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SHORT REPORT

Crohn's disease with pulmonary manifestations in children: 2 case reports and review of the literature ☆

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Abstract

Crohn's disease (CD) is a chronic granulomatous disease of unknown etiology that affects primarily the gastrointestinal system but can be associated with extraintestinal manifestations. Latent pulmonary involvement in children with CD has been described, but symptomatic pulmonary disease has rarely been reported in children. In this review, we report two pediatric cases, one with pleural effusion at the time of CD diagnosis and the other with bilateral cavitary lesions in a previously diagnosed CD patient. We review the current literature and summarize the diagnosis and management of pulmonary involvement in CD. Awareness of these pulmonary complications of CD in children may lead to more prompt diagnosis, guide appropriate therapy, and decrease morbidity.

1. Introduction

Crohn's disease (CD) is a complex, multifactorial disease characterized by chronic inflammation primarily involving the gastrointestinal system.[1] It can affect any part of the gastrointestinal tract from the mouth to the anus. Up to 25–40% of patients with CD can have a variety of extraintestinal manifestations including erythema nodosum, pyoderma gangrenosum, ankylosing spondylitis, arthritis, hepatitis, sclerosing cholangitis, pancreatitis, nephrolithiasis, uveitis, and episcleritis.[2] Pulmonary involvement in CD is often underappreciated, with the overall prevalence of broncho-pulmonary manifestations previously estimated to be as low

Abbreviations: CD, Crohn's disease; IBD, Inflammatory bowel disease; 5-ASA, 5-Amino-salicylic acid.

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as 0.2%. This figure likely is misleadingly low as pulmonary involvement is commonly not considered as part of Crohn's routine care.[3] Asymptomatic complications occurring during the course of CD are the most frequent and patients can have alteration in lung function tests and/or bronchoalveolar lavage (BAL) abnormalities.[4–7] Although asymptomatic pulmonary involvement is well described, only a minority of patients have associated symptoms or overt signs. Respiratory manifestations often, but not always, follow the onset of bowel disease and may exacerbate during gastrointestinal disease relapses.[8] Moreover, pulmonary symptoms in CD patients could also result from side effects of medications,[9] opportunistic infections[10] and also from some overlap syndromes including sarcoidosis,[31–34] thus creating diagnostic challenges and delays in initiation of appropriate therapy.

Since the first description of the association of pulmonary manifestations in patients with inflammatory bowel disease in 1976, several cases and case series have been reported in adults.[11] In pediatric patients however, the association is less well described. An extensive English literature search revealed only 15 previously reported pediatric CD patients with symptomatic pulmonary disease. This article reports two additional pediatric CD patients presenting with pulmonary symptoms and also reviews the relevant characteristics of bronchopulmonary involvement in CD patients.

1.1. Case 1

An 11-year-old female with psoriasis was admitted to our hospital with a three-week history of worsening non-productive cough. She denied any history of shortness of breath, chest pain, fever or hemoptysis. A review of systems was negative for diarrhea, vomiting, hematochezia, joint pain and weight loss. Her past medical history was significant for poorly controlled psoriasis with frequent flares that were not responding to topical therapy. Physical examination on admission revealed a well appearing girl in no apparent distress. Her height and weight percentiles were appropriate for her age. She was afebrile and had normal vital signs. Chest findings included decreased air entry at the left base on auscultation. The remainder of the systemic examination was unremarkable except for the presence of a licheniform rash in the intertriginous regions of the axilla, inframammary, and scalp areas without suppuration or exudates.

Her initial laboratory investigations revealed a white blood count of 10,800/μL, hemoglobin of 10.3 g/dL, erythrocyte sedimentation rate of 22 mm/h, and C-reactive protein of 2.2 mg/dL (reference range<1.00 mg/dL). Chest radiograph revealed a left sided consolidation and a pleural effusion. She was empirically started on intravenous cefotaxime for suspected pneumonia after obtaining blood and urine cultures. During the course of her hospital stay she developed progressive shortness of breath and worsening left-sided consolidation with increasing pleural effusion (Fig. 1) that mandated thoracentesis and chest tube placement.

The work-up including ANA, DsDNA, HLAB27, C3, C4, immunoglobulins, lymphocyte markers, uric acid, lactate dehydrogenase, thyroid profile, ferritin, celiac screen, HIV 1 and 2 antibodies, hepatitis panel, serology for Herpes simplex virus, Epstein–Barr virus and cytomegalovirus,

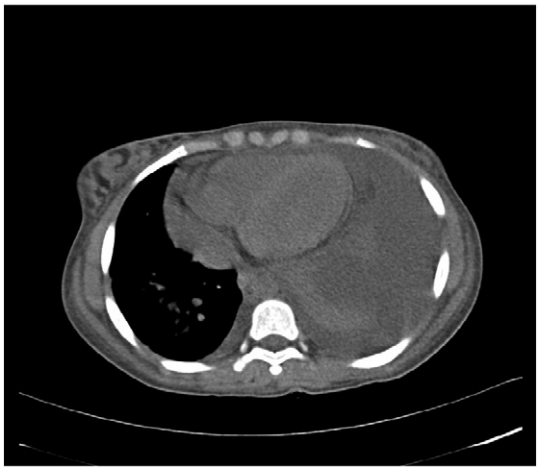

Figure 1 Computed tomographic scan revealing left pleural effusion with consolidation of the left lower lobe.

Legionella antigen, and mycoplasma titers was all normal. Purified protein derivative (PPD) and QuantiFERON®-TB Gold In-Tube tests for tuberculosis were negative. Angiotensin converting enzyme and serum lysozyme for sarcoidosis were normal. All her blood and urine cultures for bacteria, virus and fungi were negative. She underwent bronchoscopy, which revealed thick tracheal secretions. Bronchoalveolar lavage (BAL) fluid analysis revealed a total cell count of 2719/μL with 93% neutrophils, 3% lymphocytes, 2% alveolar macrophages and 2% eosinophils. Pleural fluid analysis revealed 3% neutrophils, 83% lymphocytes and 14% monocytes. BAL and pleural fluid cultures for bacteria, virus, fungi and mycobacteria were negative. Due to the new onset of diarrhea on day 10 of admission and development of hypoalbuminemia, the gastroenterology team was consulted. Her stool calprotectin level was significantly elevated at 847 μg/g but stool studies for cultures, ova, parasites, Giardia and Cryptosporidiosis were negative. Stool was also tested for *Clostridium difficile* by using toxin assay and was negative. Biopsies from esophagogastroduodenoscopy revealed active chronic gastritis and duodenitis. Colonoscopy revealed erythematous mucosa in the terminal ileum and ileocecal valve. Terminal ileal and colonic biopsies revealed signs of chronic inflammation including neutrophil cryptitis, crypt abscesses and gland distortion along with inflammatory infiltrate in the lamina propria supporting a diagnosis of Crohn's disease. However, no granulomas were identified (Fig. 2). PROMETHEUS® IBD Serology 7 was also consistent with Crohn's disease. She consequently was initiated on Crohn's therapy with intravenous steroids and infliximab with significant improvement in her pulmonary status. Her diarrhea improved in 5 days and dyspnea and cough were resolved within 2 weeks. A chest radiograph obtained at 6 weeks after discharge showed complete resolution of the pulmonary changes (Fig. 3). She remained symptom free during close follow-up for 12 months after discharge and her CD is stable on maintenance therapy with infliximab.

This case is unique for the significant pleural effusion alongside bronchial pneumonia developing prior to the onset of clinical symptoms of CD, a feature that has not been reported in pediatric literature before.