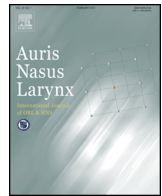




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Effect of Asian sand dust on Japanese cedar pollinosis

Kazuhiro Ogi MD, PhD^{a,*}, Tetsuji Takabayashi MD, PhD^b, Masafumi Sakashita MD, PhD^b,
Dai Susuki MD, PhD^b, Takechiyo Yamada MD, PhD^b, Yasuhiro Manabe MD, PhD^a,
Shigeharu Fujieda MD, PhD^b

^a Division of Otorhinolaryngology, Shinseikai Toyama Hospital, Toyama 939-0243, Japan

^b Division of Otorhinolaryngology Head and Neck Surgery, Department of Sensory and Locomotor Medicine, Faculty of Medical Sciences, University of Fukui, Fukui 910-1193, Japan

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ABSTRACT

Objective: Asian sand dust (ASD), originating in the deserts of Mongolia and China, spreads over large areas and is associated with adverse effects on human health in East Asia, including asthma, heart disease, and some allergic diseases. However, the effect of ASD on patients with seasonal allergic rhinitis caused by Japanese cedar pollen (SAR-JCP), the most common form of allergic rhinitis, remains unclear. The aim of this study was to investigate the effect of ASD on SAR-JCP patients.

Methods: A total of 41 patients with SAR-JCP recorded nasal and ocular allergic symptom scores in a diary. We assessed the influence of ASD events on patients with SAR-JCP during the JCP season and before and after the JCP season.

Results: ASD events did not influence nasal and ocular allergy symptoms during the JCP season. Scores for sneezing and runny nose were significantly increased by ASD events in the pre-JCP season. Ocular symptom scores were significantly increased by ASD events in the post-JCP season.

Conclusion: Our results suggest that ASD may exacerbate allergy symptoms even before mass scattering of JCP, which usually does not cause allergic symptoms in patients with SAR-JCP. ASD also induced conjunctivitis symptoms after the JCP season. However, we did not observe any adverse effects of ASD on allergic symptoms during the JCP season.

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1. Introduction

The number of patients with seasonal allergic rhinitis caused by Japanese cedar pollen (SAR-JCP) is increasing. Our data from a study of 1540 people indicated that the prevalence of SAR-JCP is 39.6% [1]. Economic losses as a result of SAR-JCP in Japan have been estimated on average to be over \$3 billion annually. Therefore, SAR-JCP is regarded as a major public health problem in Japan [2,3]. Allergic rhinitis (AR), similar to other allergic diseases, has a multi-factorial origin that includes genetic and environmental aspects. Regarding genetic factors, it has been found that an interleukin-33 genetic variant is associated with SAR-JCP, which is the most common form of AR in Japan [4], and most recently, we have demonstrated that a genetic variant of the ORMDL3 locus at chromosome 17q21 is associated with SAR-JCP [5,6]. As for the environmental factors, several researchers have reported increasing concerns about the adverse health effects of Asian sand dust (ASD).

ASD arises from the desert areas of China, Mongolia, and Kazakhstan during the spring season. The ASD aerosol spreads over downwind areas including East China, Korea, and Japan. ASD is transported not only across Asia, but also across the Pacific Ocean to the United States [7–10], and it has been reported that ASD is also transported in a full circuit around the globe [11]. The frequency of ASD storms was noted to increase rapidly after the year 2000, and ASD storms might enter a new active period [12]. Similarly, there have been reports about the adverse health effects of Saharan dust [13,14]. In East Asia, ASD events have been significantly associated with an increase in daily mortality in patients with cardiovascular and respiratory disease [15,16] and increased daily admissions and clinic visits for respiratory disease [17–19], AR [20], or conjunctivitis [21]. In Japan, adverse effects on the lower respiratory tract associated with an ASD event, especially in patients with asthma, have been reported [22,23]. JCP is the most common allergen in AR in Japan, and the JCP season almost overlaps with the usual period of ASD events. Although the precise effect of ASD events on the symptoms of SAR-JCP remains unclear, some Japanese otolaryngologists have observed an increase in clinic visits of patients with SAR-JCP who experience worsening symptoms after an ASD event.

* Corresponding author. Tel.: +81 766 52 2156; fax: +81 766 52 2197.
E-mail address: ogikazu@shinseikai.or.jp (K. Ogi).

As there are only few reports about the relationship between ASD and SAR-JCP, in this study, we have investigated the relationship between SAR-JCP symptoms and ASD events.

2. Methods

2.1. Study participants

A total of 41 participants, residents of the city of Fukui, Japan, aged ≥ 20 years, were recruited in 2006 ($n = 22$) and 2009 ($n = 19$). Patients with SAR-JCP were enrolled in this study if they had a radio-allergo-sorbent test (RAST) score ≥ 2 against JCP and allergy symptoms. All participants gave written informed consent before enrollment in the study. We designed the study as far as possible for participants who do not take anti-allergy medications. In this study, patients who took anti-allergic medicine were omitted to exclude the influence of the anti-allergic medicine. The study was approved by the ethics committee of the University of Fukui.

2.2. Measurement of environmental level of Asian sand dust

The city of Fukui is located on the west coast of Japan. Therefore, it seems to be directly affected by ASD because ASD arises from the deserts of East Asia. It is considered that the effect of ASD in Fukui is more severe than that in Tokyo, which faces the Pacific Ocean, because there is a high mountain range in the center of the Japanese Island. We defined ASD extinction days as days when visibility according to measurements of macroscopic visible horizontal distance by the Fukui Local Meteorological Observatory was < 10 km because of the effect of ASD.

2.3. Measurement of environmental levels of Japanese cedar pollen

We placed a Durham-type pollen sampler in our laboratory in a position that allowed free air movement on all sides [24]. Glass slides coated with glycerin jelly were exposed to the air for 24 h at a time, and pollen particles collected on the slides were counted daily by microscopy after staining with crystal violet solution (Polysciences, Inc., Japan). The total daily pollen count was expressed as the number of pollen particles per square centimeter.

2.4. Survey of symptoms

The participants recorded symptoms (sneezing, runny nose, stuffy nose, itchy eye, watery eye, and interference of daily life) and medication use in allergy diaries [25]. We assessed symptom changes by summing the scores of each symptom 2 or 3 days before and after ASD events.

2.5. Statistical analysis

All data analyses were performed with Wilcoxon's test using MedCalc Software (Ostend, Belgium). In this study, a p value < 0.05 was considered statistically significant.

3. Results

3.1. The effect of Asian sand dust before and during the Japanese cedar pollen season

Symptom diary data were analyzed from the surveillance period (11 February–20 March 2009), which included 5 ASD extinction days: February 15 and 21 and March 16, 17, and 18 (Fig. 1). We defined the days from February 12 to 14, the days before the ASD event in the pre-JCP season, as period I; February 15–17 as period II, the days after the ASD event in the pre-JCP season; March 13–15 as period III, the days before the ASD event during the JCP season; and March 16–18 as period IV, the days after the ASD event during the JCP season.

Sneezing scores significantly increased during period II than period I (0.82 ± 0.60 vs. 1.35 ± 0.98 , $p < 0.05$). Runny nose scores also increased significantly during this period (0.98 ± 0.89 vs. 1.45 ± 1.25 , $p < 0.05$) (Fig. 2). Scores for nasal obstruction and eye itch did not change in this period (0.40 ± 0.50 vs. 0.60 ± 0.70 , $p = 0.213$; 0.20 ± 0.30 vs. 0.50 ± 0.80 , $p = 0.260$, respectively), and there were no significant changes in any symptom score observed during period IV compared to that observed in period III (sneezing: 1.61 ± 0.90 vs. 1.53 ± 0.87 ; runny nose: 1.80 ± 1.11 vs. 1.86 ± 1.12 ; nasal obstruction: 1.20 ± 0.90 vs. 1.20 ± 0.60 ; itchy eye: 1.10 ± 0.80 vs. 1.20 ± 0.70).

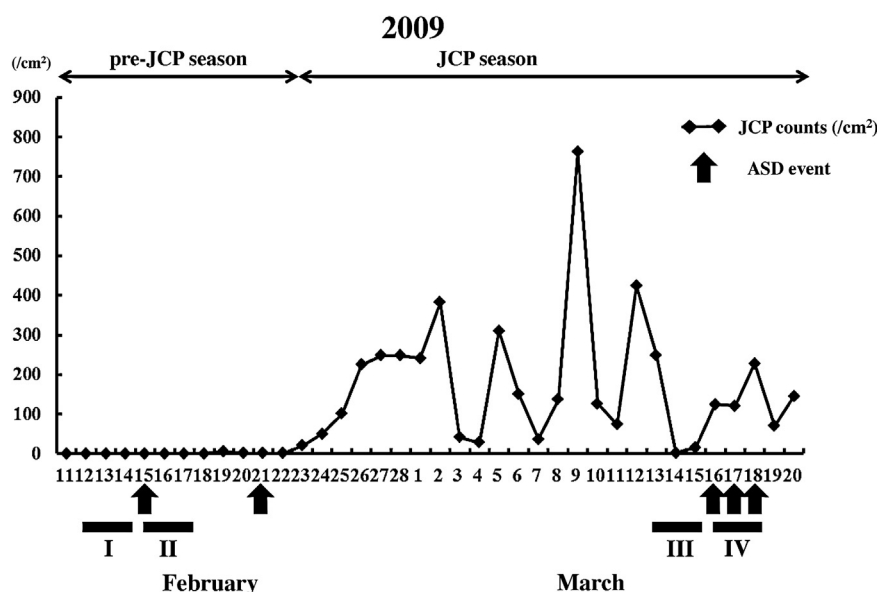


Fig. 1. Japanese cedar pollen and Asian sand dust events in 2009. We defined February 11–22 as the pre-JCP season and February 23–March 20 as the JCP season. Period I, February 12–14, indicated the days before an ASD event in the pre-JCP season, and February 15–17 as period II, the days after the ASD event in the pre-JCP season. March 13–15 as period III, the days before the ASD event during the JCP season, and March 16–18 as period IV, the days after the ASD event during the JCP season.

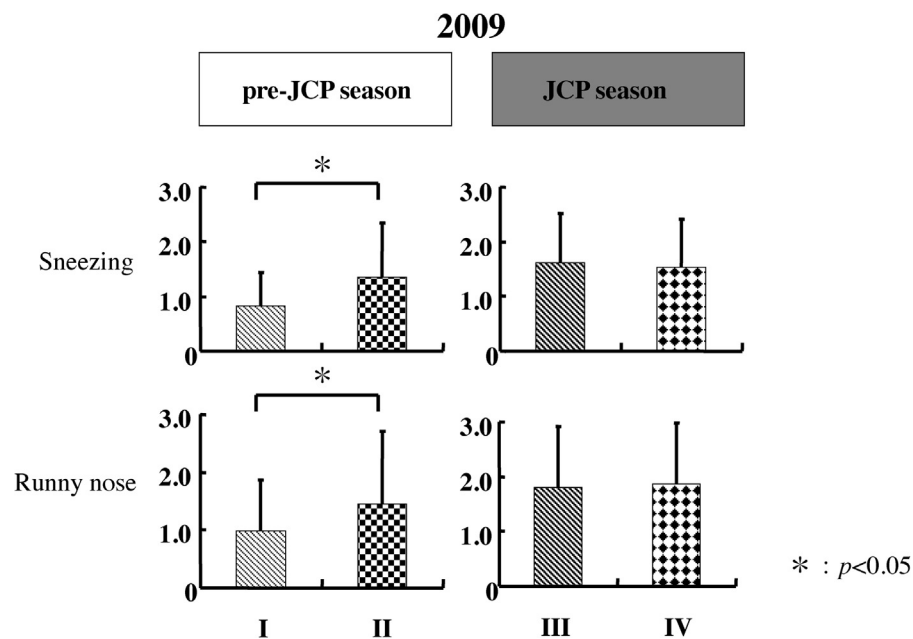


Fig. 2. Symptom changes before and after an Asian sand dust event before and during the Japanese cedar pollen season. These graphs show the symptom score data. Sneezing scores were 0.82 ± 0.60 in period I versus 1.35 ± 0.98 in period II. Sneezing scores were 1.61 ± 0.90 in period III versus 1.53 ± 0.87 in period IV. Runny nose scores were 0.98 ± 0.89 in period I versus 1.45 ± 1.25 in period II. Runny nose scores were 1.80 ± 1.11 in period III versus 1.86 ± 1.12 in period IV. Data are presented as mean $\pm$ standard error (SE).

3.2. The effect of Asian sand dust after the Japanese cedar pollen season

We also wanted to assess the effects of ASD in the post-JCP season. Unfortunately, there were no ASD events observed after the JCP season in 2009. Therefore, we investigated the allergy diary data recorded from April 2 to 19, 2006, which was a surveillance

period that included ASD extinction days. During the research period, ASD was detected according to the conditions described on 4 days, April 4, 8, 18, and 19 (Fig. 3). Thus, we defined 6 and 7 April as period I, the days before the ASD event during the JCP season. April 8 and 9 were defined as period II, the days after the ASD event during the JCP season. We defined 16 and 17 April as period III, the days before the ASD event in the post-JCP season, and 18 and 19

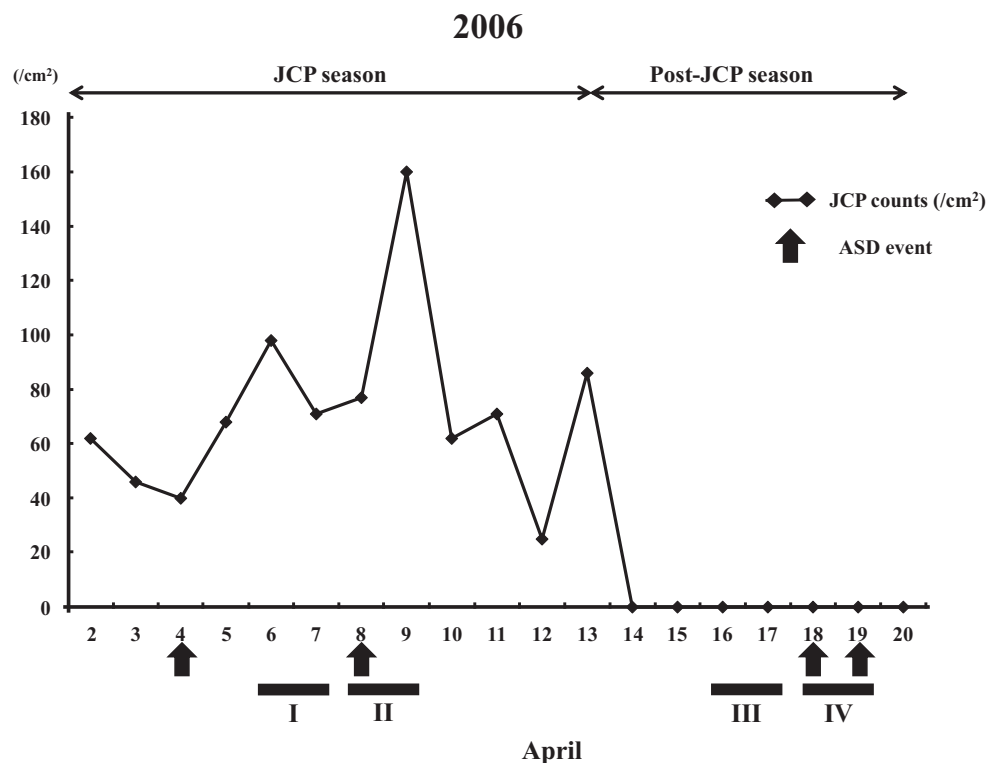


Fig. 3. Japanese cedar pollen and Asian sand dust events in 2006. We defined April 2–13 as the JCP season and April 14–20 as the post-JCP season. April 6–7 were period I, the 2 days before the ASD event during the JCP season. April 8–9 were period II, the 2 days after the ASD event during the JCP season. April 16–17 were period III, the 2 days before the ASD event in the post-JCP season, and April 18–19 were period IV, the 2 days after the ASD event in the post-JCP season.

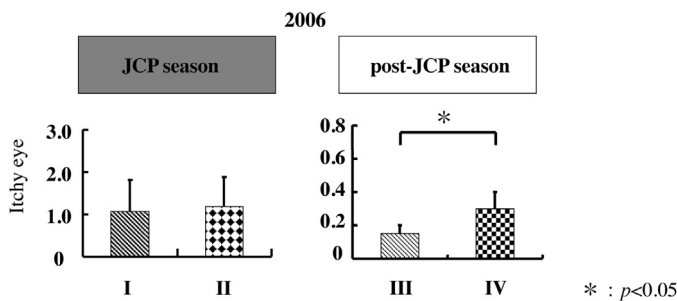


Fig. 4. Symptom changes before and after an Asian sand dust event in the post-Japanese cedar pollen season. The itchy eye score was 0.15 ± 0.05 in period III versus 0.30 ± 0.10 in period IV. Data are presented as the mean $\pm$ standard error (SE).

April were defined as period IV, the days after the ASD event in the post-JCP season.

During the 2006 surveillance period, the score for itchy eye in period IV was significantly higher than that in period III (0.15 ± 0.05 vs. 0.30 ± 0.10 , $p < 0.05$) (Fig. 4). However, none of the scores changed after the ASD event during the JCP season (sneezing: 0.65 ± 0.51 vs. 0.70 ± 0.55 ; runny nose: 0.50 ± 0.31 vs. 0.55 ± 0.40 ; nasal obstruction: 0.50 ± 0.65 vs. 0.55 ± 0.80 ; itchy eye: 1.10 ± 0.80 vs. 1.20 ± 0.70), it was just the same as in 2009, when no significant changes were observed in relation to the ASD event in any symptom scores during the JCP season.

4. Discussion

In this study, we found that ASD has an adverse effect on allergic symptoms in patients with SAR-JCP. In general, it is difficult to accurately evaluate the association of an ASD event with certain diseases because there are confounding factors and biases such as weather conditions (temperature, humidity, etc.) and the presence of coexisting air pollutants (NO_x , O_3 , SO_x , etc.) [26,27]. Moreover, there is a limited period during which we can observe ASD events through a year, which makes obtaining sufficient clinical data difficult. Many epidemiological studies about ASD have used measurements of particulate matter (PM_{10}) as an ASD extinction index. However, PM_{10} measurement includes not only ASD but also particles associated with other air pollutants, so we cannot exclude the possibility of effects originating from other air pollutants. It is reported that a light detection and ranging (LIDAR) system with a polarization analyzer can distinguish non-spherical particles from spherical particles [28]. In 2006 and 2009, the ASD events observed at the Fukui Local Meteorological Observatory were matched to LIDAR extinction coefficient data in Toyama, which is located at a distance of 137 km from the city of Fukui.

In the current study, we found that nasal allergy symptoms in patients with SAR-JCP worsened after an ASD event just before the JCP season (Fig. 2). There are several possible explanations for the finding that ASD can exacerbate symptoms of AR even before the mass scattering of JCP. Evidence from *in vitro* experiments and animal studies has revealed that ASD stimulation results in aggravation of allergy symptoms in the upper airway and lungs [29–31]. ASD contains various chemical species derived from air pollutants (SO_2 , NO_2), such as sulfate (SO_4^{2-}) and nitrate (NO_3^-), as well as microbial agents including bacteria, fungi, fungal spores, and viruses [32–34]. It has been proposed that allergy-related cytokines are released by the adjuvant effect of these agents. Ovalbumin (OVA)-sensitized mice treated with OVA and ASD showed increased OVA-specific immunoglobulin E (IgE) and immunoglobulin G1 (IgG1) production compared to mice treated with only OVA [35,36]. These results suggest that ASD induces an

adjuvant effect on type I allergy. It has also been reported that ASD is involved in mast cell degranulation [37]. Taken together, these results lead us to speculate that ASD may enhance mast cell degranulation in the presence of low levels of JCP that would not induce mast cell degranulation in a normal setting. Moreover, ASD might affect Th2 cytokine production by mast cells via a *de novo* pathway. Further investigation will be required to clarify these hypotheses.

Contrary to our expectation, we did not find any relationships between ASD events and allergy symptoms during the JCP season (Fig. 2). This result is very likely due to the masking of harmful effects of ASD during the JCP season and the milder impact of ASD on AR versus that of JCP, which has strong antigenicity. It may be difficult to augment the strong nasal allergy symptoms induced by sizeable quantities of JCP in SAR-JCP patients. Therefore, physicians might overlook the effects of an ASD event during the JCP season. Importantly, the particle size distribution of ASD in Beijing had a peak diameter of $4.7\text{--}7.0\text{ }\mu\text{m}$, while the particle size distribution of ASD in Japan had two peaks, one at $0.43\text{--}0.65\text{ }\mu\text{m}$ and the other at $3.3\text{--}4.7\text{ }\mu\text{m}$ [38]. ASD particles of both these sizes can penetrate the lower respiratory system, and particles $<2.5\text{ }\mu\text{m}$ in diameter can enter the gas-exchange region of the lungs [39]. Nitrate ions in aerosol are shown to attach to the surface of ASD particles, and the quantity of NO_3^- attached to the surface of ASD is nearly 10 times larger in Japan than in China [38]. Recent research has suggested that NO_3^- can exacerbate several respiratory diseases, including pneumonia, bronchitis, and asthma [40]. Thus, the adverse effects of ASD might vary due to differences in particle size distribution, and high concentrations of nitrate ions attaching to the surface of ASD might also be involved in the exacerbation of respiratory diseases. ASD aggravates lower respiratory tract symptoms in adult asthma patients with SAR-JCP, and ASD itself may also exacerbate the symptoms of asthma, even in patients without AR [41]. It is most likely that the exacerbation of asthma symptoms is due to the cytotoxic effects of ASD that induce neutrophilic inflammation other than type I hypersensitivity, and that nasal symptoms further increase the adverse effects of ASD because of the impairment of nasal air filtration function [42].

While an ASD event in the post-JCP season did not cause any difference in nasal symptoms, it was associated with a significant increase in scores for itchy eyes (Fig. 4). Given that ASD exhibits strong cytotoxic effects, and that even in non-atopic patients, an ASD event will exacerbate itchy eyes [37], it might be assumed that ASD cytotoxicity was involved in the increase in itchy eye symptoms in the post-JCP season. A level of minimum persistent inflammation (MPI) may be present in the nose after the JCP season, and ASD could be a trigger that increases the extent of MPI in SAR-JCP patients. Although we did not obtain data supporting ASD-related increase in nasal symptoms in the post-JCP season, clinical research should be continued to elucidate the precise effects of ASD on AR.

In conclusion, the human nose has a significant role in air filtration, humidification, and warming. Maintaining appropriate nasal breathing and blocking the harmful effects of environmental pollutants are very important to sustain human health, especially in asthma patients during spring, ASD events, and the JCP season.

Conflict of interest

None.

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