Pathogenesis of Bronchiectasis

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KEYWORDS

• Bronchiectasis • Sputum • Pathogenesis • Airway epithelium

KEY POINTS

- The pathogenesis of bronchiectasis varies by case, but generally involves a cycle of inflammation and altered immune response to infection.
- Combination of high-resolution computed tomographic imaging and sampling of the airway biology, via sputum, bronchoalveolar lavage, biopsies, or exhaled breath condensates, may target mechanisms that can be interrupted without impairing the healing stages of infection and inflammation.
- Treatment at early stages may allow for appropriate cellular and chemokine responses, reducing airway damage and harboring of virulent organisms.

In 1821, René Théophile Hyacinthe Laënnec described bronchiectasis as an "affection of the bronchia is always produced by chronic catarrh, or by some other disease attended by long, violent, and often repeated fits of coughing."[1] In 1950, Lynne Reid[2] correlated bronchographic images with pathologic specimens and defined bronchiectasis as a permanent dilation of bronchi. Systematic data for the incidence or prevalence of bronchiectasis are not available; however, it is rare in developed countries.[3] Estimates for the United States show 100,000 affected individuals, qualifying bronchiectasis as a rare disease (<200,000 affected individuals).[4] Smaller studies in isolated populations of low socioeconomic status, such as Alaskan and Australian natives, suggest a prevalence of 1% to 2%.[5,6] Although neither symptoms nor definitions have changed since the initial descriptions, numerous advancements have occurred in the pathogenesis. This review describes the changes and advancement in the pathogenesis of bronchiectasis, including mechanisms of injury and host factors.

PATHOLOGIC FEATURES OF BRONCHIECTASIS

In 1898, Ewart classified bronchiectasis into 3 forms based on the grossly dilated appearance of the large airways: (1) regular or cylindrical, (2) fusiform, and (3) globular or sacculated with a beadlike modification of the affected large airway.[7] Because of Reid's classification, bronchiectasis is grouped based on the appearance of the airways, even today. Cylindrical bronchiectasis has uniform dilation of the affected bronchi (**Fig. 1**). Varicose bronchiectasis, because of the resemblance to varicose veins, has focal areas of constriction between areas of dilation (**Fig. 2**). Cystic or saccular bronchiectasis is the most damaged form, characterized by dilated bronchi that end in cysts and grapelike clusters (**Fig. 3**).[2] The current gold standard for imaging the airways and classifying bronchiectasis is high-resolution computed tomographic (HRCT) imaging.[8,9] The pathologic terminology has been maintained and adopted when describing computed tomographic (CT) images of the chest (**Table 1**).

Because most patients are not diagnosed until an advanced stage, the gross pathology is mainly available from surgical or autopsied specimens. With the decline of surgery for bronchiectasis and autopsies over the past several decades, descriptions of the pathologic conditions of the airway mainly come from reports that were available 5 or more decades ago. The lumina contain purulent mucus and necrotic debris reflecting

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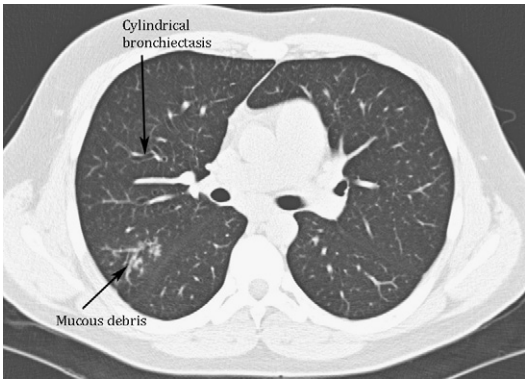

Fig. 1. Computed tomography (CT) image showing cylindrical bronchiectasis and lack of clearance of mucous debris.

impaired clearance of microbial organisms and phagocytic cells. The results of physicochemical studies of sputum from Native American children from Alaska with bronchiectasis showed sputum that was less elastic and viscous, yet had higher transportability than banked sputum of patients with cystic fibrosis and chronic bronchitis.[10] Airway walls are thickened, due to transmural inflammation. Normal mucosal and muscular layers fail to heal because of repeated infectious insult and may be replaced by a fibrotic scar. In the more proximal airways, structural cartilage is lost or replaced by the scar. With the loss or destruction of supportive mural structure, airways may be dilated out to the periphery of the lung, and bronchi and bronchioles may be tortuous or even angulated by the surrounding scar. Proximally, lymph node enlargement occurs, sometimes narrowing a lobar bronchus as in the middle lobe syndrome. Because of recurrent infection and inflammation, neovascular bronchial arterioles

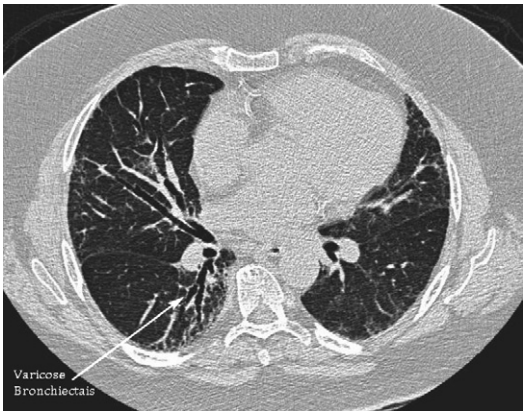

Fig. 2. High-resolution CT scan showing varicose bronchiectasis (dilated airways with fibrosis causing irregular and tortuous airways).

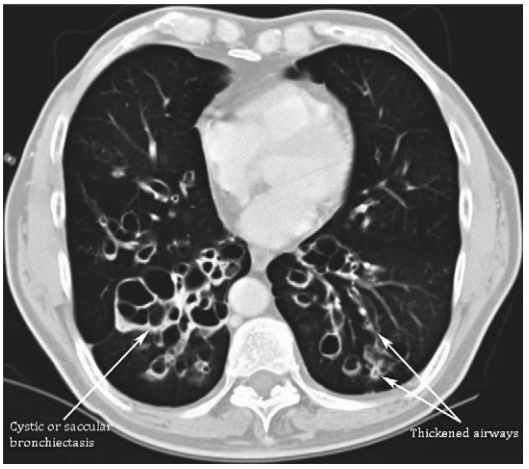

Fig. 3. CT image showing both thickened and dilated airways along with cystic bronchiectasis (grapelike clusters).

are enlarged below the mucosal surface. Erosion of the mucosa during infection contributes to the brisk bleeding sometimes seen. These changes are obviously indications of a far-advanced disease, destruction, necrosis, and attempts at repair.

Chest CT scans may provide earlier indications of susceptible or damaged airways. Patients with common variable immunodeficiency (CVID) are susceptible to recurrent bacterial infection and bronchiectasis. Inspiratory and expiratory HRCT scans were performed on 54 children aged 6 to 18 years with CVID in a stable state. The most common abnormality was expiratory air trapping (mosaic attenuation) seen in 71% to 80% of the study participants, and was the only abnormality in 9% to 15% of the study participants. The presence of air trapping in the expiratory HRCT scan results suggests that the inflammatory changes in the small airway are the cause, and raises the possibility of a reversal of these changes.[11]

Histologically, polymorphonuclear (PMN) transmural inflammation is accompanied in later stages by microabscesses of airways filled with necrotic debris, including bacteria or other infectious pathogens. Usual wavelike cilia are disrupted, fractured, or lost. Distal bronchioles may be obstructed by inflammatory debris or infected mucus. The inflammation may extend beyond airways into lung parenchyma yielding an appearance of pneumonia. Mural neovascular bronchial arterioles are recognized by their thick walls when compared with normal pulmonary capillaries. In 1952, Whitwell[12] coined the term follicular bronchiectasis. Follicular bronchiectasis has excessive formation of lymphoid tissue, and there is formation of follicles and nodes within walls of diseased bronchi.