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Case Report

The First Definition of Pulmonary Component of Hypereosinophilic Syndrome: Bronchial Casts

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Abstract

Hypereosinophilic syndrome is a heterogeneous disease characterized by eosinophilic tissue inflammation and eosinophilia. Pulmonary involvement could be seen in up to 55% among children with hypereosinophilic syndrome. A 3-year-old boy with chronic hypereosinophilia and respiratory complaints was diagnosed with idiopathic hypereosinophilic syndrome. Atelectasis was detected in the radiological evaluation, and bronchial casts with eosinophilic structures were removed by bronchoscopy. Steroid, inhaled hypertonic saline, inhaled bronchodilator, inhaled corticosteroid, and leukotriene receptor antagonist were used for 1 year in the management of hypereosinophilic syndrome, and related eosinophilic casts and repetitive bronchoscopies were administered for removal of the casts. The patient was successfully managed with an inhaled N-acetyl cysteine treatment. In children, the long-term prognosis of hypereosinophilic syndrome is uncertain. Comprehensive diagnostic tests are required for the early diagnosis and management of pediatric hypereosinophilic syndrome. In the presented case, the rare occurrence of pulmonary involvement of hypereosinophilic syndrome in a 3 year-old-boy with recurrent hypereosinophilic casts and its management were discussed.

KEYWORDS: Bronchial cast, children, hypereosinophilic syndrome
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INTRODUCTION

Hypereosinophilic syndrome (HES) is a rare disease and characterized by an absolute eosinophil count of more than 1500/mm^3 for at least 6 months and the presence of end-organ damage.[1] In the absence of an identifiable cause of eosinophilia and the presence of end-organ damage, the diagnosis of idiopathic HES should be considered. Children with HES can have pulmonary involvement in up to 55% of cases.[2]

Plastic bronchitis (PB) or cast bronchitis is a rare condition which causes partial or complete obstruction in tracheobronchial tree with the presence of mucofibrinous plugs and may result in severe respiratory distress, dyspnea, cyanosis, and wheezing.[3,4] Pathophysiology of PB may be related to alveolar–capillary barrier damage, mucosal fragility, increased venous pressure, lymphatic congestion, or decreased lymphatic drainage. Endobronchial cast which is a rubber-like or thick gelatinous-mucoid structure may cause airway obstruction, infection, or segmental atelectasis.[5] The optimal treatment of primary disease is the priority.

Plastic bronchitis has not been previously described in the pulmonary component of HES. Herein, the first definition of pulmonary involvement of HES in a 3-year-old boy with recurrent hypereosinophilic casts removed by bronchoscopic intervention is discussed.

CASE REPORT

A 3-year-old boy was admitted to our hospital with a 6-month history of dyspnea and chronic dry cough which was unresponsive to inhaled beta-2 agonist treatment. Neither the patient nor his family had any history of atopy, recurrent bronchiolitis or wheezing, cardiac disease, recurrent skin lesions, or itching. The patient had normal growth; his oxygen saturation at room air was 98%; he had no clubbing in the physical examination. He had prolonged expirium in auscultation and other system findings were normal. In laboratory findings, the eosinophil percentage was 16.5, the absolute eosinophil count was 2200/10^3, and other total blood count parameters were in the normal range. Acute phase reactants were negative. When past medical records were examined, it was observed that the hypereosinophilia persisted for more than 6 months. In chest x-ray, a double contour sign in the lower zone of the left lung and consolidation in the right upper zone were seen on admission (Figure 1A). In thorax computed tomography (CT), on the left lung lower lobe superior segment, atelectasis sitting on the pleura at the base was observed, but common ground glass opacity was not observed.

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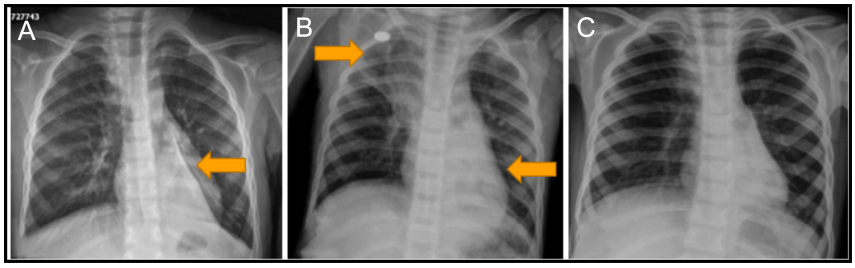

Figure 1. Left lower lobe atelectasis in the chest x-ray on admission (A). Right upper lobe and left lower lobe atelectasis on chest x-ray before the first bronchoscopy (B). Control chest x-ray a day after bronchoscopy and removal of the eosinophilic casts and a significant improvement of the atelectasis was observed (C).

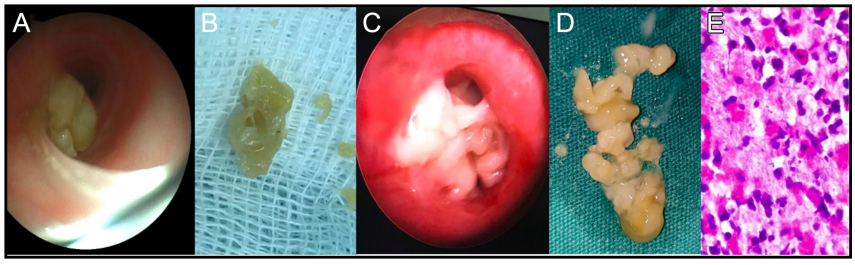

Figure 2. The appearance of the dense, mucoid structure which was in dirty yellow color at the entrance of the right lung upper lobe apical segment during fiberoptic bronchoscopy (A). The macroscopic view of eosinophilic casts removed from the right upper lobe apical segment (B). The appearance of dirty yellow tough crusty structure in the left lower lobe bronchus (C) during fiberoptic bronchoscopy and the macroscopic view after removal (D). Microscopic view of eosinophilic casts at 100× magnification with hematoxylin–eosin staining (E).

Stool parasitic investigation and serology of parasitic infections (*Toxocara canis*, *Entamoeba histolytica*, *Cryptococcus*, *Ascaris*, *Strongyloides*, *Echinococcus granulosus*) for the etiology of hypereosinophilia were negative. Abdominal ultrasound, echocardiographic examination, immunoglobulin levels (Ig G, A, M, and E), lymphocyte subgroups, serum tryptase level, and perinuclear antineutrophil cytoplasmic antibodies (p-ANCA) and cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA) values were normal. The sweat chloride test was 23 mEq/L; cystic fibrosis transmembrane regulator gene mutation and skin prick test, and food and house dust mite-specific IgE levels were negative. In the bone marrow aspiration, normocellular bone marrow, hyperplasia in myeloid cells, and an increase in eosinophils (20%) were detected. FIP1LI/PDGFRA and t (9:22) mutations were both negative. No cause of chronic hypereosinophilia was detected. The patient was diagnosed with idiopathic HES after excluding parasitic, allergic, immunological, rheumatological, and hematological diseases. The consolidation in the right upper lobe was added to the left lower lobe atelectasis, which was detected during the admission process (Figure 1B).

MAIN POINTS

- Although hypereosinophilic syndrome is very rare in children, parenchymal pulmonary involvement can be seen in 55% of patients.
- In the presented case, recurrent eosinophilic casts due to underlying hypereosinophilic syndrome were first described, while pulmonary parenchymal involvement was not observed contrary to expectations in hypereosinophilic syndrome.
- Atelectasis appearing in different regions at different times on chest x-ray may be an indicator of bronchial casts.
- The basic approach for the diagnosis of a bronchial cast is bronchoscopy and cytopathological examination of the extracted cast.

The patient underwent bronchoscopy and a dense, mucoid structure which was dirty yellow in color was observed at the entrance of the right lung upper lobe apical segment (Figure 2A). Inside the left lower lobe bronchus, a dirty yellow tough crusty structure, approximately 0.5 × 1 cm in size, was detected (Figure 2C). They were removed by rigid bronchoscopy (Figure 2B and D). Eosinophilia not exceeding 15% was detected in the bronchoalveolar lavage fluid and no microorganisms were observed. After the removal of the bronchial casts, radiological appearance improved (Figure 1C). The pathological assessment of the bronchial casts showed eosinophilic mucinous structure with 80% eosinophilic infiltration (Figure 2E). Systemic steroid treatment was started as HES treatment (1 mg/kg/day). Systemic steroid, inhaled hypertonic saline, inhaled bronchodilator, inhaled corticosteroid, and leukotriene receptor antagonist were used for 1 year in the management of HES-related eosinophilic casts (Figure 3). However, 3 more fiberoptic bronchoscopy (FOB)s were required due to recurrent casts and respiratory problems in the first year of follow-up. Inhaled N-acetyl cysteine (NAC) was added to the patient's treatment and eosinophilic casts did not repeat. The patient, who was followed without treatment for the last 3 years, had no complaints during the final check-up and had an absolute eosinophil count of 800 and eosinophilia of 7.5%. Written consent was obtained from parents.

DISCUSSION

In children, small case series of HES have been described in the literature. The presentation of the disease is diverse. There could be dermatologic, pulmonary, gastrointestinal system, cardiac, and/or neurologic involvement.[6] The presentation of idiopathic HES is heterogeneous and may vary from

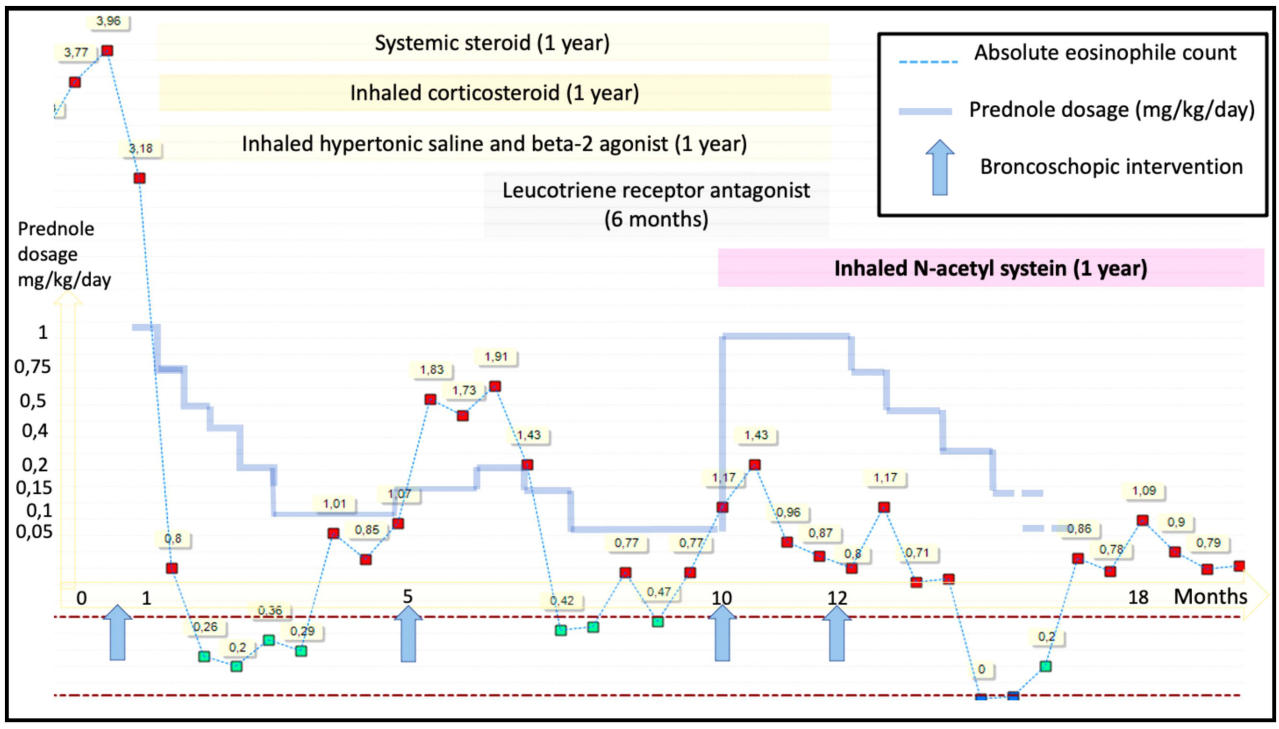

Figure 3. Figure showing the relationship between the patient's treatment scheme, peripheral blood eosinophil counts, and bronchoscopic interventions.

nonspecific complaints such as fatigue, cough, dyspnea, itching, and skin rash to life-threatening cardiac and/or neurologic findings. Cardiac, pulmonary, and skin are known to be the most common involvements in the pediatric age group.[7] The most common pulmonary findings of HES are dyspnea, cough, and wheezing. Abnormal chest x-ray and CT findings such as parenchymal infiltrates, patchy ground glass opacities, pleural effusion, intrathoracic lymphadenopathy, and pulmonary emboli could be seen.[8] In one of the largest series with 49 patients aged 12 to 88 years with HES, 45% of patients with pulmonary involvement had dyspnea, 39% had cough, and 24% had wheezing.[8] Pulmonary involvements during childhood vary from 27.5% to 55.3%.[7,9] In the study conducted by Tavil et al.[2] half of the pediatric patients had pulmonary involvement presented as cyanosis, crackles on auscultation, and thorax CT findings.[2] In the presented case, the patient had only dry cough and respiratory distress. There were no findings of parenchymal infiltration, ground glass opacity, lymphadenopathy, or pulmonary embolism on the CT scan. Atelectasis was detected only in the distal of the existing casts. In the present case diagnosed with idiopathic HES, we determined bronchial casts without parenchymal lesions. Pulmonary involvement of HES associated with recurrent casts has not been defined so far.

Plastic bronchitis, fibrinous bronchitis, bronchitis pseudomembranosa, and Hoffmann bronchitis are all terms used to describe bronchial casts. In children, it has been reported in association with a variety of cardiorespiratory disorders, such as cystic fibrosis, asthma, allergic bronchopulmonary aspergillosis, respiratory infections (H1N1, severe coronavirus disease 2019, etc.), congenital heart disease (CHD), and acute chest syndrome associated with sickle cell disease.[10,11] The presented case had no history of recurrent wheezing or atopy and did not respond to the asthma treatment. All these disorders and diseases including asthma were excluded with a detailed examination of the patient.

Bronchial casts are classified clinically and pathologically in various ways. Based on cast histology, a pathological approach was adopted by Seear et al[12], and casts were classified into type 1 or inflammatory casts and type 2 or acellular casts. Inflammatory casts were often developed due to bronchial diseases and presentation of this type was often acute. Acellular casts could be seen in idiopathic cases and cyanotic CHD. Madsen et al[13] attempted to categorize bronchial casts based on the underlying condition and form of the casts. Mucinous, inflammatory, and chylous casts may develop in patients with structural CHD. The patients without structural CHD were classified as lymphatic disease or chylous casts, acute chest syndrome associated with sickle cell disease or fibrinous casts, and atopy or eosinophilic casts.[13] In the existing literature, eosinophilic casts are commonly associated with atopy, allergy, and underlying inflammatory diseases of the lung.[13,14] We can evaluate the hypereosinophilic casts due to idiopathic HES in this group.

Management of bronchial casts can be defined as the treatment of an underlying disease.[5] In addition to the removal of the casts with rigid or flexible bronchoscopy, it has been experienced in the literature that some medical treatments may be beneficial in type 1 casts. Fibrinolytic agents and anticoagulants (tPA, unfractionated heparin, and urokinase), dornase alpha against cellular DNA and NAC as mucolytic can be administered by nebulization or intraoperatively through bronchoscope.[5,11] Systemic steroids to decrease secretions and anti-inflammatory activity and bronchodilators to assist in airway clearance and to reduce bronchospasm can be given.[5,12] Hypertonic saline with chest physiotherapy can be employed in airway clearance.[5] In addition to these

medications, oral macrolides may help reduce inflammation and secretions of the cast.[5] Type 2 casts can be removed with bronchoscopy in terms of symptomatic relief.[5] Bronchoscopy, steroids, and inhaled NAC were experienced beneficial in one of the most extensive case series with 9 children.[12] The presented case was treated with systemic steroid, inhaler hypertonic saline, inhaled bronchodilator, inhaled corticosteroid, and leukotriene receptor antagonist; however, the most effective treatment option was inhaled NAC.

The long-term prognosis of HES is unknown in children. For the early detection and management of complications in pediatric HES, comprehensive diagnostic investigations are essential. In this case, we wanted to share the rare occurrence of HES-based eosinophilic cast in the bronchial tree and how it was managed to contribute to the existing literature.

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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