



Pneumomediastinum as a presenting feature of allergic bronchopulmonary aspergillosis in a child with cystic fibrosis

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We describe the first report of pneumomediastinum as a presentation of allergic bronchopulmonary aspergillosis (ABPA) in a child with cystic fibrosis (CF).

Case report

Our patient is a 10-year-old girl with CF who was found to be homozygous for $\delta F508$ on newborn screening. Her early life was uneventful. Her growth centiles from the first years of life were between 50th to 75th centiles. There were no concerns or issues during her annual assessments in the early years.

She grew *Pseudomonas aeruginosa* for the first time at three years of age in 2003. By the age of eight years she became chronically infected with *Pseudomonas aeruginosa*.

Her lung function prior to annual assessment in early 2008 showed an FEV1 of 1.94 litres (percentage predicted of 105%) and an FVC of 1.99 litres (percentage predicted of 92%). She was noted to have a rise in IgE at 345 kU/L with aspergillus precipitins of 64 mgA/L. She was started on itraconazole and a reducing course of prednisolone as a part of treatment for ABPA. During that stage, her lung function declined slightly showing an FEV1 of 1.67 litres (percentage predicted of 85%) and FVC of 1.94 litres (percentage predicted of 85%).

At nine years of age, in September 2009, she presented to her local hospital with cough and wheeze. She was considered to have a mild infective exacerbation and was treated with flucloxacillin and prednisolone. She gave a history

of handling garden mulch a day before her presentation.

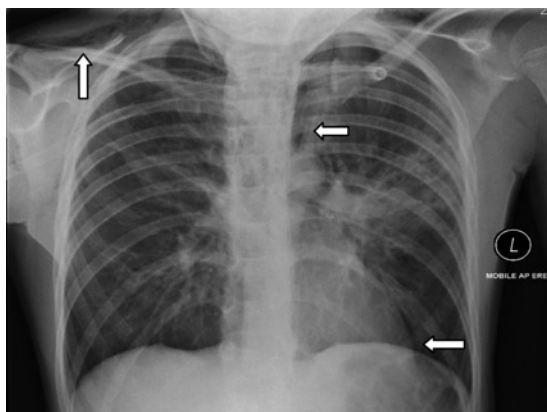
She represented three days later with vomiting and wheeze. Her respiratory distress worsened. A chest X-ray (Figure 1) was taken which showed surgical emphysema and pneumomediastinum. She later had a CT chest (Figure 2) which confirmed pneumomediastinum and bronchiectasis within the left lung.

She also had an upper GI contrast study to rule out an oesophageal rupture as a cause of her pneumomediastinum which did not reveal any oesophageal tears. She was subsequently transferred to the paediatric intensive care unit (PICU) at the CF centre. Here she received high flow oxygen for her pneumomediastinum, and commenced on intravenous ceftazidime, tobramycin, aminophylline and hydrocortisone. Oral itraconazole was restarted due to the evidence of the re-emergence of ABPA as shown in the graphs below (Graphs 1 and 2).

The pneumomediastinum spontaneously resolved in four days. Her recovery was uncomplicated. She was gradually weaned to salbutamol given four hourly and discontinued oxygen 9 days after admission. She was discharged on a weaning regimen of Prednisolone for 2 months and Itraconazole for 3 months. During this episode of admission, except for a CRP of 76 mg/L and a WCC of $17 \times 10^9/L$, other blood tests were unremarkable. Her respiratory microbiology was negative.

She made good progress on discharge. On follow-up after 2 months her FEV1 was 2.10 litres (percentage predicted of 99%) and FVC 2.13 litres (percentage predicted of 89%) (Graph 3). She was weaned off her Prednisolone.

Figure 1
Chest X-ray. Note the surgical emphysema above the right clavicle. Also note the pneumomediastinum shown by the remaining two arrows



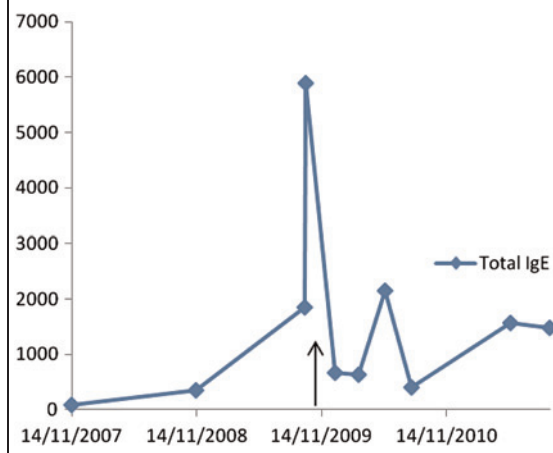
She is currently 12 years-old. She had one further recurrence of ABPA without pneumomediastinum but has been off treatment for ABPA since December 2010.

Discussion

Air leaks are not uncommon in advanced CF¹ and usually present as pneumothoraces. It is rare in young children with CF. The youngest reported case in the literature was 4 years of age.²

Spontaneous pneumothorax in CF has an average annual incidence of 0.64%.³ The median age for pneumothorax is 21 years, and 72.4%

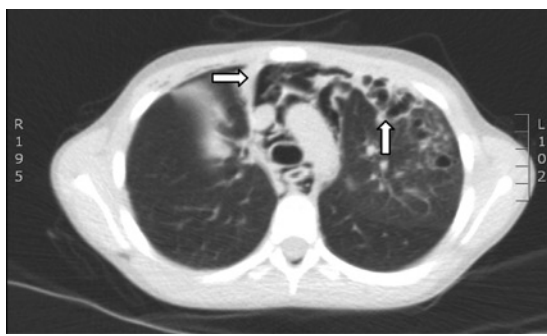
Graph 1
Total IgE over time



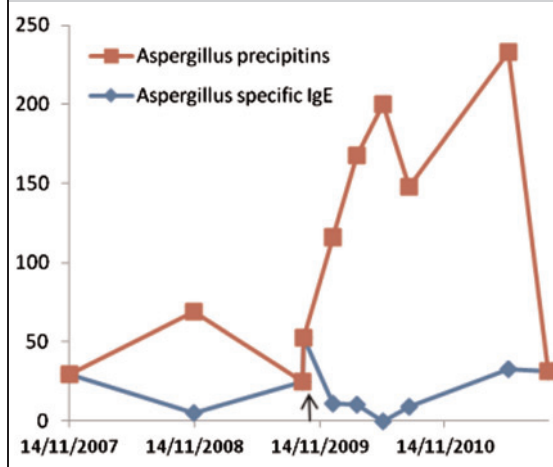
occurred in patients greater than 18 years of age.³ The diagnosis is confirmed via a chest radiograph and or a computed chest tomography.⁴ If a patient does not respond to treatment such as observation, needle aspiration or chest tube⁵⁻⁷ then an early, more definitive procedure such as surgical or chemical pleurodesis should be considered.

Pneumomediastinum has not been reported in these advanced CF lung diseases and we are aware of only one published case report of a pneumomediastinum as a presenting feature of CF.⁸ Spontaneous pneumomediastinum is rare in

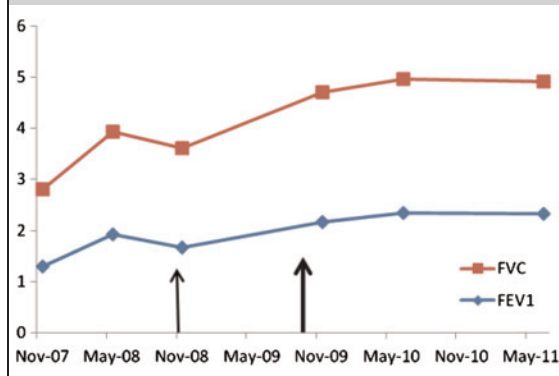
Figure 2
CT Chest. Note the top arrow showing the pneumomediastinum and the other arrow showing bronchiectatic changes in the left lung



Graph 2
Aspergillus precipitins and Aspergillus specific IgE over time



Graph 3
Lung function over time. 1st arrow indicating
ABPA for the 1st time. 2nd arrow indicating
Pneumomediastinum, ABPA and PICU
admission



children.⁹ It is generally a benign condition in young children caused by alveolar rupture and dissection of air into the mediastinum and hilum.¹⁰ Many physiological events like inducing a valsalva manoeuvre, coughing, forceful vomiting and pathological events like wheezing can lead to alveolar rupture.^{9,10} The clinical diagnosis is based on the symptom triad of chest pain, dyspnoea and subcutaneous emphysema and is also based on Hamman's sign.⁹ The diagnosis is confirmed by chest radiography. The main differential diagnosis is oesophageal perforation, which should be investigated, requires an oesophagogram with contrast.⁹ Spontaneous pneumomediastinum generally resolves spontaneously within a few days. Management consists of treating the underlying cause (if identified), rest, analgesics and simple clinical monitoring.⁹

In all, 1–15% of CF patients may develop ABPA.¹¹ Among patients with CF, ABPA is more commonly seen in those who are males, have a history of asthma or atopy, have lower lung function or have *Pseudomonas* in sputum cultures.¹²

ABPA is usually suspected on clinical grounds.¹³ The diagnosis is confirmed by radiological and serological testing.

The following diagnostic criteria are based on a combination of the UK CF trust and US CF Foundation guidelines for diagnosis of ABPA in CF.^{12,14} (1) Acute/sub acute clinical deterioration (cough, wheeze, exercise intolerance, exercise-induced asthma, and decline in lung function or increased

sputum production) not attributable to other etiology. (2) Total serum IgE >500 IU/ml or a fourfold increase in IgE titres. (3) Immediate cutaneous reactivity to *A. fumigatus* >3 mm or raised aspergillus specific IgE to *A. fumigatus* greater or equal to than grade 4. (4) Precipitating IgG antibodies to *A. fumigatus*. (5) New or recent (infiltrates, mucus plugging or central bronchiectasis) changes on chest radiograph/CT that have not cleared with antibiotics and standard physiotherapy. Positive respiratory culture for aspergillus is not an essential pre-requisite for diagnosis of ABPA.¹⁵

Treatment of ABPA aims to treat acute exacerbations of the disease and limit progressive lung disease and bronchiectasis.¹³ This is achieved by attenuation of the allergic inflammation with oral corticosteroids and reduction of the antigen burden with antifungal therapy. Two weeks of daily therapy of oral prednisolone, followed by gradual tapering, has been recommended for new ABPA-related infiltrates. The duration of treatment should be individualised according to the patient's clinical condition.¹³ Total serum IgE serves as a marker of ABPA disease activity.¹³

Itraconazole has been used as the antifungal agent to reduce the antigen burden. Voriconazole is a new antifungal agent with better absorption than Itraconazole. It may be used as a second line agent in patients who fail to respond to itraconazole.¹⁶ There are some case reports of other therapy like pulsed methylprednisolone and omalizumab being used.

Our case has definite exposure to garden mulch,¹⁷ which is a recognized source of aspergillus spores, had acute deterioration in her lung disease and a pneumomediastinum. She had definite serological evidence of ABPA with a significant rise of total and aspergillus specific IgE, and hence we describe the first report of pneumomediastinum as a presenting feature of ABPA.

Conclusion

Patients with Cystic Fibrosis can have an air leak as a complication usually in the advanced stages of the disease, when they are older. Our patient had air leak but did not have advanced lung disease. Diagnostic criteria for ABPA in her included acute/subacute deterioration not attributable to other aetiologies along with supportive

clinical, radiological and serological evidence present. Pneumomediastinum is not a commonly recognized feature in the established diagnostic criteria.

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