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Case report

Two cases of non-cystic fibrosis (CF) bronchiectasis with allergic bronchopulmonary aspergillosis

Hriday De [a, *], Syed Md. Azad [a], Prabhas P. Giri [a], Priyankar Pal [a], Apurba Ghosh [a], Anirban Maitra [b]

[a] Institute of Child Health, Kolkata, India
[b] Royal Manchester Children's Hospital, United Kingdom

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ABSTRACT

Allergic bronchopulmonary aspergillosis (ABPA) is a complex hypersensitivity reaction in patients with asthma or cystic fibrosis (CF), which is associated with bronchi colonized by the fungus Aspergillus species, most often Aspergillus fumigatus. ABPA is an important consideration for asthmatics that do not respond to asthma management or with recurrent chest infections and deteriorating lung function in children with cystic fibrosis. We present two cases of non CF bronchiectasis associated with ABPA who presented to our hospital with recurrent hospitalisations of undiagnosed aetiology.

1. Introduction

Bronchiectasis is defined as the permanent dilatation of bronchi that results from a vicious cycle of inflammatory and infectious damage to the bronchial and bronchiolar walls [1]. While cystic fibrosis (CF) is the most common cause of bronchiectasis in childhood in the developed world, non-CF bronchiectasis is may result from a number of other conditions that include tuberculosis and pertussis sequelae, immunodeficiency, connective tissue disorders and allergic bronchopulmonary aspergillosis etc.[2, 3].

ABPA is characterized by type I and type III hypersensitivity reactions. Repeated episodes of bronchial obstruction, inflammation and mucoid impaction can lead to bronchiectasis, fibrosis and respiratory compromise. A number of cases of ABPA have been described in the Indian adult population, but only a handful has been reported in the paediatric age group.

Herein this article, we describe two children with prolonged respiratory illness necessitating recurrent hospitalisations and failure to respond to standard asthma management that were subsequently diagnosed with ABPA.

2. Case report

2.1. Case 1

The first case involves a six year old girl who was apparently well until the age of six months. Thereafter, she had started developing repeated episodes of cough and cold, respiratory distress with wheezing and was hospitalised on many occasions where she was treated with antibiotics, inhaled bronchodilators and inhaled corticosteroids. Her symptoms responded only to recur again in a few weeks interval. There was no history of exposure to pets or home exposure to smokes. She was then referred to our institution for further evaluation and management for ongoing symptoms. There is no history of contact with tuberculosis.

On admission, the patient was noted to be pale, clubbed but not cyanosed with faltering weight gain (height and weight both below the 5th percentile). Examination of the chest revealed a pectus carinatum deformity (Fig. 1) and increased work of breathing (tachypneic at 32/min, bilateral wheeze and recessions). A Chest x-ray performed on admission revealed bilateral patchy opacities (Fig. 2). Her total leukocyte counts were elevated at 10,650/mm^3 with 9% eosinophil in peripheral smear (absolute eosinophil count of 850/mm^3). Serum IgE level was elevated at 1020 ng/mL. Sputum for acid fast tubercular bacilli and TB NAAT was negative. Flexible bronchoscopy revealed intra-bronchial mucus plugs. A high

* Corresponding author. Institute of Child Health, India.
E-mail address: hridayde2010@gmail.com (H. De).

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resolution chest CT scan (HRCT) showed 'tram track' bronchial dilatation and, 'tree in bud appearance' confirming bronchiectasis (Fig. 3). Her sweat chloride estimation and CFTR gene mutation (for ΔF508) for cystic fibrosis was reported as negative. Her skin prick test to aspergillus (what reagent and what was the reading) serum IgE specific to aspergillus fumigatus were positive e. A diagnosis of ABPA was made and she was treated with oral prednisolone started at the dose of 0.75mg/kg/day over 2 week then gradually tapered over next 2 months and oral itraconazole 200 mg twice daily for 4 months. She responded favourably with progressive resolution of radiological opacities in serial chest x-rays.

2.2. Case 2

A seven year old boy presented with history of recurrent respiratory distress with wheezing since five years of age. There is a history of an allergic rash since two year of age that has often accompanied these episodes. Moreover, there was family history of atopy and asthma. In this case also there was no socio-environmental cause of asthma exacerbation. On clinical examination there was clubbing and evidence of increased work of breathing (subcostal suction, bilateral wheeze and crepitations). A chest x-ray revealed bilateral patchy pulmonary opacities (Fig. 4). A transient improvement was recorded post bronchodilator therapy.

Investigations revealed a total leukocyte count of 13,500/mm^3 with 6% eosinophil (absolute eosinophil count of 800/mm^3). Serum IgE level was elevated at 2500ng/ml. Tests were negative for tuberculosis. Sweat chloride estimation and CFTR gene mutation was negative thereby ruling out cystic fibrosis. HRCT chest showed changes suggestive of bronchiectasis, 'signet ring sign' (Fig. 5). Skin

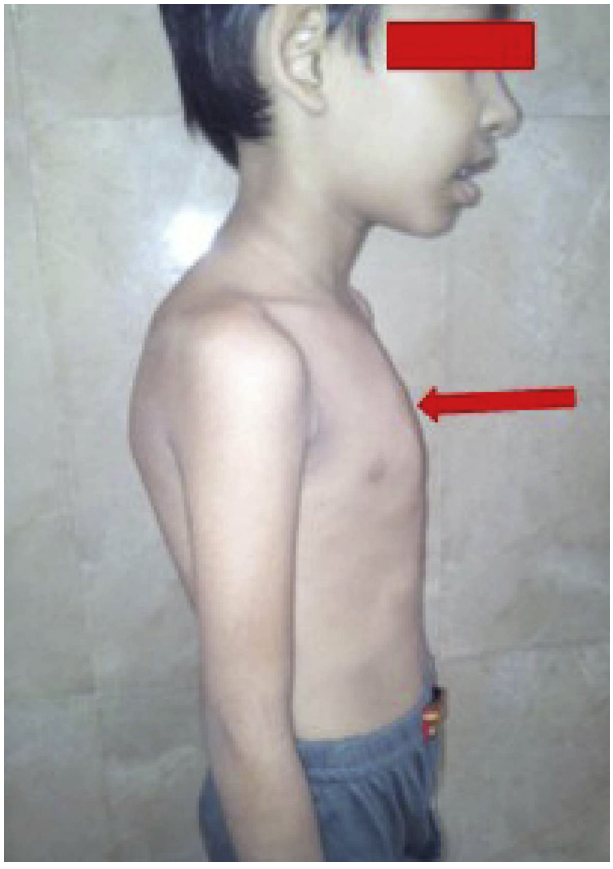

Fig. 1. Pectus Carinatum deformity of chest.

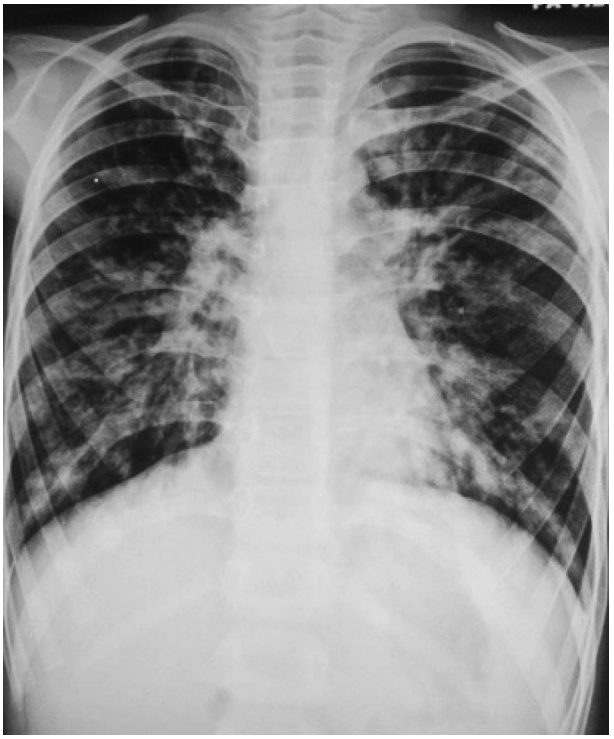

Fig. 2. CXR showing B/L opacities.

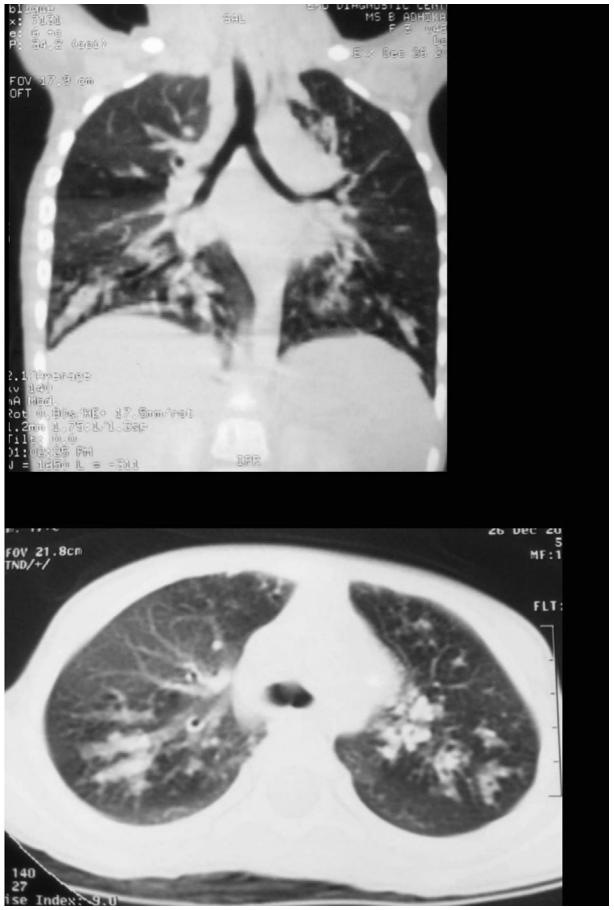

Fig. 3. Chest CT scan (HRCT) showed 'tram track' bronchial dilatation and, 'tree in bud appearance' confirming bronchiectasis.

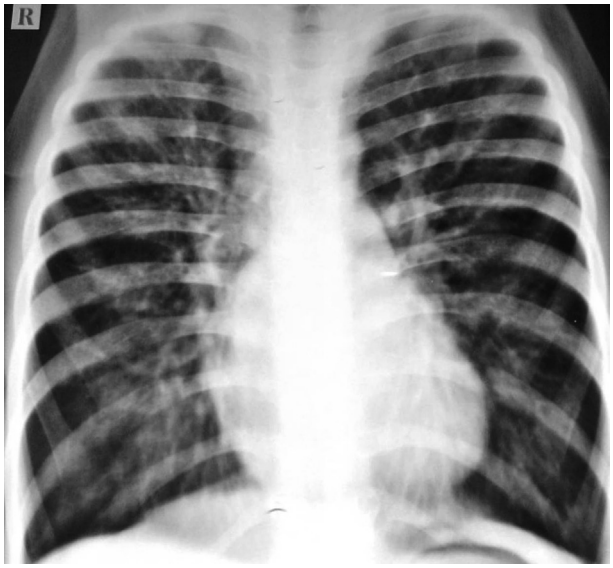

Fig. 4. CXRshowing B/L opacities.

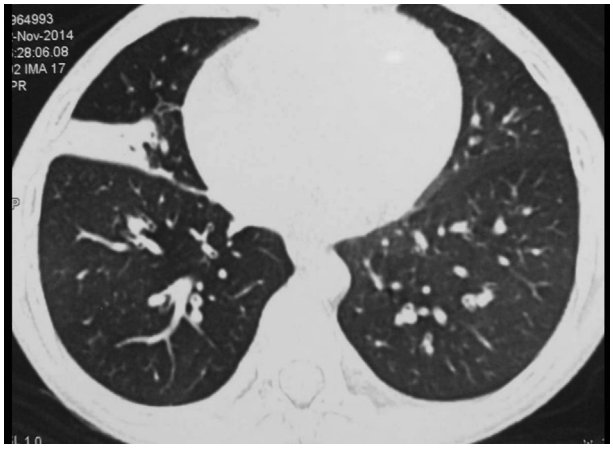

Fig. 5. HRCT chest showing 'signet ring sign'.

prick tests were positive for Aspergillus fumigatus and Aspergillus versicolor. Serum IgE antibodies specific against Aspergillus fumigatus was found to be positive. As like the other patient, the patients responded favourably to treatment (oral corticosteroids alone of total 2 months duration).

3. Discussion

Allergic bronchopulmonary aspergillosis (ABPA) is a characterized by a hypersensitivity reaction to antigens of the Aspergillus species (most frequently Aspergillus fumigatus). First described in 1952 by Hinson et al., the pathogenesis of ABPA is complex with both host immune and genetic factors being implicated [4]. For reasons unclear, colonization prompts vigorous antibody (IgE and IgG) and cell-mediated immune responses (type I, III, and IV hypersensitivity reactions to *Aspergillus* antigens, leading to a vicious cycle of inflammation and bronchial wall damage. Clinically, this leads to frequent exacerbations, recurrent disease activity and ultimately permanent airway damage with bronchiectasis. ABPA most commonly affects patients with asthma (1–2% of ABPA patients) or cystic fibrosis (5–15% of ABPA patients) [5]. ABPA should be suspected in asthmatic children of any age with frequent exacerbations and suboptimal response to asthma therapy. As ABPA is very rarely diagnosed, in patients without a history of asthma, no data on the incidence are available [6]. With the development of ABPA, children with asthma or CF typically worsens clinically and may present with a new onset or worsening cough or an increase in sputum production or wheezing. Haemoptysis may occur secondary to airway inflammation and bronchiectasis. Systemic symptoms of low-grade fever, malaise, and weight loss and growth failure are variably associated with ABPA.

Management is conservative and is heavily reliant on reducing the airway inflammation by oral corticosteroids for prolonged periods. Antifungal agents like Itraconazole are often added, especially in cases where oral corticosteroids are contraindicated or are ineffective alone.

The diagnosis of ABPA is based on clinical and immunologic reactivity to Aspergillus. Fumigatus. The minimal criteria required for the diagnosis of ABPA are mentioned in Table 1 [7]. The designation of ABPA-seropositive (ABPA-S) may be used to classify asthmatic patients who meet the required criteria but lack the proximal or central bronchiectasis (ABPA-CB).

Only a handful number of studies have reported of ABPA in children. About 15% of children with bronchial asthma fulfilled four or more criteria for the diagnosis of ABPA [8,9]. The youngest reported patient with ABPA was a 22-month-old toddler with peripheral blood eosinophilia, elevated total serum IgE level, serum precipitin against *A fumigatus*, and immediate and late skin reactivity to *A fumigatus* antigens [10]. Another case report by Gaur et all relates to a case of ABPA from the Indian subcontinent where a 4 year old female child presented with recurrent wheeze and growth failure [11] In a study from India done by Kumar et al. eighty children with non-cystic fibrosis bronchiectasis were identified and 6 patients among them was diagnosed as ABPA [12]. All our cases presented with recurrent wheeze and growth failure, had a history suggestive of asthma and were negative for CF. Subsequently they were demonstrated as having bronchiectasis on HRCT. They had evidence of peripheral eosinophilia, elevated total IgE and skin prick test positivity to aspergillus fumigatus. The first case had an elevated serum IgE specific to aspergillus whilst the later had an elevated serum precipitins to aspergillus. Both responded

Table 1
Criteria for diagnosis of allergic bronchopulmonary aspergillosis in asthma.

(1) Asthma
(2) Chest radiographic infiltrate(s)
(3) Allergy prick skin reactivity to A. Fumigates
(4) Elevated total serum IgE level ≥1000 IU/mL. Some groups recommend IgE ≥1000 ng/mL (416 IU/mL)
(5) Precipitating IgG antibodies to A. Fumigates
(6) Peripheral blood eosinophilia
(7) Elevated serum specific IgE anti-A. fumiatus antibodies greater than twice non-ABPA IgE A. fumigatus-positive asthmatic serum pool
(8) Elevated serum specific IgG anti-A. fumiatus antibodies
(9) Central bronchiectasis

(i) Criteria 1–9, ABPA-central bronchiectasis, ABPA-CB (ii) Criteria 1–8, ABPA-seropositive, ABPA-S.

favourably to ABPA therapy and remains in long term remission.

In summary, ABPA often complicates asthma and rarely CF in the Indian children. A high index of suspicion is required to investigate suboptimal response to asthma therapy. A prompt evaluation of failure to respond asthma coupled with proper anti-inflammatory and antifungal therapy can prevent from permanent destruction of airways with long term morbidity.

Contributors

Dr. Priyankar Pal: Concept and designed the study, **Dr. S M Azad**: analyzed data and drafted the manuscript; **Dr. Prabhas P Giri**: Helped in Diagnosis and management; **Dr. A Ghosh, Dr. Anirban Maitra**: Reviewed the case report.

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