

Asymptomatic Developments of Pulmonary Infiltrates and Central Bronchiectasis in a Patient with Allergic Bronchopulmonary Aspergillosis

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알레르기성 기관지폐 아스페르길루스증(allergic bronchopulmonary aspergillosis, ABPA)에서 일시적 또는 영구적인 폐병변이 나타날 수 있다. 저자들은 ABPA 증상 악화 없이 새로운 폐침윤과 중심성 기관지확장증이 발생한 증례를 경험하여 이를 보고하는 바이다. 46세 남자로 천식으로 진단 받고 규칙적으로 항천식약물을 복용하고 있던 중, 추적관찰 목적으로 검사한 흉부방사선사진에서 우연히 우상엽에 고립성 폐결절이 관찰되었다. 호흡기증상 또는 폐기능 악화의 소견은 동반되지 않았다. 말초혈액 호산구, 혈청 총 IgE, *Aspergillus fumigatus*-특이 IgG 등이 증가되었고,

경흉부세침생검 검사에서 폐결절은 ABPA 폐침윤이었다. 폐침윤은 경구용 스테로이드 사용 후 없어졌으며, 흉부 고해상전산화단층사진에서 폐침윤이 생겼던 부위에 과거에 보이지 않았던 중심성 기관지확장증 병변이 새롭게 발견되었다. 본 증례를 통하여 ABPA 환자에서 악화 증상이 없더라도 단순 흉부방사선 추적관찰은 폐침윤을 조기에 발견할 수 있으며, 결국 영구적 폐손상을 예방 또는 최소화하는데 도움이 될 수 있을 것으로 생각된다. (Korean J Asthma Allergy Clin Immunol 2009;29:293-297)

Key words: Asthma, Allergic bronchopulmonary aspergillosis, Bronchiectasis

INTRODUCTION

Allergic bronchopulmonary aspergillosis (ABPA) is characterized by immunologic reactions to antigens of *Aspergillus fumigatus* (*Af*) that are present in the bronchial tree, which result in pulmonary infiltrations and central bronchiectasis. ABPA has been estimated to occur in 1~2% of chronic asthmatics. Chest radiographic changes in ABPA may be transient or permanent. Transient changes, which may clear with or without oral corticosteroid therapy, appear to be the result of parenchymal infiltrates, mucoid impactions, or secretions in damaged bronchi. Permanent changes include central bronchiectasis, cavitation, and pulmonary fibrosis, which may occur as a result of repeated pulmonary infiltrations.¹⁾

A new bronchiectasis can develop in areas of pulmonary infiltrates, especially if no oral steroids have been used to treat the infiltration.²⁾ It is important to detect and treat the ABPA infiltrations promptly, so as to prevent or minimize bronchiectasis that develops at the sites of infiltrates. However, ABPA infiltration

may not be associated with any symptoms or signs related to exacerbations in up to 33% of cases.^{3,4)} We hereby described a case of the developments of pulmonary infiltrates and then a new central bronchiectasis under the absence of symptoms or signs of exacerbations in a patient with ABPA.

CASE REPORT

A 46-year-old man was diagnosed as having asthma based on a significant bronchodilator response (increase in FEV₁ of 15.4% and 220 mL) in September 2003 and was given regular asthma medications, including inhaled corticosteroids, long-acting beta2 agonists, theophyllines and leukotriene receptor antagonists. His best FEV₁ was recorded to be 2.2 L (57% of predicted). At the time of the diagnosis of asthma, he had total serum IgE of 647 IU/mL (1,552 ng/mL), blood eosinophils of 900/mm³ (5.9%) and central bronchiectasis on chest high resolution computed tomography (HRCT) (Fig. 1), which may be suggestive of ABPA. However, he had no immediate skin reactivity or precipitating antibodies to *Af* (Green Cross Company, Yongin, South Korea). His asthma was well controlled with the medications, although lung function was low due to fixed airway obstruction. He had asthma duration of 15 years, smoking amounts of 15 pack-years, and diffuse bronchiectasis.

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He regularly visited our outpatient clinic for asthma control. In November 2007, chest radiographic examinations were performed for the purpose of routine follow-up assessments. He had no respiratory symptoms. However, chest radiographs showed around 4 cm-sized mass-like lesion in right upper lobe (Fig. 2). Spirometry revealed FEV₁ of 2.06 L, which was 93.6% of the previous best FEV₁, and FEV₁/FVC of 64.1% (Spiro Analyzer ST-75, Fukuda Sangyo, Tokyo, Japan). Blood tests showed leukocytes of 7,600/mm³,

with 11.6% eosinophils, and total serum IgE of 499 IU/mL (1,197 ng/mL). Stool examinations and ELISA tests (Green Cross Company) were negative for ova and parasites. No mycobacteria and fungi were found in sputum stains and cultures. Skin prick tests to common allergens, including *Af*, and intradermal test to *Af* were negative (Allergopharma, Reinbek, Germany). *Af*-specific IgE was not detected in his serum (ImmunoCAP 100, Phadia AB, Uppsala, Sweden), but *Af*-specific IgG was 14 U/mL (reference range 0~10 U/mL; Green Cross Company). Chest CT revealed about 3.5 cm-



Fig. 1. Chest HRCT obtained in September 2003 showed central bronchiectasis mostly located in inner two-thirds of the right lung field.

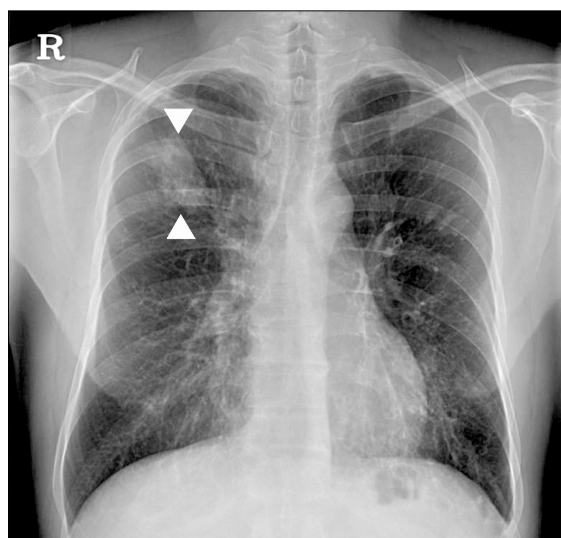


Fig. 2. Chest PA showed about 4 cm-sized solitary pulmonary nodule (arrows) in right upper lung field.

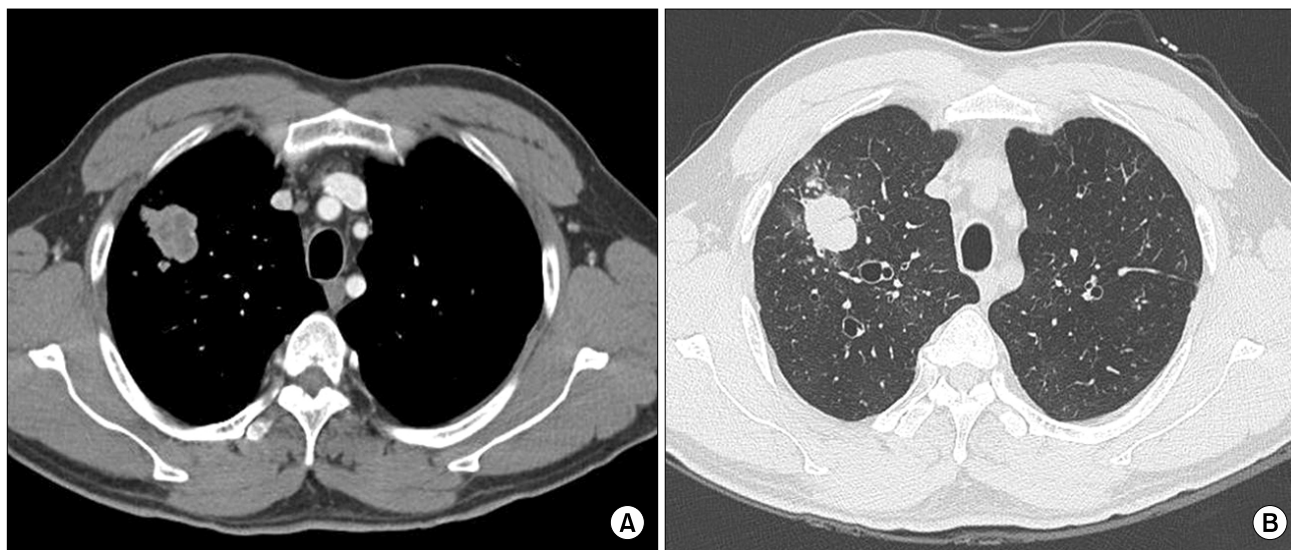


Fig. 3. Chest CT revealed peripheral rim enhancing, low attenuation mass-like lesion in anterior segment of right upper lobe (A) and small centrilobular nodules and linear branching opacities in surrounding lung parenchyma (B).

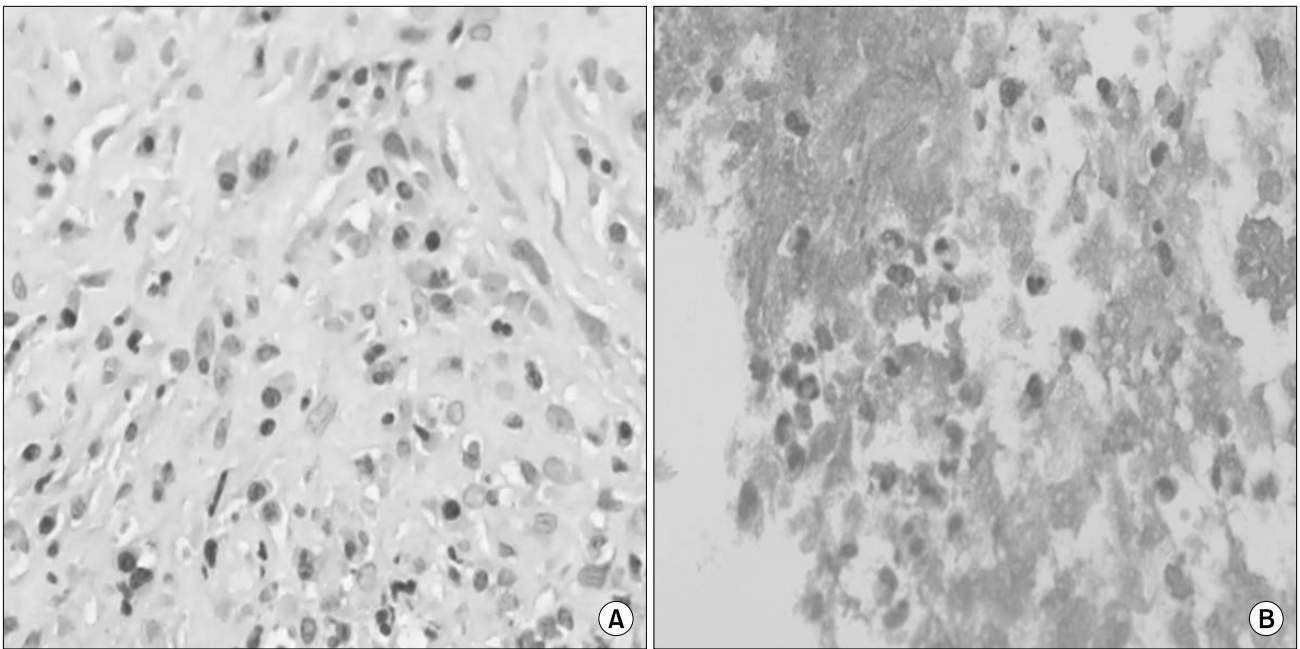


Fig. 4. CT-guided transthoracic fine needle biopsy revealed that alveolar interstitium (A) and mucoid impaction (B) were infiltrated with numerous eosinophils (H&E, $\times 400$).

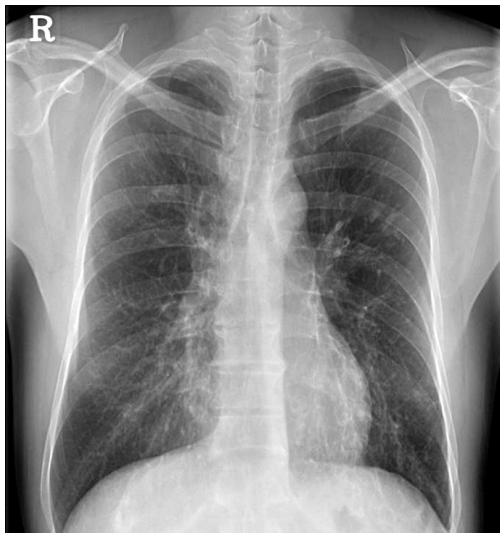


Fig. 5. Chest PA showed that the pulmonary nodule previously seen in right upper lung disappeared following 3-week treatment with oral corticosteroids.

sized mass-like lesion in anterior segment of right upper lobe (Fig. 3).

Next, bronchoscopic examination was done, showing no abnormal findings except for mucous secretions within the bronchi. No mycobacterial and fungal species were observed in stains and cultures of bronchoalveolar lavage fluids. No malignant cells were found in the fluids. Transbronchial lung biopsies were not done.

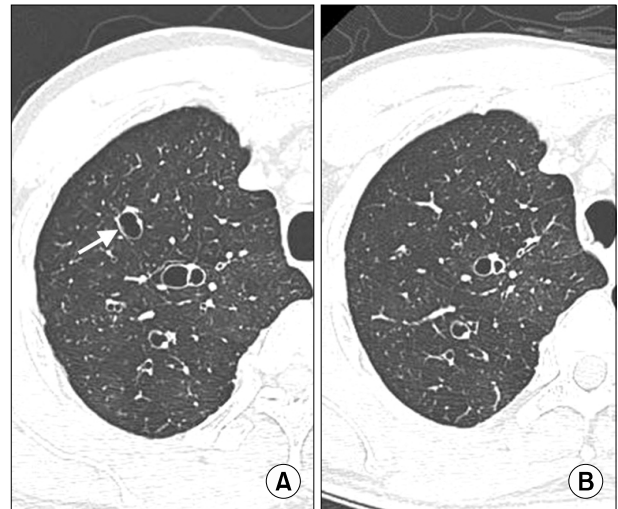


Fig. 6. Chest HRCT obtained in June 2008 revealed that a new central bronchiectasis (arrow) developed in the site of pulmonary infiltrates in anterior segment of right upper lobe (A, see Fig. 3B), which was absolutely not seen in the previous chest HRCT obtained in September 2003 (B).

Instead, CT-guided transthoracic fine needle biopsy was performed, showing that alveolar interstitium was infiltrated with many eosinophils (Fig. 4A). Mucoid impaction was also observed, which was infiltrated with numerous eosinophils (Fig. 4B). No malignant cells were found in the lung tissue. No hyphae were stained with methenamine-silver or Periodic acid-Schiff in the tissue. No fungi

or mycobacteria were cultured in the aspirates.

Finally, he could be diagnosed as having ABPA on the basis of the presence of the following criteria; asthma, peripheral blood eosinophilia, elevated total serum IgE, elevated *Af*-specific IgG, central bronchiectasis and pulmonary infiltrates with eosinophils, although there was no skin reaction or serum IgE to *Af*. He was treated with 30 mg prednisolone daily for 3 weeks. The nodule in right upper lobe disappeared on chest radiographs (Fig. 5). In June 2008, follow-up chest HRCT was obtained, showing a new central bronchiectasis in the site of the infiltrates in anterior segment of right upper lobe (Fig. 6A), which was absolutely not seen in the previous chest HRCT obtained in 2003 (Fig. 6B). Recently, total serum IgE level was 402 IU/mL (964 ng/mL). His asthma has been well controlled with asthma medications.

DISCUSSION

In the present case, the new central bronchiectasis, which was absolutely not seen in the previous chest HRCT, was found in the area where ABPA pulmonary infiltrates occurred. The central bronchiectasis should occur before or in concurrence with the pulmonary infiltrates.

It is known that radiographic exacerbations may result in bronchiectasis in involved areas in ABPA, if not treated with oral steroids.²⁾ Early treatment with oral steroids for the radiographic infiltrates can prevent or minimize the development of bronchiectasis. Thus, prompt detection of the radiographic infiltrates is required to prevent disease progression in ABPA. However, ABPA pulmonary infiltrations may not be associated with symptoms of exacerbations in up to 33% of cases,^{3,4)} and symptoms and physical findings may be insufficient to detect all ABPA infiltrations. Indeed, it is known that in ABPA, there is a lack of relationship between the chest radiographs and clinical symptoms. Our case showed no symptoms related to ABPA exacerbations or changes in lung function in spite of the pulmonary infiltrates.

It has been known that serial measurements of serum total IgE concentrations may be useful in that sharp elevations (100% over baseline) are frequently associated with new pulmonary infiltrations.⁵⁾ However, in the present case, total IgE level was not increased by 100% over baseline, although being a little elevated (24%). Therefore, our case suggests that regular chest radiographic examinations besides total serum IgE measurement may be required for early detection of pulmonary infiltrates in patients with ABPA. Repeated pulmonary infiltrations may result in the development of

end-stage lung diseases, including cavitation, bullae, blebs, and pulmonary fibrosis.⁵⁾ Only prompt detection and treatment of pulmonary infiltrations may prevent the progression to fibrotic stage in ABPA. It might be reasonable to recommend that chest radiographs should be repeated at least yearly even in asymptomatic ABPA patients, based on suggestion⁶⁾ that spirometry should be obtained yearly in patients with ABPA. Although, in the present case, early detection of pulmonary infiltrations and treatment with oral steroids did not prevent the development of bronchiectasis, regular follow-ups with serum IgE measurement, spirometry, and/or chest radiographic examination may be the best way to prevent or minimize the development of end-stage lung diseases in ABPA.

Our case met criteria for ABPA, including asthma, pulmonary infiltrates, peripheral blood eosinophilia, elevated total serum IgE concentration, elevated *Af*-specific IgG, and central bronchiectasis.^{1,5,6)} Particularly, the presence of central bronchiectasis may be pathognomonic finding for diagnosis of ABPA.⁷⁾ On the other hand, the pulmonary infiltrates in the present case presented as solitary pulmonary nodule, which was proven to be ABPA infiltrates with eosinophils and mucin and resolved with oral steroids. Radiographic ABPA infiltrates may be considered in the differential diagnosis of solitary pulmonary nodules in asthmatics.

However, in the present case, no immediate cutaneous reactivity to *Af* or elevated serum *Af*-specific IgE was found. Several factors must be considered. First, the quality of *Aspergillus* extracts used for skin testing or in vitro specific IgE assays might be poor in that few relevant *Aspergillus* epitopes could be present. *Af* is a very heterogeneous antigen, with immunoreactive components ranging from 10 to 100 kD. It has some 40 components that bind to IgE.⁸⁾ The Allergen Nomenclature Subcommittee of the International Union on Standardization has recognized 22 *Af* allergens.⁹⁾ Second, it is possible that the levels of specific IgE are too low to be reactive to *Af* in vivo or in vitro tests. Our case have regularly used medium to high doses of inhaled corticosteroids at least for 4 years, which might suppress IgE immune responses.¹⁰⁾ Serum total IgE levels were not so high in the patient, although being over 417 IU/mL (1,000 ng/mL). Third, other fungi except *Af* might be involved in the occurrence of ABPA. *Af* is involved in the majority of ABPA cases. However, clinical and radiological features similar to those observed in *Af* ABPA cases are occasionally seen in association with other fungi, such as *Stemphylium lanuginosum*, *Helminthosporium species*, *Candida species*, *Curvularia species*, *Schizophyllum commune*, *Drechslera hawaiiensis*, *Fusarium vasinfectum* and other species of *Aspergillus*.^{11,12)} However, we could not identify hyphae or fungi in aspirate

obtained with CT-guided fine needle aspiration. This may be because the amount of aspirates is not enough to detect them in stains or cultures. Surgical resection might provide more opportunities to identify them.

CONCLUSION

Taken together, our case showed that ABPA pulmonary infiltrates occurred without symptoms or signs of exacerbations and new central bronchiectasis developed in the site of the pulmonary infiltrates. We can infer from the findings that regular follow-up with radiographic chest examinations may also be required for earlier detection of pulmonary infiltrates in ABPA patients without symptoms or signs related to exacerbations, which will prevent or minimize the development of irreversible permanent changes in the lung. Additionally, ABPA infiltrates may be considered in the differential diagnosis of pulmonary nodules in asthmatics.

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