Rapidly progressive bronchiectasis complicating ulcerative colitis in a child

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Patients with ulcerative colitis may have a presentation dominated by extraintestinal manifestations. These manifestations, particularly bronchiectasis, are very rarely seen in pediatric patients. A 13-year-old boy with ulcerative colitis who was diagnosed by colonic mucosa biopsy is presented. He developed unexplained productive cough after the appearance of colonic disease. He was treated and followed up at his primary care hospital with the sole diagnosis of ulcerative colitis, with little attention given to the chest symptoms. The relation of the bronchial involvement to the ulcerative colitis was not established until two years after the onset of disease. Thoracal computed tomography (CT) examination after this period showed evidence of bronchiectasis and pulmonary involvement. Despite prophylactic inhaled corticosteroid treatment, no clinical or radiographic improvement was observed and widespread bronchial destruction developed very rapidly. More effective treatment with oral steroids was probably necessary in this patient, if the early chest symptoms were related to the ulcerative colitis.

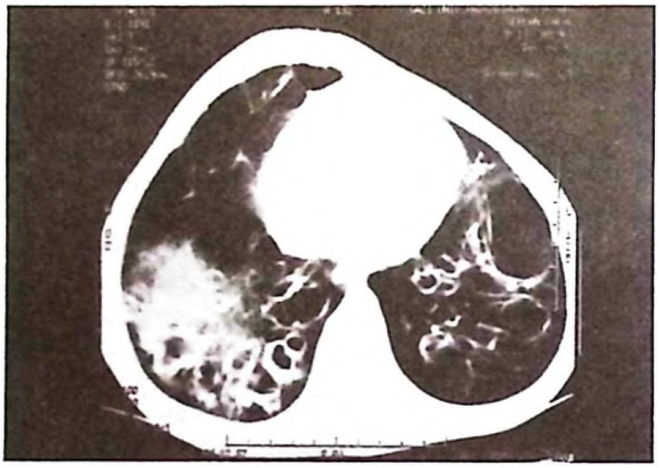
Key words: bronchiectasis, inhaled corticosteroid, ulcerative colitis.

Over the course of the past 20 years, varied patterns of pulmonary involvement in ulcerative colitis have been identified in case reports[1-4]. These manifestations, particularly bronchiectasis which is the characteristic pulmonary lesion of adult ulcerative colitis, are very rarely seen in pediatric patients. We present a 13-year-old boy with ulcerative colitis who developed a rapidly progressive bronchiectasis after the appearance of colonic disease despite inhaled corticosteroid treatment.

Case Report

A 13-year-old boy was admitted to the emergency room in December because of a productive cough, cyanosis and dyspnea at rest. Colonic mucosa biopsy proven ulcerative colitis had been diagnosed in 1993 with a one-year history of persistent mucous diarrhea, abdominal pain and intermittent rectal bleeding, and sulfasalazine treatment was started. Within three months of his medication he had an unexplained productive cough. There was no history of significant respiratory illness (including no sinusitis, wheezy bronchitis or asthma, or gastroesophageal reflux), nor family history of pulmonary disease. A switch from sulfasalazine to mesalazine produced no change in respiratory symptoms. In 1995, he experienced hepatic dysfunction and transient, multiple joint swelling and tenderness which involved the large joint and was asymmetric in distribution without exacerbation of the colitis. Investigations included hepatic biopsy which confirmed the chronic active hepatitis diagnosis. During follow-up, there were two minor exacerbations of his chronic hepatitis, but arthritis did not reappear. He experienced three to four episodes of gastrointestinal disturbance each year which responded to intermittent oral corticosteroid therapy. However, increase in his productive cough and dyspnea continued with progressive changes on the chest X-ray. In June 1995 thoracal computed tomography (CT) scan showed newly developing cystic bronchiectasis (Fig. 1). Subsequently, prophylactic treatment was started with inlaled budesonide, 800 μg/day. Between 1995-1998 he was hospitalized several

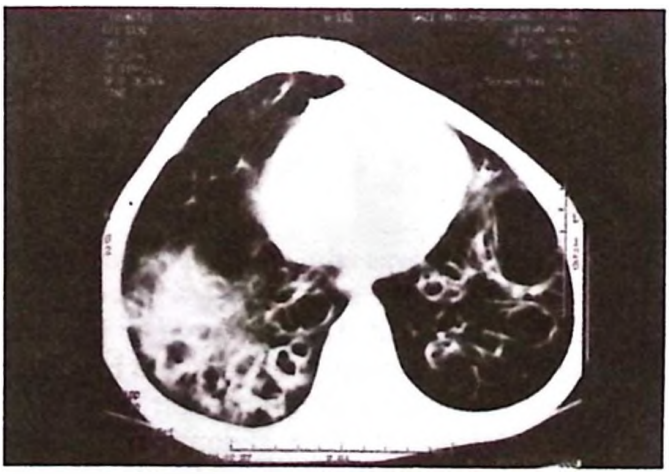
times for pulmonary disease, and had received prednisone in doses ranging from 20 mg to 30 mg daily for treatment periods of seven to 10 days, with dramatic improvement. The other intermittent medications included mesalazine, antibiotics and bronchodilators. Despite prophylactic inhaled corticosteroid treatment, productive cough and dyspnea increased and home oxygen treatment was started, seven months prior to our evaluation.



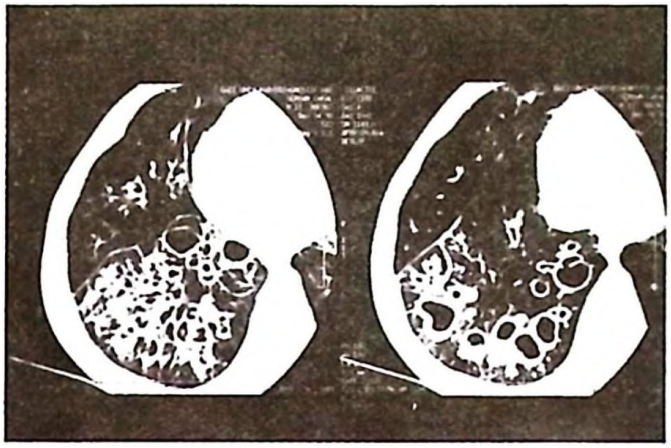
Fg. 1. Thoracal computed tomography (CT) scan in 1995 demonstrated newly developing cystic bronchiectasis affecting both the lower lobes and the middle lobe. The bronchiectasis was more severe in the left paracardiac region (arrow).

At the time of admission, his parents reported the above history. On his examination, the patient's general condition was poor. He was unable to walk and could not do his normal activities. He was cyanotic and orthopneic with intercostal retractions. Physical examination showed a thin and weak boy, with a blood pressure of 110/79 mmHg and a heart rate of 88 beat/min. Examination of the chest revealed widespread wheezing and crackles at both lungs. There was considerable finger clubbing and pectus carinatum. The liver was palpable 2 cm below the costal margin; the spleen was not palpable.

The arterial blood gas values on room air showed an arterial oxygen tension (PaO_2) of 65 mmHg, arterial carbon dioxide tension ($PaCO_2$) of 40 mmHg and pH of 7.4. Hemoglobin was 10 g/dl. White blood cell count, serum electrolytes, liver function tests, autoantibody screen (ANA, SMA, LKM-1, cANCA, pANCA) and sweat sodium levels were negative. Hepatitis B surface antigen and anti-hepatitis C antibody were negative. HLA B27 was negative. Erythrocyte sedimentation rate was 60 mm in the first hour, and C-reactive protein was 38 mg/dl. His serum IgE was 20 IU/L; other quantitative immunoglobulins, including IgG subclasses, were normal. There was no serological evidence for bronchopulmonary aspergillosis at the time of evaluation. In addition, sputum cultures did not reveal Aspergillus organisms or other fungi, and dermal hypersensitivity to Aspergillus antigen was absent. Skin-prick tests for the other common allergens were negative. Repeated bacteriologic studies of sputum, including cultures for mycobacteria, were negative. The cell type was neutrophils. A tuberculin skin test (ppd, 5 TU) was negative. Repeated colonic mucosal biopsies showed ulcerative colitis in remission. Abdominal ultrasonography showed multiple gallstones in gallbladder, of which the greatest was 1x1 cm. Consecutive CT scans of the thorax showed progression to widespread, severe cystic bronchiectasis (Figs. 2a, 2b). Treatment with parenteral fluid, oxygen, cefuroxime, nebulized salbutamol and budesonide (200 µg/day) and intravenous methylprednisolone (40 mg/day) was started. Three weeks later, the patient's clinical condition was somewhat improved and he was able to perform the pulmonary function test: forced expiratory volume in ones (FEV_1) was 0.50 L (31% of predicted), forced vital capacity (FVC) was 1.10 L (62%) of predicted), FEV_1/FVC: 45% and 25-75% of forced expiratory flow (FEF_{25-75}) was 0.25 L/sec (12% of predicted). FEV_1 increased to 0.57 L after inhaling 5 mg nebulized salbutamol (an increase of 15%). Intravenous methylprednisolone was changed to oral methylprednisolone without dose change, and



Fg. 2a. Repeated thoracal CT scan at the same level through the lower lobes three years after diagnosis showed progression to widespread severe cystic bronchiectasis.



Fg. 2b. A thoracal high resolution CT scan shows multiple rounded lucencies with discrete walls representing severe cystic brnochiectasis with prominent bronchial wall thickening almost entirely replacing the right lower lobe.

then was gradually tapered off while he continued inhaled budesonide (2000 µg/day). He was discharged with inhaled budesonide, salbutamol, continuous oxygen, and oral methylprednisolone (30 mg/day).

Discussion

Occasionally, patients with ulcerative colitis may have a presentation dominated by extraintestinal manifestations. This accounts for less than five percent of pediatric disease[5]. Camus et al.[1] recently described the largest series of patients with inflammatory bowel disease-associated large airway disease, which included 28 patients with ulcerative colitis. In that series, only six patients developed bronchiectasis. A study in 1998, the second largest case series of such patients, reported by Spira et al.[2], included a series of six ulcerative colitis adult patients who had new, persistent and unexplained symptoms of respiratory disease, particularly chronic productive cough. In four patients, a subsequent diagnosis of ulcerative colitis-associated bronchiectasis was made using CT scan. The pattern of ventilatory impairment was predominantly obstructive in patients with ulcerative colitis[3,4]. Generally, the course and severity of the extraintestinal involvement do not correlate with the colonic disease[1,2]. On long-term follow-up, our patient had experienced three to four colonic attaks each year, whereas supurative pulmonary disease progressed very rapidly. Concurrent exacerbations of bowel, hepatic and airway disease never occurred. Only pulmonary disease was severe enough to require hospital treatment.

The mechanisms of bronchiectasis in patients with ulcerative colitis has not been clearly defined yet, but it may simply represent inflammation at two different sites of common embryological roots[1]. There is accumulating evidence for a cell-mediated pattern of immune response with infiltration of activated CD4+ or CD8+ T lymphocytes within the bronchial mucosa in bronchiectasis[6]. These cells have been noted in a number of other systemic diseases including ulcerative colitis[6]. The similarities of the mucosal immune system of the lung (bronchial-associated lymphoid tissue) and intestine (gut-associated lymphoid tissue) suggest that the immune cells may migrate from the gut to the lung, possibly leading to inflammatory damage at both the bronchial and colonic mucosa[7]. Gaga et al.[8] clearly demonstrated that in patients with bronchiectasis treated with inhaled corticosteroids, the T cell infiltrate (CD4+ T cells) was significantly lower than in untreated patients. This finding supports a role for cell-mediated immune mechanisms in the pathogenesis of ongoing airway damage in bronchiectasis.

Our patient had no prior viral or bacterial infections of the lungs, including no mycobacterial infections, which could predispose to development of recurrent infections and bronchiectasis. The absence of alternative factors to account for his bronchiectasis; failure to isolate bacterial pathogens on repeated sputum culture; presence of bowel disease preceding the onset of pulmonary symptoms; and an impressive response to oral steroids, particularly during the onset of disease, all support that the pathogenesis of bronchiectasis in ulcerative colitis may be primarily autoimmune. It is possible that his bronchiectasis may have represented, the end stage of an active inflammatory process seen in all of the bronchia. Cholelithiasis and chronic active hepatitis were associated with ulcerative colitis in our patient. The relationship between chronic active hepatitis and inflammatory bowel disease remains unclear. Although there was no autoantibody positivity in our patient, the type of chronic active hepatitis found to be associated with inflammatory bowel disease has usually been the so-called autoimmune type[9].

In our patient, the relation of the bronchial involvement to the ulcerative colitis was not established until two years after the onset of disease. Thoracal CT examination after this period showed evidence of bronchiectasis and pulmonary

involvement, leading to bronchial destruction after only three years. Inflammatory bowel disease-associated lung disease is generally responsive to inhaled[2] and oral steroids[1-3]. Our patient received the minimal dose of systemic steroid medication for periods too short in duration. He was treated with inhaled corticosteroids for a period of about three years, but no clinical or radiographic improvement was observed and widespread bronchial destruction developed very rapidly. Probably more effective treatment with oral steroids was necessary in this patient.

Some of the pulmonary involvements make a substantial contribution to the considerable fatality[4,10]. It is impotant to recognize this association in patients with ulcerative colitis who have had unexplained persistent pulmonary symptoms. To our knowledge, in inflammatory bowel diseases, so destructive and rapid a pulmonary complication as seen in our case has not been reported previously. Because of its extremely rapid progression, proper anti-inflammatory treatment should be started immediately in the early stage in such patients.

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