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Climate Change to Blame in Severe Oral Corticosteroid-Dependent Asthma? A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Funds Collection G

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Patient: Female, 63-year-old
Final Diagnosis: Asthma
Symptoms: Wheeze
Medication: —
Clinical Procedure: —
Specialty: Pulmonology

Objective: Unusual clinical course

Background: Despite the availability of inhaled corticosteroid and the development of various biological treatment agents, severe asthma patients are still at high risk of recurrent and life-threatening exacerbations, which results in morbidity and mortality. In addition to treatment response variability, incorrect inhaler technique, poor adherence, and major psychological problems, environmental factors such as climate change also are contributory factors for worsen symptoms of asthma and acute exacerbation. We present here, a case of a 63-year-old female patient who had oral corticosteroid-dependent severe asthma and recurrent attacks in spring and autumn.

Case report: A 63-year-old Chinese female was diagnosed with asthma when she was 3 years old. During 2007–2011, she was admitted to the hospital once a year because of asthma exacerbation; she was on a regular treatment regimen of inhaled corticosteroids (ICS) plus long-acting beta-agonist (LABA). In October 2018, she was admitted to our Department for aggravating symptoms due to "sudden climate change". She was discharged on tapering doses of oral methylprednisolone from 32 mg once daily, but the reduced methylprednisolone resulted in aggravation of wheezing. However, when the weather warmed up, her symptoms were relieved, and she stopped taking methylprednisolone (after the tapering).

Conclusions: This study suggests an association between the common causes of weather changes and acute severe asthma exacerbation. Patients and clinicians should be aware that keeping warm and avoiding exposure to cold air and airborne allergens might reduce the frequency of asthma exacerbations.

MeSH Keywords: Asthma • Climate Change • Disease Progression

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Background

Asthma is a common airway disease that affects 4.2% of Chinese adults [1]. Severe asthma is defined as asthma uncontrolled despite adherence with maximal optimized therapy or asthma that worsens when high dose treatment is tapered [2]. Severe asthma patients make up 3% to 10% of adults with asthma worldwide and have a higher risk of recurrent and potentially life-threatening exacerbations. This group represents much of the morbidity and mortality burden, and more than 60% of the total medical cost of asthma care [3,4]. Despite the increase in available biological agents in addition to inhaled glucocorticoids, long-acting beta-2 receptor agonists and leukotriene receptor antagonists, the management of severe asthma is complicated by the heterogeneity of the disease, treatment response variability, incorrect inhaler technique, poor patient adherence, major psychological or socioeconomic problems [5], environmental factors and medical or psychiatric conditions such as gastroesophageal reflux, chronic sinusitis [6,7]. It remains a major challenge for both clinicians and patients that needs to be resolved. Cold air exposure is one of the causes of airway contractions and asthma attacks [8]. Previous studies have identified low temperature as a trigger of childhood asthma. Zhang et al., in an epidemic study in Shanghai, China, found that the most important triggers of asthma attacks were cold air, followed by respiratory infection and dust [9], indicating the potential role of cold air exposure as a risk factor in asthma exacerbation. The aim of this work was to present the case of a severe corticosteroid-dependent difficult-to-control patient with asthma due to recurrent attacks that occurred in the spring and autumn.

Case Report

The patient was a 63-year-old Chinese female who was first referred to our pulmonary clinic approximately 2 years ago for evaluation and management of uncontrolled bronchial asthma. Aside from asthma, she had hypertension, coronary heart disease, and gastroesophageal reflux. She took olmesartan 20 mg, amlodipine besylate 10 mg, verapamil 40 mg, rosuvastatin 5 mg, and rabeprazole 10 mg once daily.

The patient was diagnosed with asthma when she was 3 years old. Her symptoms were well-controlled except occasional exacerbation until she was 18 years old when recurrent exacerbations occurred, after which the patient regularly used aminophylline and cromolyn. Her exacerbations started to increase when she was 50 years old (2006), especially in the spring and autumn. She was admitted to the hospital once a year because of asthma exacerbation during the following 5 years (2007 to 2011); she had access to inhalation budesonide and terbutaline irregularly. Since 2013, she had been prescribed with regular Seretide (250 μg) twice daily, Spiriva 18 μg daily, cetirizine and montelukast 10 mg daily. In 2015, Seretide was switched to Symbicort 320 μg twice daily. From 2015 to 2018, she experienced several exacerbations in the spring and autumn, when there was an abrupt change in the weather; oral prednisone (5~10 mg) was used to relief chest tightness and wheezing.

In October 2018, with a sudden break in the weather, she presented to our Department for hospitalization because of worsening dyspnea and wheezing. At presentation, the patient's lungs were filled, she had wheezing on auscultation, and a slight increase in the proportion of eosinophils (4.3%) in her peripheral blood was detected, but no abnormalities were found in serum biochemistry tests. Chest x-ray showed increased lung markings. Chest computed tomography (CT) scan showed increased lung markings and a micro nodule on the left lower lobe. After treatment with intravenous levofloxacin, methylprednisolone, aminophylline, and ambroxol, she was discharged after 1 month, and administrated with tapering doses of oral methylprednisolone from 32 mg once daily. In January 2019, she experienced aggravated wheezing once the dose of methylprednisolone was reduced to 8 mg. Thereafter, she was treated with maintenance therapy (methylprednisolone 12 mg once daily, Symbicort 320 μg twice daily, Spiriva 18 μg once daily, cetirizine and montelukast 10 mg once daily and salbutamol on an as-needed basis to control symptoms) until June 2019, at which time, the weather warmed up and her symptoms were relieved. After that, she began tapering her methylprednisolone, and 3 weeks later she stopped taking it. Her symptoms were then under control with no wheezing in the bilateral lung on auscultation; she took her other medications regularly, including Symbicort 320 μg twice daily, Spiriva 18 μg once daily, and cetirizine and montelukast 10 mg once daily. Her weight had remained stable, and her glycosylated hemoglobin fluctuated in the range of 5.6~7.1 during her treatment with oral methylprednisolone.

Her level of fractional exhaled nitric oxide (FeNO) reached 19 ppb in 2015, followed by a reduction to 7 ppb in 2019 (Figure 1). Her pulmonary function tests showed a slight fluctuation from 2011 to 2019: forced expiratory volume in one second (FEV1) 1.35 to 1.12 L, forced vital capacity (FVC) 2.29 to 2.18 L, and FEV1% pre decreased from 60% to 50% (Figure 2). A bronchoscopy showed no abnormality. RAST (radio allergo sorbent test) demonstrated normal total immunoglobulin (Ig)E level (53.6 kU/L), increased serum specific IgE levels to Dermatophagoides pteronyssinus (0.21 kUA/L), D. farina (0.22 kUA/L) and egg white (0.35 kUA/L), and increased IgE level to Aspergillus fumigatus (0.91 kUA/L). Induced sputum inflammatory cell count showed eosinophil 1% and neutrophil 51%.

The diagnosis of asthma for this patient was based on the following evidence: 1) recurrent episodes of wheezing,

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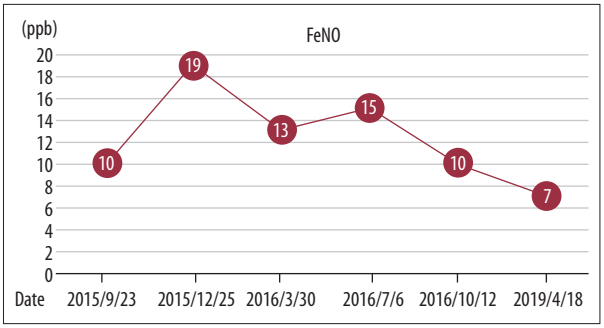

Figure 1. The number in the blue circle represented fractional exhaled nitric oxide (FeNO) levels of the patient.

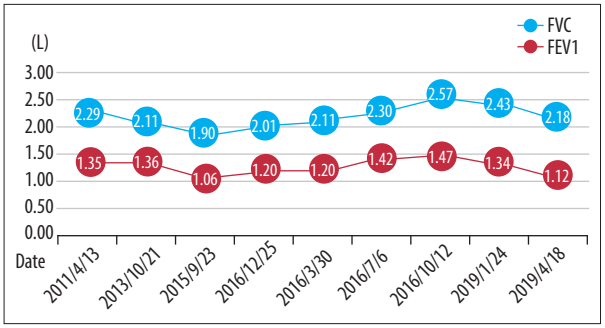

Figure 2. The number in the circles represented levels of. forced expiratory volume in one second (FEV1) (red) and forced vital capacity (FVC) (blue).

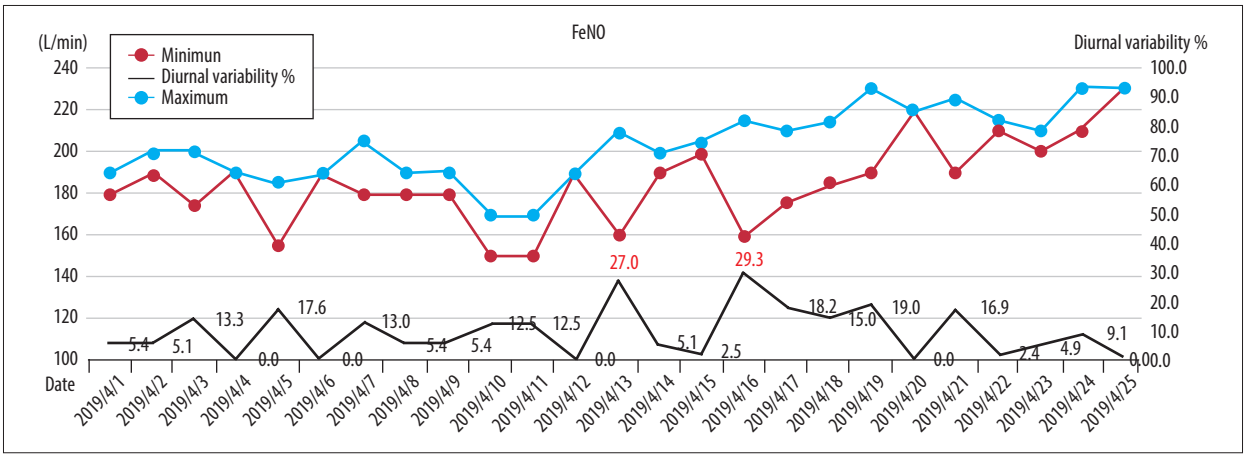

Figure 3. Peak expiratory flow (PEF) levels (blue and red) and diurnal variability of PEF (black) of the patient in consecutive 25 days.

breathlessness, chest tightness, and coughing; 2) diffuse wheezing in expiratory phase in bilateral lung on auscultation; 3) these symptoms could be relieved by corticosteroids; 4) diurnal variability of peak expiratory flow (PEF) >20% (Figure 3); and 5) x-ray or CT scan did not show evidence of chronic obstructive pulmonary disease (COPD), pneumonia or congenital abnormality of lung (Figure 4).

Discussion

Asthma is a heterogeneous disorder and its control varies because of treatment response variability. Severe asthma refers to failure to achieve remission with aggressive therapy, such as inhaled corticosteroid (ICS) treatment, namely poor corticosteroids responsiveness. Variability of responsiveness to ICS treatment is the main obstacle to successful asthma management.

Risk factors for severe asthma in general involve environmental factors including weather changes, airborne pollen, airborne fungal spores, air pollutants, and passive smoking. Climate change might be a major contributing factor to oral corticosteroid dependence due to the fact that more severe or worsening symptoms and aggravations of asthma occur after sudden climate change in autumn and spring observed since 2006. Moreover, in our patient's case, it is worth noting that acute asthma exacerbation happened when the weather abruptly changed, and the patient's symptoms were relieved when the weather warmed up, which may suggest, in our case, a potential predominant role of environmental factors in poor asthma control, although the association between exacerbations of asthma and weather or air pollution is not well understood. However, low temperature or a sudden fall in temperature is a well-known risk factor for asthma exacerbations provoking aggravated airway spasms by airway cooling or irritation [8,9]. Factors involving climate change (temperature, wind speed, humidity) can affect both biological and chemical components in the air, including airborne pollen, fungal spores, and pollutants. For instance, temperature and wind play important roles in determining patterns and concentrations of air pollution [10]. In addition, air pollutants were associated with asthma incidence and exacerbation [10]. It has been demonstrated that there is a PM2.5 (particulate matter smaller than 2.5 μm in diameters) explosive growth triggered by some chemical components during late autumn and winter in Shanghai [11], which is consistent with the occurrence of

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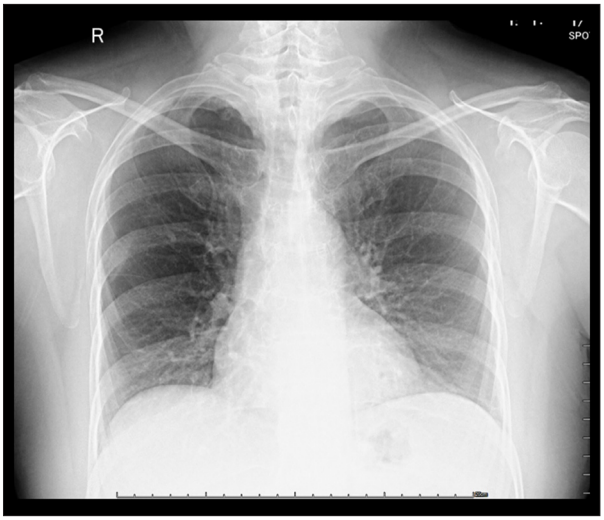

Figure 4. A chest x-ray revealed increased lung markings.

exacerbations of our patient. Airborne allergens such as pollen and fungal spores have also been shown to correlate with asthma hospital admissions [12]. In view of the epidemiological and experimental studies on the effects of climate changes on respiratory allergy, our case suggests a potential causal relationship between severe asthma and environmental factors.

A cross-sectional, community-based study with a large sample population of 27 042 participants in Shanghai demonstrated that cold air was the most prominent cause of asthma attacks, exceeding other recognized risk factors for asthma exacerbation such as respiratory infection, dust inhalation and exercise [9]. Another study conducted in Shanghai also ascertained a negative relationship between ambient temperature and risk of asthma attacks [13]. These studies provided additional evidence for the association of climate change (cold air) with the exacerbation of our patient who resided in the same sample district (Shanghai). Recently, Chan et al. measured the effects of environmental exposure on asthma episodes and revealed a significant association between the perceptions of cold temperature and asthma symptoms [14]. Several underlying mechanisms should be taken into consideration about this topic. Cold air exposure is a cause of airway contraction which could result in an asthma attack; low temperature is connected with worse lung function such as lower lung capacity [15]; airways in low temperature scenarios are more susceptible to respiratory virus, which is an important driver in asthma exacerbation through increasing airway inflammation [16,17]. At the same time, a suppressed immune system worsens this situation [18]; cold temperature can increase the mRNA level and secretion of mucin protein-MUC5AC, which can activate downstream molecular signaling pathways to induce exacerbations of asthma [19]. Therefore, asthma patients are sensitive to temperature.

In this patient case, other factors which might lead to poorly controlled severe asthma could be ruled out by evidence of the patient's correct inhalation, good adherence, support of her family, and no other major psychological or socioeconomic problems. Therefore, these study findings suggest an association between common causes of weather change (cold air/low temperature) and acute severe asthma exacerbation. Patients and clinicians should be aware that keeping warm and avoiding exposure to cold air and airborne allergens might reduce the frequency of asthma exacerbations.

Conclusions

This case suggests that climate change (cold air/low temperature) might be identified by asthmatic patients as an important trigger of an asthma attack. Apart from the aforementioned mechanisms described, other reasons such as changes in chemical and biologic components of air breathed might also deserve consideration and need epidemiological studies with large groups to confirm.

Conflict of interest

None.

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