Raj Kumar[1], Mohammed Noufal Poongadan[2], Mandeep Singh[2]

[1]Department of Respiratory Allergy and Applied Immunology, National Centre of Respiratory Allergy, Asthma and Immunology, India
[2]Department of Respiratory Allergy and Applied Immunology V P Chest Institute, University of Delhi, India

Allergic Bronchopulmonary Aspergillosis presenting as lobar or total lung collapse

Alergiczna aspergiloza oskrzelowo-płucna w postaci niedodmy płuc

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Abstract

Introduction: Allergic bronchopulmonary aspergillosis (ABPA) is a T-helper cell 2 (Th2) mediated hypersensitive lung disorder in response to *Aspergillus* that usually affects asthmatic and cystic fibrosis (CF) patients. ABPA rarely presents as lung collapse and such kind of presentation is very rare in non asthmatic patients. We are presenting a series of three cases in which ABPA presented as lobar or total lung collapse. ABPA presenting as opaque hemithorax is a rarity with only a few of them reported in the literature.
Case series — the first case described is a 45-year non-smoker with history suggestive of bronchial asthma and on chest radiological examination was found to have opaque right hemithorax. The second case is of 62-year non-smoker non-asthmatic patient who presented to us as left lung collapse. The last case is of middle lobe collapse in asthmatic male. All cases ultimately were proved to be having ABPA and after treatment showed marked clinical and radiological improvement.
Conclusions: The present case series highlights the need for aggressive approach in diagnosing this treatable condition in cases presenting as segmental or total lung collapse. The condition has a good prognosis if detected early.

Key words: ABPA, lung collapse, allergic bronchopulmonary aspergillosis, asthma

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Streszczenie

Wstęp: Alergiczna aspergiloza oskrzelowo-płucna (AAOP) to choroba wywołana nadwrażliwością na antygeny *Aspergillus fumigatus*. Jest mediowana przez limfocyty pomocnicze Th2 i występuje zazwyczaj u chorych na astmę i mukowiscydozę. Alergiczna aspergiloza oskrzelowo-płucna rzadko prowadzi do niedodmy płuc, szczególnie u osób niechorujących na astmę, i w postaci całkowitej niedodmy płuca jest wyjątkową rzadkością — w piśmiennictwie przedstawiono tylko pojedyncze przypadki.
Seria przypadków: Pierwszy dotyczy 45-letniego chorego na astmę, nigdy niepalącego, u którego w badaniu radiologicznym klatki piersiowej uwidoczniono niedodmę płuca prawego. W drugim przypadku u 62-letniego mężczyzny, również nigdy niepalącego i niechorującego na astmę stwierdzono niedodmę płuca lewego. Natomiast w trzecim wykryto niedodmę płata środkowego u mężczyzny chorego na astmę. U wszystkich chorych ustalono rozpoznanie AAOP, a po zastosowaniu odpowiedniego leczenia uzyskano poprawę kliniczną i radiologiczną.
Wnioski: Prezentowana seria przypadków podkreśla potrzebę diagnostyki pod kątem AAOP chorych z obrazem radiologicznym niedodmy części lub całego płuca. Choroba cechuje się dobrą odpowiedzią na leczenie i dobrym rokowaniem, szczególnie gdy zostanie wcześnie rozpoznana.

Słowa kluczowe: AAOP, alergiczna aspergiloza oskrzelowo-płucna, niedodma płuca, astma

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Address for correspondence: Raj Kumar, MD, Professor and Head of the Department of Respiratory Allergy and Applied Immunology National Centre of Respiratory Allergy, Asthma and Immunology, V P Chest Institute, University of Delhi, Delhi 110007, India
Tel.: 9810146835; 91-011-27667667 Ext. 144, fax No: 91-011-27667420, e-mail: rajkumarvpci@gmail.com
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Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is a T-helper cell 2 (Th2) mediated hypersensitive lung disorder in response to Aspergillus fumigatus that affects asthmatic and cystic fibrosis (CF) patients [1]. It is one of the most frequently recognized manifestation of allergic aspergillosis, occurs worldwide and is now seen as an important emerging disease in India [2]. This potentially destructive lung disease was first reported in England in 1952 and since then it has been reported from all the continents [3]. The first case of ABPA in India was reported in 1971 [4], subsequently many cases have been reported. In 2000, Kumar and Gaur estimated that the prevalence of ABPA in patients with asthma is 16% [5]. ABPA has been classified into ABPA Seropositive (ABPA-S), ABPA-Central Bronchiectasis (ABPA-CB) and ABPA Other Radiological Findings (ABPA-CB-ORF) based on the radiological picture, with both the severity of the radiological and serologic findings increasing from patients with ABPA-S to those with ABPA-CB-ORF [6]. ABPA was diagnosed in 27.2% of asthmatics attending pulmonary clinic at a referral level hospital in north India. Amongst them 27% were ABPA-S, 33.3% ABPA-CB and 39.6% were ABPA-CB-ORF [7]. A recent study by Kumar et al found the relative incidence of ABPA, ABPA-CB and ABPA-ORF to be 22.32, 43.75 and 33.92 percent respectively [8]. The chest radiographic findings depend on the clinical presentation of the disease. During acute exacerbations of the disease, transient and fleeting opacities are characteristically found, whereas fixed abnormalities are encountered in chronic stages of the disease. Common findings include consolidation, mucoid impaction of bronchi, and areas of atelectasis, whereas rare findings include pleural effusion, perihilar bronchoceles mimicking adenopathy, miliary nodules and unilateral lung collapse. Chest radiographic findings are non-specific and high resolution computed tomography (HRCT) of the chest is the radiological investigation of choice in ABPA. The findings on chest HRCT include central bronchiectasis, mucus plugging with bronchocele formation and others [9]. ABPA rarely presents as lung collapse and such kind of presentation is very rare in non-asthmatic patients. We describe here three cases, one with complete lung collapse in non-asthmatic patient and two cases in asthmatic patients, one with complete lung collapse and the other with middle lobe collapse.

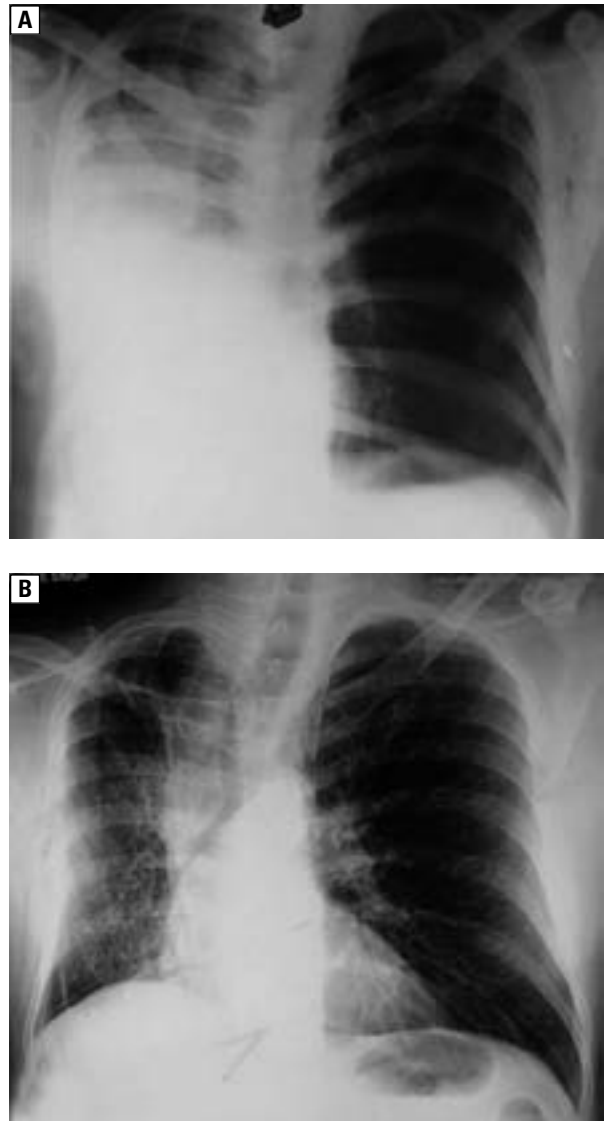

Figure 1. Chest radiogram of the patient in case 1, showing (**A**) Collapsed right lung at presentation; (**B**) Re-expanded right lung after treatment

Case 1

A 45-year-old non-smoker male presented to us with 10 year history of episodic cough and breathlessness aggravated with change of season. He was a known diabetic on regular treatment. On examination vitals were within normal range, mediastinum was shifted to the right and breath sounds were found to be absent on the right side. A previous chest radiogram of the patient showed total right lung collapse (Fig. 1A). High resolution computed tomography (HRCT) showed right lung collapse with mediastinal shift to the right (Fig. 2A). At presentation patient was on antitubercular therapy for the last five months based on chest radiogram and lung HRCT while

Table 1. Diagnostic features of ABPA in each of the three cases

S.No	Criteria	Case 1	Case 2	Case 3
1	Bronchial asthma	Present	Absent	Present
2	Serum Total IgE* (IU/ml**)	2345	1930	8064
3	Skin prick test against *Aspergillus species*	Positive	Positive	Positive
4	Specific IgE against *Aspergillus Fumigatus* (KUA/l)#	56.5	5.02	39.8
5	Specific IgG## against *Aspergillus Fumigatus*	Positive	Positive	Positive
6	Serum precipitin against Aspergillus Fumigatus	Positive	Positive	Positive
7	Central bronchiectasis	Absent	Present	Present
8	Absolute eosinophil count (per mm^3)	2500	2750	150

*Immunoglobulin E; **International Units/millilitre; #kilounits of *Aspergillus fumigatus*; ##specific IgE antibody per litre

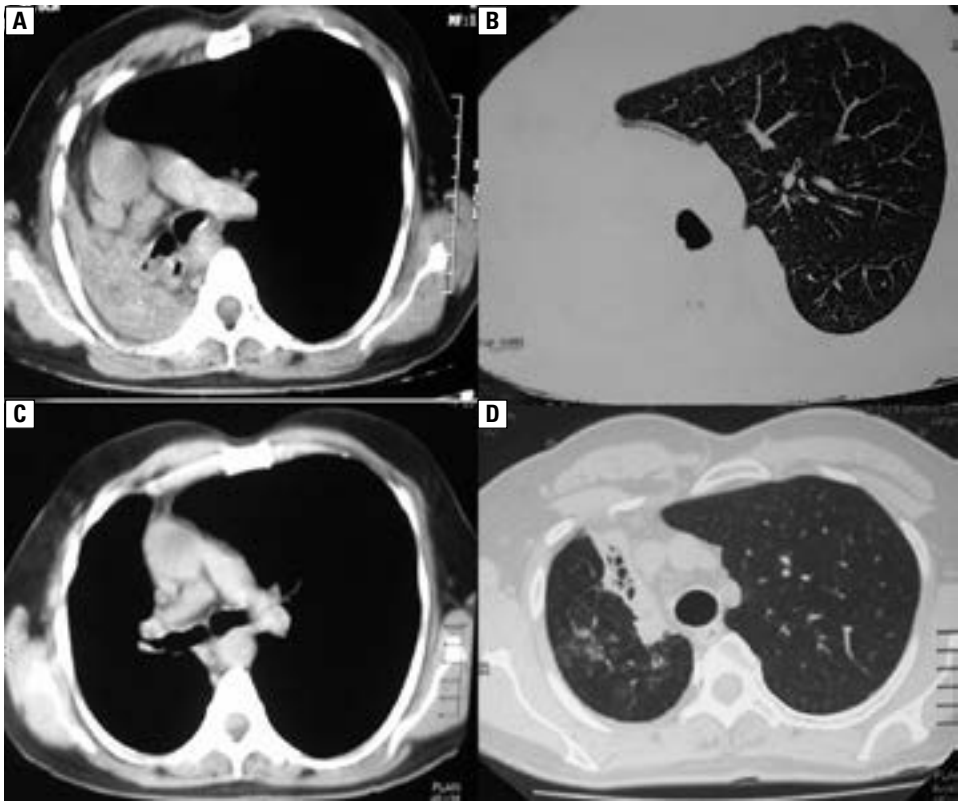

Figure 2. High resolution computed tomography of the lung of patient in case1 (**A**, **B**) Collapsed right lung at presentation with mediastinal shift to right (**C**, **D**) Re-expanded right lung after treatment

sputum was negative for acid fast bacilli at that time. No symptomatic relief was achieved with treatment. He was suspected to have ABPA with mucus plugging of the right main bronchus due to a characteristic intra luminal density in the proximal right main bronchus and was diagnosed to have ABPA based on the characteristic investigations (Table 1). Chest physiotherapy, oral corticosteroids and oral and inhaled bronchodilators were started. A reassessment radiogram done after five days of therapy showed aeration of the right lung, a repeat HRCT lung showed re expansion of right lung and evidence of central bronchiectasis in the right lung (Figs 1B, 2B).

Case 2

A 62-year-old non-smoker farmer presented with dry cough and intermittent low grade fever for the past six months. He was prescribed some

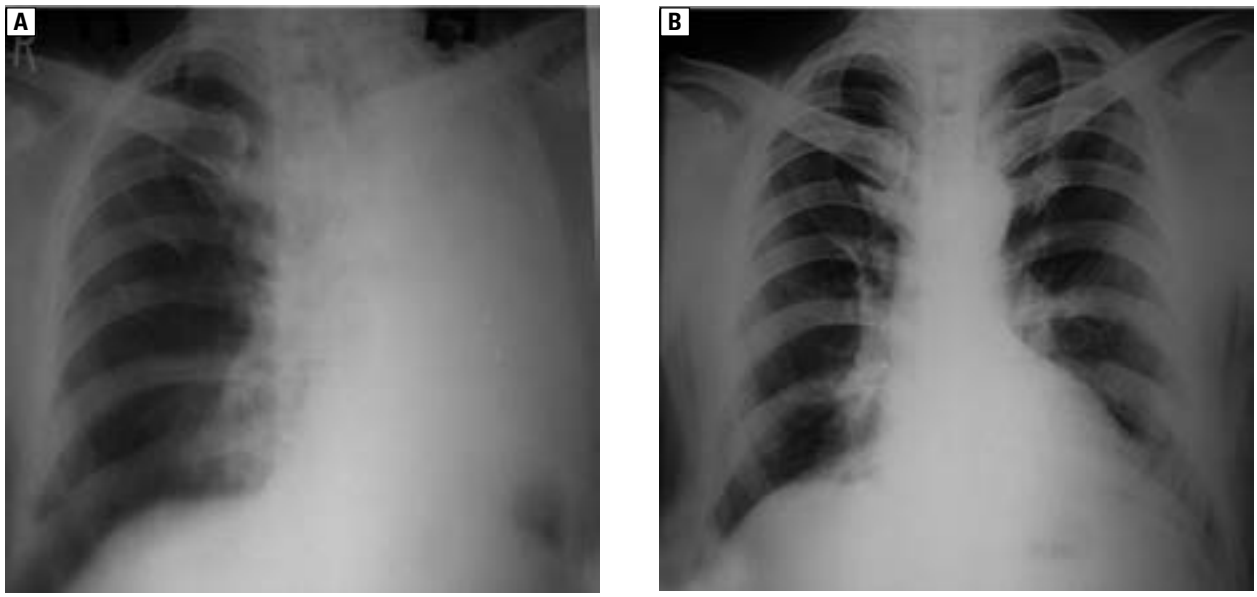

Figure 3. Chest radiogram of the patient in Case 2, showing (**A**) Collapsed left lung at presentation; (**B**) Re-expanded left lung after bronchoscopy

oral medications and inhaled bronchodilators, which did not lead to relief in his symptoms. There was no personal or family history suggestive of atopy. He started producing thick white casts in sputum along with weight loss after 5 months of dry cough. He was admitted to a hospital with sudden onset breathlessness and heaviness over the left side of chest. On chest radiogram, left sided complete lung collapse was present. The patient was investigated for pulmonary tuberculosis and bronchogenic carcinoma but repeated sputum examinations for acid fast bacilli and malignant cells were negative. Because of the persistence of his symptoms and inadequate relief with various forms of treatment he was referred to our institution. He presented to us with sudden worsening of dyspnea, cough with thick golden brown casts in sputum, along with left sided chest pain. On examination there were signs of volume loss and breath sounds were absent on the left side. Chest radiogram showed left sided collapse (Fig. 3A). Routine investigations were significant for eosinophilia of 3340 cells/μL. Fiberoptic bronchoscopy was performed which revealed blockage of left main bronchus by thick mucus plug and necrotic debris sticking to underlying inflamed mucosa. Bronchial aspirate and endobronchial biopsy showed eosinophilia (48%) with acute on chronic infiltrate and Charcot Leyden crystals with PAS +ve branching fungal hyphae admixed in necrotic debris. Bronchial aspirate was negative for acid fast bacilli and malignant cells. Further, patient was evaluated for ABPA and was found to be positive for both type 1 and type 3 reactions (Table 1). Spirometry showed no airflow limitation with forced expiratory volume in 1 second (FEV_1) of 1.94 litres (78% of predicted), forced vital capacity (FVC) of 2.56 litres (83% of predicted) and FEV_1/FVC of 95% of predicted. A repeat chest radiogram showed full expansion of the left side of chest (Fig. 3B). HRCT showed bilateral central bronchiectasis with areas of mucous plugging in the left lung (Fig. 4). Thus, diagnosis of ABPA without bronchial asthma was established and patient was started on oral prednisolone and itraconazole 200 mg/day. He was followed up regularly with improvement in symptoms and a fall in total serum IgE to 939 IU/ml from the initial levels of 1930 IU/ml. The dose of steroid was tapered off and total IgE level reached a plateau of 909 IU/ml after 7 months of treatment.

Case 3

45-year-old non-smoker chemist presented with complaints of episodic breathlessness and wheeze for 5 years which were persistent for one year prior to presentation. On examination, vitals were within normal range and auscultation revealed decreased breath sounds in the right mammary area and inspiratory crepitations. On chest radiogram, right middle lobe collapse was present (Fig. 5A). HRCT lung showed collapse of right middle lobe (Fig. 6A, B). Fibreoptic bronchoscopy was performed which revealed right middle lobe medial segment irregular narrowing and transbronchial lung biopsy showed chronic

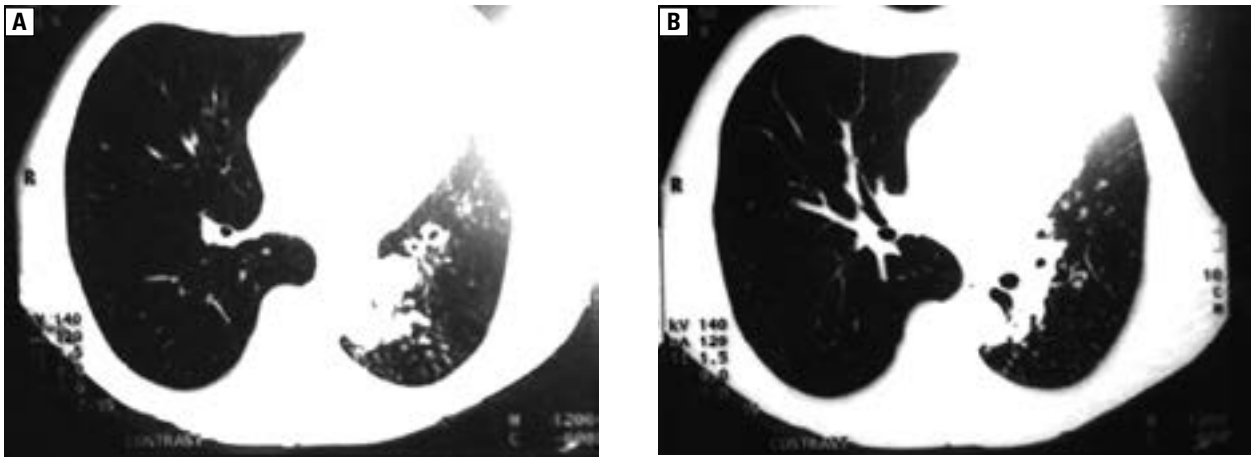

Figure 4. High resolution computed tomography of the lung of patient in Case 2 showing bronchiectasis and mucus plugging

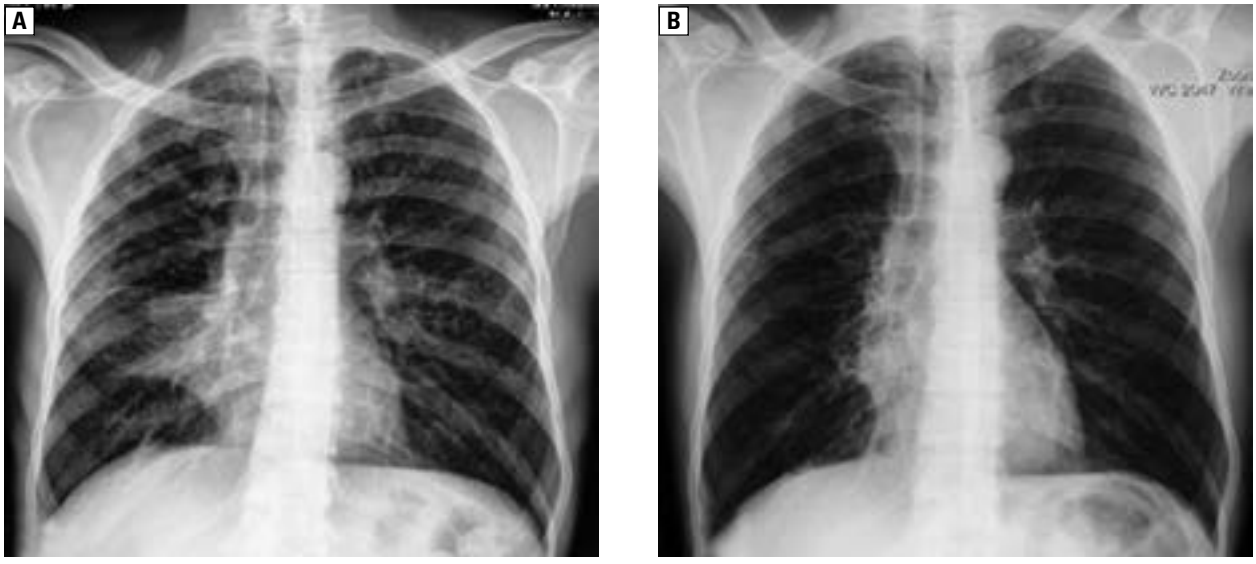

Figure 5. Chest radiogram of the patient in case 3, showing (**A**) Collapsed right middle lobe at presentation; (**B**) Re-expanded right middle lobe after treatment

sub epithelial inflammation. Computed tomography guided fine needle aspiration was done which showed liquid necrotic material only. Patient was investigated and found positive for ABPA (Table 1). Thus, diagnosis of ABPA was established and patient was started on oral steroids. He was followed up regularly with improvement in symptoms and a fall in total IgE levels to 1024 IU/ml from initial level of 8046 IU/ml. A repeat chest roentgenogram and chest HRCT showed re-expansion of the middle lobe and empty dilated bronchus (Fig. 5B, 6C, D).

Discussion

ABPA is often indolent and may be present for years before diagnosis. When diagnosis is made early and treatment with prednisolone is started, irreversible lung damage can be prevented. Prednisolone controls the asthma and causes the sputum (which is the culture medium for Aspergillus fumigatus) to disappear. It eliminates the inflammatory reactions of the bronchi and lung parenchyma so that the patient's condition improves clinically [10].

The increasing frequency with which the diagnosis of ABPA is being made is probably the result of increasing recognition of the disease entity, and perhaps some liberalization of the criteria required for diagnosis [11]. The diagnostic criteria for ABPA are divided into major and minor ones. The major criteria includes asthma, fleeting shadows on chest radiograms, immediate cutaneous reactivity to *Aspergillus fumigatus*,

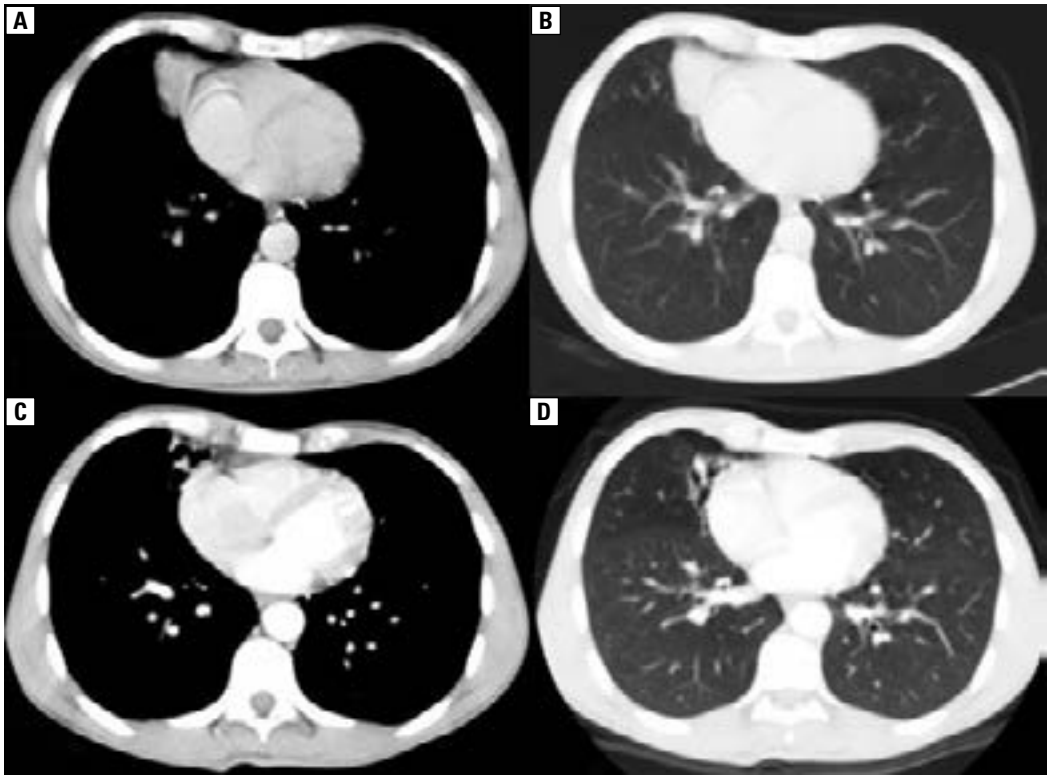

Figure 6. High resolution computed tomography of the lung of patient in case 3 (**A, B**) Collapsed medial segment of right middle lobe at presentation (**C, D**) Re-expanded medial segment of right middle after treatment

elevated total serum IgE, precipitating antibodies against *Aspergillus fumigatus*, peripheral blood eosinophilia, elevated serum IgE and IgG to *Aspergillus fumigatus*, central/proximal bronchiectasis with normal tapering of distal bronchi. The minor criteria are expectoration of golden brownish sputum plugs, positive sputum culture for *Aspergillus species*, and delayed skin reactivity to *Aspergillus fumigatus*. A minimum essential set of criteria has also been advocated that includes asthma, immediate cutaneous reactivity to *Aspergillus fumigatus* and central bronchiectasis in the absence of distal bronchiectasis, elevated total IgE, specific IgE against *Aspergillus fumigatus* [12, 13].

A literature search for ABPA presenting as opaque hemithorax could yield only four such cases [14–16]. In a case series of five patients of lung collapse caused by ABPA in non-asthmatic by Berkin et al., two cases presented as opaque hemithorax [14]. A case of total collapse of right lung in a patient with ABPA has been reported from Japan by Nomura et al in a 29 year old man with bronchial asthma [15]. Agarwal et al described a 22-year-old female without any prior respiratory symptom history who presented with respiratory failure secondary to left lung collapse, necessitating rigid bronchoscopy for diagnosis and management of ABPA [16]. In eight out of the nineteen cases of ABPA in non-asthmatic patients [14, 17–19], bronchogenic carcinoma was initially suspected due to abnormality in the chest roentgenogram (mostly atelectasis), but bronchoscopy revealed typical mucus plugs containing macrophages, several eosinophils, fungal hyphae, scaled-off epithelium (crushman spirals) and calcium oxalate crystals [20]. The microscopic finding of mucoid impaction of bronchi in conjunction with non-invasive fungal hyphae is highly suggestive of ABPA [20]. Many times these patients are confused with tuberculosis and repeatedly treated with anti-tuberculosis drugs [21].

The radiographs of 100 patients with ABPA were examined to assess the type and distribution of abnormalities seen during long-term follow-up by Phelan et al [22]. Lobar shrinkage occurred almost exclusively in the upper zones but other abnormalities were distributed throughout both lungs. Bronchial wall thickening was the commonest lesion observed and was usually a permanent finding. Consolidation was commonest in the perihilar regions. Episodes of transient collapse were segmental, lobar or involved a whole

lung. Permanent collapse was always segmental. Massive shadowing, band shadows and 'gloved fingers' were seen less frequently than expected and cavitation was rare. In some patients the chest radiograph was normal between exacerbations of the disease. It should also be considered that although pulmonary infiltrates and segmental collapse are the usual radiological picture, it can rarely present as lung collapse as in our case.

On computed tomography, the mucoid impaction of the bronchial tree generally shows slightly hyper-hydric density [20]. Computed tomography has a sensitivity of 83% and a specificity of 92% in detecting central bronchiectasis in patients with ABPA [23]. Computed tomography appearances can be sub-divided into bronchial, parenchymal and pleural abnormalities. Bronchial abnormalities include central bronchiectasis, dilated and totally occluded bronchi, air-fluid levels within the dilated bronchi, bronchial wall thickening and parallel-line shadows. Parenchymal abnormalities, which have a predilection for upper lobes, include consolidation, collapse and parenchymal scarring. Parenchymal lesions can extend up to the pleura [24].

Itraconazole is a potential adjunctive treatment for ABPA. Itraconazole treatment of subjects with stable ABPA reduces eosinophilic airway inflammation, systemic immune activation, and exacerbations [25].

Conclusions

The present case series highlights the need for aggressive approach in diagnosing this treatable condition in cases presenting as segmental or total lung collapse even in patients without prior history of bronchial asthma. The condition has a good prognosis if detected early. The collapse can be managed by aggressive pulmonary toileting to cause mobilization of secretions by physiotherapy, postural drainage and/or bronchoscopy along with treatment with drugs like corticosteroids and/or antifungal agents. We hereby recommend that ABPA should be kept as a differential diagnosis of lung collapse.

Conflict of interest

The authors declare no conflict of interest.

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