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Case Report Open Access

Asthma Exacerbation Caused by Bacterial Infection in Two Elderly Patients

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Abstract

Background: The role of airway bacterial infection in the asthma exacerbation has been reported in addition to that of viral infection. However, the effect of bacterial infections on asthma exacerbation has received less attention than that of viral infections, and clinical features have not been well reported.

Case presentation: Here, we describe the clinical features of two cases of asthma exacerbation that were thought to involve airway and/or lung bacterial infection and that improved with treatment including antibiotics, glucocorticoids and bronchodilators.

Conclusion: The examination data suggested that neutrophilic inflammation caused by bacterial infections may have an important role in the development of asthma exacerbations.

Keywords: Bacterial infection; Bronchial asthma; Exacerbation; Neutrophilic inflammation

Background

A variety of factors are associated with the exacerbation of asthma, including antigen inhalation, cigarette smoking, cold air, non-steroidal anti-inflammatory drugs and airway infections [1-6]. Among airway infections, viral infections such as rhinoviruses are major causes of asthma exacerbation [3-6]. Airway infections by bacteria, such as *Streptocccus pneumoniae* and *Haemophilus influenzae*, have also been found in patients with asthma exacerbation [7,8]. However, the role of bacterial infections in asthma exacerbation is less clear [9] and has received less attention than that of viruses [10]. Furthermore, the clinical features of asthma exacerbation caused by bacterial infections have not been well documented.

Here, we describe two elderly individuals with asthma exacerbation who received treatment for bronchial asthma and were infected with bacteria in the lung and/or airway. They improved with treatment with antibiotics, glucocorticoids and bronchodilators. Both patients consented to our report.

Case Presentation

Case 1

An 80 year-old Male patient presented with a fever (38.0˚C) and dyspnea with severe wheezing and purulent sputum and was transferred to the Tohoku University Hospital from Kurihara Central Hospital. The patient had received treatment for bronchial asthma for 20 years. At his first visit to Tohoku University Hospital 20 y ago, he presented with wheezes and dyspnea while sleeping and initially after waking. The number of eosinophils in the peripheral blood (17%) and the sputum (90%) were high [11,12]. The serum immunoglobulin E (IgE) level was elevated (Table 1), and specific IgE antibodies against house dust mite (*Dermatophagoides pteronyssinus*) were detected using a radioallergosorbent test. The patient was treated with an inhaled corticosteroid plus oral intake of a short-acting β2 agonist and theophylline. However, auscultation of the lungs revealed occasional weak wheezes in both lung fields. The results of a pulmonary function test before exacerbation also showed obstructive impairment even after the start of treatment (Table 1), although the results indicated normal pulmonary function when he presented without wheezes (FVC, 2.65 L (84%); FEV1, 2.00 L/s; FEV1/FVC, 75%). He was introduced to Kurihara Central Hospital, which is in his city of residence.

At Kurihara Central Hospital, oral intake of a short-acting β2 agonist was replaced by inhalation of a long-acting β2 agonist (LABA) and treatment with oral corticosteroid, after which treatment with anti-IgE antibody was added. Furthermore, treatment with an inhaled corticosteroid was continued. He was maintained on this regimen until one year ago, when he presented with symptoms of exacerbation and was admitted to the Tohoku University Hospital.

During exacerbation, the chest radiographs and a computed tomography (CT) scan showed diffuse micronodular shadows in the lower parts of the lung (Figures 1A and 1B). Peripheral blood and serum examination data showed inflammation with an elevated white blood cell (WBC) count and serum C-reactive protein (CRP) levels (Table 1). *Pseudomonas aeruginosa* was isolated in the sputum, which was sensitive to many types of antibiotics tested, including tazobactam/piperacillin with which the patient was treated. The number of eosinophils in the peripheral blood and sputum was low, the number of neutrophils in the peripheral blood was high, and the serum IgE

level was mildly elevated (Table 1). Although an *Aspergillus* antigen was detected, the antibody titer against *Aspergillus* was below the detection level. Antigens from *Legionella pneumophila* and *Streptocccus pneumoniae* in the urine, influenza virus in the nasal cavity swabs, rhinovirus and respiratory syncytial (RS) virus in the sputum, and serum *Mycoplasma pneumoniae* antibody were not detected (Table 1). Exhaled nitric oxide (FeNO) could not be measured during exacerbation because of the patient's poor condition (Table 1).

Case 2

An 85 year-old Female patient was admitted to Kurihara Central Hospital because of fever (37.8˚C) and dyspnea with wheezing, purulent sputum and cough. The patient had received treatment for bronchial asthma in a clinic for three years, but occasionally presented with wheezes. At the time of admission, the chest radiographs and CT scans showed infiltrative shadows in the right middle and lower regions and the left lower region of the lung (Figures 1C and 1D), indicating the presence of bronchopneumonia. Elevated levels of WBC and neutrophil in the peripheral blood and CRP of the serum were observed and the FeNO value was mildly elevated (Table 1). *Klebsiella pneumoniae* was detected in the sputum, which was sensitive to many types of antibiotics tested, including tazobactam/piperacillin with which the patient was treated. In contrast, Antigens from *Legionella pneumophila* and *Streptocccus pneumoniae* in the urine, influenza virus in the nasal cavity swabs, rhinovirus and RS virus in the sputum, and serum *Mycoplasma pneumoniae* antibody were not detected (Table 1). The number of eosinophils in the peripheral blood and sputum during exacerbation and the serum IgE level at the stable condition after treatment of exacerbation were low (Table 1).

	Case 1	**Case 2**
Characteristics		
Age	80	85
Gender	Male	Female
Smoking history	Non-smoker	Non-smoker
Comorbidities	Chronic sinusitis	Hypertension
Pulmonary function[1]		
FVC, L (%)	3.19 (103)	1.35 (79)
FEV1, L/s	1.83	0.61
FEV1/FVC, %	57	45
%FEV1, %	88	49
Laboratory data		
Hematological and biochemical properties at exacerbation		
WBC (/μL)	11,000	9,740
Neutrophil (%)	93.6	79.3
Eosinophil (%)	0.0	0.3
CRP (mg/dL)	3.9	15.3
Sputum bacteria	*P. aeruginosa*	*K. pneumoniae*
Antigens and antibody of microorganisms	SP (-), LP (-), MP (-)	SP (-), LP (-), MP (-)
Sputum eosinophil (%)		
At the first visit[2]	90	-
At the exacerbation	<3	<3
At the stable condition[3]	<3	<3
IgE (IU/mL)		
At the first visit[2]	921	-
At the exacerbation	188	-
At the stable condition[3]	-	13
FeNO (ppb)		
At the exacerbation	NP	46
At the stable condition[3]	15	19

Table 1: Characteristics, pulmonary function and laboratory data for the patients. CRP: C-Reactive Protein; FeNO: Exhaled Nitric Oxide; FEV1: Forced Expiratory Volume in One Second; FVC: Forced Vital Capacity; *K. pneumoniae*: *Klebsiella pneumoniae*; LP: *Legionella pneumophila*; MP: *Mycoplasma pneumoniae*; NP: Tried but could not be performed; *P. aeruginosa*: *Pseudomonas aeruginosa*; SP: *Streptocccus pneumoniae*; WBC: white blood cell.1) Pulmonary function test eight years after treatment at the Tohoku University Hospital in case 1 and 12 months after treatment of asthma exacerbation in case 2. 2) During the first visit to the Tohoku University Hospital 20 years prior to admission to the hospital because of exacerbation in case 1. No data before exacerbation in case 2.3)12 months after treatment of asthma exacerbation.

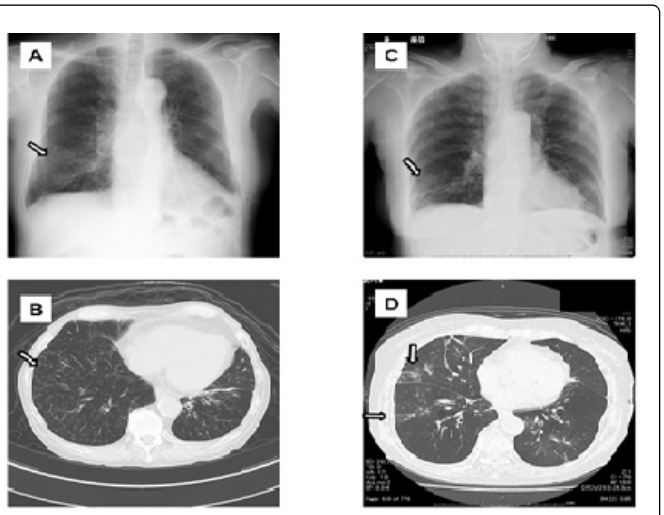

Figure 1: Chest radiographs (A and C) and computed tomography scans (B and D) of case 1 (A and B) and case 2 (C and D) show diffuse microgranular shadows (case 1) and infiltrative shadows (case 2) (arrows).

Treatments and outcomes

The two cases were treated with tazobactam/piperacillin for 8 days (in case 1) or for 7 days (in case 2) and with either oral (in case 1) or a drip infusion of (in case 2) corticosteroids and LABA. After the treatment, the shadows in the lungs diminished on chest radiographs and CT scans, and fever and dyspnea with wheezing improved, although the results of the pulmonary function test in case 2 still showed an obstructive impairment (Table 1). *Pseudomonas aeruginosa* (in case 1) and *Klebsiella pneumoniae* (in case 2) were not detected in the sputum at the stable condition after treatment of exacerbation. Treatment with an inhaled corticosteroid plus LABA (ICS/LABA) was started before discharge from the hospital. Case 1 was also prescribed a long-acting anti-cholinergic (LAMA: long-acting muscarinic antagonist) drug for the treatment of bronchial asthma [13]. In both cases, FeNO examination results showed a normal value 12 months after treatment of asthma exacerbation (Table 1).

Discussion

These two patients had received treatment for bronchial asthma. The diagnoses of bronchial asthma were based on the symptoms of wheezing, cough, chest tightness, or dyspnea, as well as reversible airflow limitation after inhalation of a β2 agonist [1,14]. During exacerbation, the patients received treatment with systemic steroids and LABA in addition to antibiotics for bacterial bronchitis and bronchiolitis (case 1) or for bronchopneumonia (case 2), based on the symptoms and the findings of the chest radiographs and CT scans. After treatment, the shadows in the lungs diminished on chest radiographs and CT scans, and fever and dyspnea with wheezing improved.

COPD and heart failure were ruled out based on the symptoms, smoking history, the findings of the pulmonary function test, chest radiographs and CT scans. *Aspergillus* antigen was detected in the sputum of case 1. However, allergic bronchopulmonary aspergillosis was ruled out because of low levels of an antibody against *Aspergillus*. By contrast, case 1 was thought to have had eosinophilic inflammation 20 years ago because the number of eosinophils in the peripheral blood and sputum was elevated [11,12]. However, treatment with an oral steroid for more than three years might reduce the number of eosinophils in the peripheral blood and sputum as well as the serum IgE level in this case.

In case 2, mild FeNO elevation was observed during the exacerbation. Furthermore, the obstructive impairment of pulmonary function after treatment of exacerbation might have been caused by persistent airway narrowing due to bronchial asthma in spite of the treatment.

Bacteria detected in these cases and in previous reports [7-9] enhance mucus secretion [15], inhibit the ciliary beat frequency, and cause airway epithelial injury, thereby impairing mucociliary clearance [16]. Infection with these bacteria also stimulates the cells in the airways and the lung parenchyma to induce pro-inflammatory substrates such as interleukin (IL)-8 and leukotriene B4 [17]. These substrates induce inflammation by causing neutrophils to infiltrate the airways and alveoli and by activating neutrophils to release cytotoxic products and neutrophil elastase [17].

Similar to previous findings [7-9], bacteria were detected in the sputum in these cases. In addition, the number of eosinophils in the peripheral blood and sputum was low, and the patients presented with neutrophilia.

Conclusion

The findings in these cases suggest that a bacterial infection in the airway and lung may induce asthma exacerbation with neutrophilic inflammation, as previously reported [11,18].

Competing of Interest

All authors have no competing interest.

Author's Contribution

All authors made substantial contributions to the investigations presented in this manuscript. MY wrote the article. MY, HY, KM, SN and MI collected clinical data. MY drafted the manuscript with contribution of MI. All authors read and approved the final manuscript.

Acknowledgment

Both patients consented to our report.

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