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Childhood Bronchiectasis : A Review

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More than two decades ago, bronchiectasis unrelated to cystic fibrosis (CF) was termed "Orphan disease", because it had become an uncommon clinical entity among children in the developed world. It is more common among children in lower socioeconomic classes and in developing countries, due to more frequent recurrent respiratory infections, environmental airway irritants, poor immunization, and malnutrition. The pathophysiology includes airway inflammation, mucous production, and regional airway obstruction, but the reasons some children develop bronchiectasis while other do not is not clear. Public measures aimed at improving living conditions for children and prevention of respiratory infections with anti-viral vaccines will have a good impact on childhood bronchiectasis than medical treatment.

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Definition

Bronchiectasis is a condition in which there is abnormal and often permanent dilatation of the bronchi. The affected sub-segmental airway may have become tortuous, flabby, and are partially obstructed by purulent or viscid exudates. It typically involves the second to the sixth order of segmental bronchi, sparing the proximal ones[1]. It was first described by Laënnec in 1819. He provided the first pathologic description based on examination of postmortem specimens[1-4.]

Incidence

Bierrring in 1956 studied 151 patients in Copenhagen following pneumonia and found only one child (0.7 percent) to have bronchiectasis[2]. Rubermanm and colleagues (1957) evaluated with bronchoscopy 69 patients with persistent abnormalities on chest radiographs out of 1711 young adults (18 to 25 years of age) treated for pneumonia at a U.S. army hospital[3]. They found 29 (1.7 %) have bronchiectatic changes. Most series indicate a male/female ratio about 1:1.4[5].

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Fileld in 1961 noted a dramatic decrease in admission rates, for bronchiectasis at five British hospitals from an average of 48 per 10,000 in 1952 to 10 per 10,000 of total pediatric admissions in 1960[6]. She speculated that improved treatment of lower respiratory tract infections made possible by the increased availability of broad-spectrum antibiotics during that period accounted for the decreased incidence[6]. Other contributing factors include the prevention of measles and pertussis through the immunization and the marked decrease in primary pulmonary tuberculosis in the pediatric population brought about by better public health measures and improved treatment regimens for this disease.

Pathology

The macroscopic abnormality is that of fusiform or cylindrical dilation of sub-segmental bronchi. Also described are alternation areas of dilation and constriction, called *varicose bronchiectasis*[5,6]. In later stages, saccular dilation occurs. There is often accompanying atelectasis of the involved lobe, with pleural thickening and adhesions. In addition, the bronchi are often tortuous and filled with mucopurulent material. The small distal airways may be obliterated as the result of longstanding obstruction, being replaced by a discrete cord of fibrous tissue containing muscle, elastic tissue, capillaries, and occasionally plates of cartilage. As a process progresses, there is continued inflammatory infiltration, damage to the muscles layers, and eventually destruction of the supportive cartilage surrounding the airways. Having lost their supportive structures, the airway takes on a saccular appearance. The affected area itself is no longer lined by columnar epithelium, instead cuboidal cells and, in more advanced (saccular) disease, squamos epithelium, which is often ulcerated, fibrosed, or denuded. There is associated hypertrophy of bronchial glands, lymphoid hyperplasia, and hypertrophy of mucous glands, occasionally to the point of bronchial obstruction. The investigators hypothesized that the enlargement and anastomosis are the result of engorgement of the bronchial capillary bed (in response to local inflammation) near the pulmonary arterial vessels[5-12].

Pathogenesis

The various mechanistic theories have been divided into four groups[7-12].

The *pressure-of-secretion theory*: Thick secretions first obstruct, then mechanically distend the airway in such a way that the dilation persists after the clearance of the obstruction.
The *atelectasis theory*: It suggests that bronchial dilation is the result of increasingly negative intrapleural pressure brought about by collapse of lung parenchyma surrounding the bronchus in question.
Traction theory: contends that fibrosis and scarring from parenchymal disease exert traction on the bronchial walls.
Infection theory: holds that it is largely infection and the inflammatory response to infection that result in damage to the supportive structures of the bronchial wall and subsequent bronchiectasis.

Of these theories, only the infection theory is supported by animal models of this disease. Researchers concluded that early dilation was the result of entrapment of secretions and was reversible with relief of the bronchial obstruction. Irreversible dilation (i.e., bronchiectasis was the result of bronchial wall alterations from the pressure of entrapped secretions, concomitant

infection, or both. Bronchial obstruction with retention of secretions and infection appear to be the major factors in its development in most cases.

Etiology

Infection is by far the most common, and, until relatively recently, tuberculosis was the most common infectious agent responsible for post infectious bronchiectatic changes[1-5]. The hilar and peribronchial lymphadenopathy associated with it results in bronchial obstruction, which, when coupled with parenchymal damage from that or from subsequent infections with other organisms, can lead to bronchial wall destruction and bronchiectasis. Pertussis and, more commonly, measles complicated by pneumonia have been associated previously with subsequent development of bronchiectasis. Lees in 1950, in examining the incidence of bronchiectasis and atelectasis in 150 consecutive cases of pertussis, found that only four patients (2.6%) developed bronchiectatic changes; three of these later had spontaneous resolution[13]. Fawcitt and Party in 1957 similar reviewed 956 cases of pertussis and 897 cases of measles and found atelectasis in 48 percent and 28 percent, respectively[14]. At a later follow-up, 17 percent of the pertussis patients and 15 percent of the measles patients had residual atelectasis. Concomitant or subsequent infection with other agents, particularly adenovirus and herpervisrus, that mediates the injury resulting in bronchiectasis. Herbert, et al. in 1977 has documented bronchiectasis in 20 to 64 percent of children following pneumonia from adenovirus (types 1,3,4,7, and 21) alone[15]. Other infectious agents that have been linked to the development of bronchiectasis include *Aspergillus fumigatus* and *Mycoplasma pneumoniae*[16].

Congenital and Genetic Disorders

By far the most common genetic disorder that results in bronchiectasis is Cystic fibrosis (CF), as a result of the chronic bronchial obstruction with inspissated mucus, infection, and inflammation associated with CF (2, 17-20). Williams and Campbell syndrome has been described to cause bronchiectasis with onset of lung disease, including bronchiectasis in infancy[21]. Mitchell and Bury in 1975 described a case in which, in addition to deficiency of cartilage, obliterative bronchiolitis was noted[21]. They suggest that, although infection plays an important role in the outcome of these patients, it is lack of cartilage that is primarily responsible for the bronchiectasis. Tracheomegaly has been found to occur more frequently in individuals with bronchietasis. Bronchoscopy confirms the tracheobronchial dilation and often reveals the airway walls to be floppy and redundant, with occasional outcropping or diverticula[21].

Ciliary Abnormalities

Kartagener syndrome, the most well known, is recognizable clinically as the triad of situs inversus sinusitis, and bronchiectasis. Also associated with it is abnormal ciliary function, which is responsible for the suppurative aspects of the syndrome[22-24].

Immuno-deficiencies

Deficiency of IgG, either in total or of one or more subclasses (most often IgG2), is often associated with recurrent respiratory tract infections and the potential development of bronchiectasis. A normal serum level of total IgG does not preclude a deficiency in one of the subclasses; IgG subclasses should be evaluated separately. IgA deficiency is infrequently associated with bronchiectasis. However, IgA deficiency may be associated with IgG2

subclass deficiency and recurrent pyogenic pulmonary infections. Immunoglobulin replacement must be monitored closely in these patients, as they may become immunized against IgA. Deficiencies of complement and abnormalities of neutrophil function may also lead to recurrent pulmonary infections. Hilton and Doyle in 1978 found that 42 of 53 patients (79%) with bronchiectasis had at least one abnormality of immunoglobulins, typically an elevation in serum levels of IgA, IgG, or IgM; eight patients (15%) had elevations of all three classes[25,26].

Foreign Body Aspiration

The prolonged presence of a foreign body within the airway can result in chronic obstruction and inflammation, both major factors in the development of bronchiectasis. In a review of 500 patients with bronchiectasis, Kürklü and colleagues in 1973 found eight (1.6%) to have a long-retained foreign body as the cause[27,28].

Right Middle Lobe Syndrome

Persistent right middle lobe atelectasis can be associated with the development of bronchiectasis. Bertelsen and colleagues (1980) reported a 10-year study. A total of 135 patients (predominantly adults) with isolated right middle lobe atelectasis. Forty-six of 135 patients had nonmalignant disease, eight of the latter 46 patients (17%) had bronchiectasis[29].

Asthma

Field in 1949 and Clarke in 1963 described asthma in 6.9% and 7.8%, respectively, of children with bronchiectasis[6,24]. Bahous in 1984 found that there is increased airway reactivity in 45-69% of patients with positive methacholine challenge test with decrease in forced vital capacity (FVC) and forced expiratory volume in one second (FEV1)[30,31,32].

Other Causes

Developmental abnormalities of the lung, such as intralobar pulmonary sequestration or bronchiectasis by causing extrinsic obstruction of the airway, or in association with chronic infection of the cyst itself if it communicates with the tracheobronchial tree[33-36]. Chronic sinusitis has previously been associated with bronchiectasis. Whether chronic aspiration of purulent sinus drainage leads to bronchiectasis or chronic expectoration of purulent sputum causes recurrent contamination of the sinuses or both are not known. Sever or recurrent aspiration may lead to the development of bronchiectasis. Anatomic abnormalities, such as tracheoesophageal fistula, or neurologic deficits, such as cerebral palsy, may be associated with chronic aspiration and the subsequent development of bronchiectasis. Aspiration following general anesthesia, especially for tonsillectomy and adenoidectomy, has in the past been linked to bronchiectasis. Pulmonary injury from inhalation of noxious gases may predispose to bronchiectasis. Anhydrous ammonia and sulfur dioxide have both been implicated in this regard. Concomitant or subsequent infection may be important cofactors for these events[33-36]. HIV, lipid pneumonia, and scoliosis have been described to cause bronchiectasis[37-44].

Presentation

Age

The majority of children with bronchiectasis present in the preschool and early school-age years. Field found that 40 % of the 160 patients in her review presented before seven years of age, with 20 percent presenting between age six and seven years[6,12]. Of the 116 children with bronchiectasis reviewed by Clark, 84 % presented before age six and 50 % before three[24].

Symptoms

Cough, not surprisingly, is an almost universal finding and can often be dated from an acute respiratory illness. The incidence of sputum production is likely much higher than listed, because many patients present before an age when sputum is normally expectorated. Hemoptysis characterized as mild, slight, or streaking. Other symptoms noted with less frequency include weight loss (although most children with bronchiectasis maintain adequate weight gain) and intermittent fever. Field found a median duration of approximately three years[6]. Frequently present, a history of recurrent pneumonia especially when restricted to a single lobe or segment. Except in diffuse disease, the auscultatory findings are usually localized to the involved areas. In addition to these physical findings, the author described various deformities of the chest wall, the most common being a linear area of depression circumscribing the lower third of the chest wall (Harrison's Sulcus)[6]. The author also found postural deformities (rounded shoulders, lordosis, protuberant abdomen) to be common[6]. The author also found that in long-term follow-up the incidence of clubbing had fallen from 43.7 % to 6.5%, although she points out that the death of the most severely affected patients might have influenced the change in these figures.

Diagnosis

Although not diagnostic, bronchiectasis can be suspected on the basis of abnormalities on chest radiographs[45-47]. Bronchial dilatation (present in 100%); volume loss (97%); bronchial wall thickening (92%); signet ring sign (the presence of a thick-walled, end-on bronchus larger than its companion end-on artery) (79%); compensatory hypeinflation (58%); mucoid impaction (45%); and cyst formation (42%). Other nonspecific findings said to be suggestive of bronchiectasis include segmental accentuation and loss of definition of lung markings and loss of lung volume, manifested by crowding of lung markings. Another finding is the "tram-track" sign; parallel linear markings that represent thickened bronchial walls viewed in their longitudinal dimension. Flexible fiberoptic bronchoscopy has become an extremely valuable diagnostic modality for the pediatric pulmonary subspecialist.

Computed tomography (CT) in the evaluation of bronchiectasis[45-47].

Four findings characteristic of the disease: 1) air-fluid levels in distended bronchi, 2) a linear array of cluster of cysts, 3) dilated peripheral bronchi, and 4) thickened bronchial walls. Using medium-thickness cuts (4mm) at medium slice intervals (5mm). Joharjy and co-workers in 1987 found a specificity of 100% for all types of bronchiectasis and sensitivities of 100% for cystic and 94% for cylindrical disease when compared with bronchograms in 20 patients[48,49]. Lung scintigraphy appears to be a useful screening measure when combined with plain chest radiography. The left lower lobe, the upper lobes are commonly involved, probably because mucociliary clearance is facilitated by gravity. Multilobar involvement is common, with left lower lobe and lingual the most common combination.

Ventilations/ Perfusion lung scan

There are marked reductions in ventilation and less severe reductions in perfusion in patients with bronchiectasis[50]. The study showed that, Scintigraphy had a sensitivity of 89 percent for bronchiectasis as compared with 71 percent for chest radiographs. The study concluded that lung scintigraphy is useful screening test for diagnosis and prognosis of bronchiectasis.

Other diagnostic tests

Viral and bacteriologic studies not only provide epidemiologic data but also may guide therapy. Evaluating the presence of a foreign body, obtaining samples of respiratory epithelium for ciliary studies, and providing information regarding endobronchial anatomy. Evaluation of immunodeficiency, cystic fibrosis, aspiration, mycobacterial or fungal disease, or other predisposing factors is also important and should proceed as guided by the clinical picture.

Treatment

The emphasis is on removal of excess secretions, treatment of intercurrent infection, and good nutrition. Surgical management, utilized less frequently than in the past because of improved medical management, may offer significant benefits to those children with localized disease but persistent symptoms[51-54].

Medical Therapy

Chest percussion and postural drainage (or chest physiotherapy) are effective in facilitating clearance of secretions in those patients whose bronchiectatis is associated with excessive sputum production (greater than 30 ml/day). Physiotherapy results in more rapid and complete clearance of a radioactive aerosol than coughing alone. Some studies have shown improvement in pulmonary function following chest physiotherapy[3,51-54]. Autogenic drainage may also be helpful in those children old enough to master this technique. Newer methods of airway clearance, such as the use of a flutter valve device or positive expiratory pressure valve, have been found to be helpful in some patients with CF. Mucolytic agents, such as *N*-acetylcysteine, may not penetrate the mucous blanket enough to be effective and, more important, may be potent bronchial irritants. There is some evidence, however, that ß-adrenergic agonists improve mucociliary clearance. More recently the use of aerosolized recombinant deoxyribonuclease (Dnase) has been shown to result in an improvement in pulmonary function and a reduction in the frequency of respiratory exacerbations in patients with CF. Although antibiotic therapy is clearly indicated for acute infections (increased cough and sputum production, fever, malaise, etc.), its use on a continuous basis is generally discouraged. Long-term antibiotic therapy may be of benefit to those individuals whose bronchiectasis has an underlying cause (e.g., cystic fibrosis, immotile cilia syndrome), those who experience a marked increase in pulmonary symptoms on withdrawal of antibiotics, or those who have frequent bouts of lower respiratory tract infection.

Antibiotic therapy should be directed at specific pathogens and guided by sputum cultures and sensitivity studies. Pending the outcome of microbiologic studies, empiric antibiotic therapy should be directed against those organism commonly found in the sputum of patients with bronchiectasis[54-61] : *Haemophilus influenzae, Streptococcus pneumoniae,* and *staphylococcus aureus*. Organisms found less commonly include *Pseudomonas aeruginosa* and *Proteus*

vulgaris. The role of anti-inflammatory therapy is unclear. There are studies that suggest that indomethacin and inhaled corticosteroids may reduce sputum production and, in the case of indomethacin, reduce sputum concentration of inflammatory mediators. Sanderson and co-workers in 1974 reviewed 393 patients (88 of them less than 15 years of age) and compared outcomes in the surgically and conservatively treated groups[62]. They found that surgically treated patients overall had better outcomes, although with milder disease the difference between the groups was less striking. Most investigators agree that aggressive medical therapy should be carried out for at least two years before considering surgery. Depending on the cause of bronchiectasis, surgical resection is an option even in patients with bilateral disease. Such patients generally undergo resection in two stages, with the more severely affected area being removed first. Occasionally, the second resection can be deferred because of satisfactory improvement achieved with the first procedure. The most important factor in determining outcome following pulmonary resection for bronchiectasis is patient selection. Others have suggested that children with localized disease accompanied by significant persistent symptoms are the best surgical candidates[3,54-61].

Complications

Common in the preantibiotic era but now are rare: brain and lung abscess, empyema and pyopneumothorax, bronchopleural fistula, severe atypical pneumonia, hemoptysis, amyloidosis, and, in advanced disease, cor pulmonale[63]. Serious complications from surgical therapy are uncommon, but less severe problems are more common. Sanderson and colleagues had an overall complication rate of 30.5%[62].

Prognosis

The prognosis for children with bronchiectasis, in general, is quite good. Clark reviewed the outcome in 116 children at five to 14 years after diagnosis. In 79 of the children, repeat bronchograms had been performed at intervals from six months to eight years. Of these children, 46 (58%) showed no change, 27 (34%) had deteriorated, and seven (9%) had improved. Only 15 of the 27 patients who had deteriorated demonstrated involvement of previously normal airways. There were five deaths, two postoperatively. Of the 80 children treated surgically, 55% recovered completely and 16% had only minimal symptoms. In the medically treated group (six of whom were considered candidates for surgery), 81% were improved, although 12 of these patients had only mild disease initially. Field found similar results in her initial follow-up series[6].

Landau and colleagues in 1974 evaluated pulmonary mechanics in 69 children and young adults with bronchiectasis[64]. Their results suggest that generalized small airways obstruction is common in bronchiectasis that has been present since childhood, independent of the treatment modality used.

CONCLUSION

From the standpoint of social functioning (employment, marriage, and family life), there is general agreement that the majority of patients with bronchiectasis can lead relatively normal lives if they are provided with appropriate medical support and care.

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