.[17] Over time, a number of other microorganisms get established , particularly *Streptococcus pneumonae* and *Pseudomonas aeruginosa.* Persistent infection and chronic inflammation lead to systemic complications.

INVESTIGATION

1.CT Scan - High resolution CT scan of the chest is the confirmatory test for diagnosis of bronchiectasis. Findings include bronchial wall thickening with dilatation of bronchi to a diameter greater than that of accompanying arteriole (signet ring sign), lack of normal tapering of bronchi on sequential slices and visualization of bronchi in the the outer 1-2 cm.[8,18,19] Cases of allergic broncho pulmonary aspergillosis have central bronchiectasis while cystic fibrosis cases have upper zone bronchiectasis.

2. Chest X-ray - This is useful as a baseline to monitor disease progression and at times of exacerbations. X-rays may show tram lines or ring shadows.[20]

Table 1. **Cases of Bronchiectasis**

Structural lung conditions	William-campbell syndrome Mounier-kuhn syndrome Ehlers Danlos syndrome
Toxic damage to airways	Inhalational injury Aspiration secondary to neuromuscular diseaseGastro-intestinal reflux disease
Obstruction of single bronchus	Tumour Foreign body
Obstructive airways disease	Asthma Chronic obstructive airways disease Alfa 1 antitrypsin deficiency
Defects of mucociliary clearance	Ciliary diskinesia Primary ciliary diskinesia Secondary ciliary diskinesia
Channelopathies	Cystic fibrosis tans membrane conductance regulator dysfunctions Epithelial Sodium Channel dysfunction
Allergic bronchopulmonary Aspergillosis	
Immunodefficiency	Common variable immunodefficiency X-linked agammaglobulinaemia Chronic granulomatous disease Antibody deficiency with normal Immunoglobulin Secondary immunodefficiency Haematological malignancy Post allogenic bone marrow transplant Drug induced immunosuppression
Infection	Childhood infection Tuberculosis Pneumonia Measles Whooping cough Non tuberculous Mycobacteria
Bronchiectasis in systemic disease	Inflammatory bowel disease Connective tissue disease Yellow nail syndrome
Idiopathic bronchiectasis	

3. Blood tests - Full blood count may show anaemia (of chronic disease). IgE levels may be raised in cases of allergic broncho-pulmonary Aspergillosis associated bronchiectasis. Aspergillus precipitin tests, Immunoglobulin levels and subclasses, Alfa 1 antitrypsin levels are other tests done to investigate aetiology of brocnhiectasis.

4. Sweat tests and genetic tests may be done if cystic fibrosis is suspected.Other specific genetic tests and tests of ciliary functions are requested in appropriate clinical contexts.

5. Sputum examinations: Routine cultures are helpful in finding the colonizing bacteria e.g. *H influenza, S pneumonae and Pseudomonas aeruginosa*. AFB cultures are done to exclude *Mycobacterium tuberculosis* and also to consider the possibility of infection by Environmental Mycobacteria.

6. Lung function tests - These are useful in assessing severity of airflow obstruction and in monitoring disease progression.
ter 1-2 cm (8,18,19).

MANAGEMENT

1. Sputum clearance techniques - Sputum clearance is the mainstay of treatment of bronchiectasis. Various strategies like postural drainage, breathing exercises, flutter valves have been traditionally used with varying success. Adequate clearance improves quality of life and reduces frequency of exacerbations.

2. Inhalers - Bronchodilators and steroid inhalers may be used to improve symptom control. There is no good evidence base for use of steroid inhaler as an anti-inflammatory agent. Response to inhalers should be assessed both subjectively and objectively. The decision regarding whether to continue it long term should be decided on individual case by case basis.

3. Antibiotics - Antibiotics are the mainstay of treatment in exacerbations caused by infections. Choice of antibiotics depends on previous and current sputum culture results. Intravenous antibiotics may be used in cases with severe exacerbations or in cases not responding to oral antibiotics.

Infective exacerbation is characterized by increasing sputum volume and change in colour, increasing breathlessness, fever etc. Appropriate treatment often reverts the symptoms back to pre-exacerbation state. Short courses of steroid are used in patients who have significant bronchospasm. Nebulised bronchodilators are used as necessary.

Patients who have had frequent (more than 3 per year) exacerbations despite optimal conventional treatment may benefit from long term antibiotic therapy. The choice could be based on sputum microbiology results. They reduce exacerbation rates and improve quality of life. Macrolides like Azithromycin have been used with good outcomes and they are considered as having immunomodulatory effects.[21] One strategy is to use Azithromycin 250 mgs three times in a week.

Nebulised antibiotics e.g. Colomycin, gentamycin etc may have a role in cases with chronic pseudomonas colonisation and frequent exacerbations. The largest published study using nebulised antibiotic was published by Barker et al where pateints were randomly assigned to Tobramycin or placebo.22 62% of Tobramycin treated pateints showed improvement in Medical condition versus 38 % of placebo pateints but there was no significant difference in lung function tests.

Colonisation with pseudomonas is associated with increasing morbidity, exacerbations, declining lung functions and poor quality of lives. Various strategies have been tried to eradicate infections e.g. Ciprofloxacin plus nebulied colistin, intravenous Tazobactam etc.[23]

4. Mucolytics - Hypertonic Saline accelerates mucociliary clearance in both healthy subjects and patients with cystic fibrosis as demonstrated in radioaerosal studies.[24-27] In a randomised cross over trial, Kellett et al evaluated the effect of hypertonic saline as an adjunct to physiotherapy in 24 stable bronchiectatic patients.[28] This demonstrated increased ease of sputum clearance and reduced sputum viscocity. There is good evidence of benefits of hypertonic saline in patients with cystic fibrosis.[29] Currently the evidence base in non cystic fibrosis bronchiectasis is not as strong as in cystic fibrosis but it is well tolerated.

There is emerging evidence that mannitol is an effective treatment in non CF bronchiectasis. Daviskas et al showed improved health related quality of life with its use and it is well tolerated.[30]

Evidence base for n- Acetyl cysteine is very limited. Dornase-alfa may be harmful in non cystic fibrosis bronchiectasis althogh it is well established in cystic fibrosis.[31]

The evidence base for long term humidification is weak. Rea et al showed fewer exacerbation days, improved quality of life and lung functions. There was no significant decrease in exacerbation frequency.[32]

5. Surgery - Surgical resection should be reserved for cases with localized disease who do not respond to medical management. Lung transplant may be considered in selected cases.

6. Immunoglobulin - Patients with immunoglobulin deficiency and bronchiectasis can be treated with immunoglobulin replacement therapy.

7. Bronchiectasis with Allergic broncho pulmonary Aspergillosis - These cases are treated with steroid inhalers as well as oral steroids depending on symptom control in addition to other measures as mentioned above. The role of antifungal therapy is not estabished. Itraconazole may be used in selected cases and has often been used in addition to steroids.

8. Atypical Mycobacteria -Persistent colonisation with progressive lung involvement may need specific anti Mycobacterial therapy.

9. Haemoptysis - Patients with bronchiectasis can sometimes have massive haemoptysis. Massive haemoptysis may be treated by angiogram and embolisation or emergency surgery.

CONCLUSIONS

Bronchiectasis is chronic, progressive obstructive airways disease involving bronchioles characterized by destruction and dilatation of bronchi and is associated with chronic infection and inflammation. This brief review looks at current concepts in pathophysiology and management of bronchiectasis. Current knowledge is limited by paucity of clinical trials data and some of the concepts are extrapolated from trials involving patients with cystic fibrosis. Chest physiotherapy and mucus clearance are the mainstay of management strategy.

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