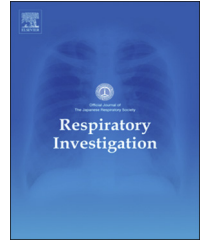




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Short Communication

Association between typhoon and asthma symptoms in Japan



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1. Introduction

A typhoon is a tropical cyclone that develops in the western Pacific or Indian Oceans and occurs yearly between September and October in Japan. In 2013, 31 typhoons developed and, of those, 10 were in close proximity to Japan and 2 struck Japan directly. Research has shown that an impending typhoon is a factor associated with asthma attacks [1]. In Okinawa, Hanashiro et al. analyzed the relationship between asthma attack outbreaks and typhoons [2]. They discovered that, as a typhoon approaches, changes in meteorological parameters, especially decreases in temperature and barometric pressure, are related to induction of asthma attacks. By contrast, in past reports, meteorological parameters of

interest were vapor density, temperature, and barometric pressure. However, we hypothesized that there may be other risk factors that contribute to typhoon-related worsening of asthma, similar to the relationship between pollen allergy and thunderstorm-associated asthma [3]. We retrospectively analyzed asthmatic subjects who presented with worsening of symptoms related to the approach of typhoons between September and October 2013.

2. Materials and methods

In our study, we retrospectively reviewed 58 asthmatics (26 males and 32 females; average age = 61.7 ± 15.5 [SD] years) in

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an outpatient setting who had regular follow-ups with the Department of Pulmonary Medicine at Fukushima Medical University Hospital. Between November and December 2013, we asked subjects whether they were aware of any symptom changes, such as onset of wheezing, shortness of breath, chest tightness, and persistent coughing, or if they took reliever medication on days when typhoons passed through the Fukushima Prefecture between September and October 2013. Worsening of symptoms was defined as a condition where a subject has become aware of at least one symptom change or took reliever medication. All subjects were undergoing asthma treatment, including inhaled corticosteroids (ICS). Severity of asthma, based on the Japanese guidelines for adult asthma [4], for all 58 subjects was determined: 4 subjects had mild intermittent asthma, 12 subjects had mild persistent asthma, 26 subjects had moderate persistent asthma, and 16 subjects had severe persistent asthma. Use of rescue oral or intravenous corticosteroids (systemic corticosteroids) between September 2012 and August 2013 was evaluated. Asthmatics who suffered from upper or lower airway infections and those who changed their regular asthma treatment regimen between September and October 2013 were excluded from our study. The Fukushima Medical University Ethics Committee approved our study [No. 2391].

3. Results

During the study period, 17 of the 58 subjects (29.3%) noted worsening of symptoms (worsened group) while the other 41 subjects did not note any symptom changes (stable group). A comparison of baseline characteristics between both groups is shown in Table 1. There were no significant differences in age, gender, body mass index, age of asthma onset, duration of asthmatic treatment, smoking history, and incidences of allergic rhinitis and chronic sinusitis between the groups. No significant differences were observed in daily dosage of ICS and proportion of long-acting β -agonists, theophylline, leukotriene receptor antagonists, oral corticosteroids, and antihistamine agents during their regular treatment. However, the proportion of subjects who received systemic corticosteroids as rescue medication over the study period of 1 year was significantly higher in the worsened group than in the stable group (8/17 [47.0%] and 8/41 [19.5%], respectively; $p=0.033$). Pulmonary function, exhaled nitric oxide, and laboratory data obtained during a stable period within 1 year were compared between both groups; there were no differences in pulmonary function and exhaled nitric oxide levels.

Laboratory data revealed that serum total IgE levels were significantly higher in the worsened group than in the stable group (556 ± 564 [SD] IU/mL and 440 ± 824 IU/mL, respectively, $p=0.035$; Mann–Whitney U test). Levels of serum IgE specific for Japanese cedar (*Cryptomeria japonica*; sugi tree) and Japanese cypress were also significantly higher in the worsened group than in the stable group ($p=0.004$ and $p=0.02$, respectively; Mann–Whitney U test; Fig. 1). Additionally, the number of subjects with positive Japanese cedar- or cypress-specific IgE (>0.7 UA/mL) was also significantly higher in the worsened group than in the stable group (13/17 [76.5%] and 16/41 [39.0%], respectively, $p=0.02$; Fisher's exact test). We also

Table 1 – Clinical characteristics of asthmatics in the worsened and stable groups.

	Worsened group (n=17)	Stable group (n=41)	p Value
Age (year)	55 $\pm$ 19	65 $\pm$ 13	0.083
Gender (male/female)	6/11	20/21	0.387
BMI (kg/m ²)	24.1 $\pm$ 5.1	24.1 $\pm$ 5.0	0.878
Age of asthma onset (year)	45 $\pm$ 18	51 $\pm$ 16	0.180
Duration of treatment (year)	4.1 $\pm$ 2.3	5.2 $\pm$ 3.2	0.242
Smoking history (never/former/current)	13/4/0	23/14/4	0.234
Allergic rhinitis (+/–)	12/5	20/21	0.080
Chronic sinusitis (+/–)	5/12	13/28	1.000
WBC count (cells/ μ L)	6900 $\pm$ 1655	6573 $\pm$ 1875	0.469
Blood eosinophil (%)	4.9 $\pm$ 3.7	4.7 $\pm$ 3.7	0.780
Serum total IgE level (IU/mL)	647 $\pm$ 663	456 $\pm$ 811	0.033*
Serum antigen specific IgE			
House dust mite (+ ^a /–)	9/8	11/30	0.073
Weeds pollen (+ ^a /–)	2/15	3/38	0.624
Poaceae (+ ^a /–)	4/13	10/31	1.000
Dog or cat (+ ^a /–)	5/12	5/36	0.139
Molds (+ ^a /–)	4/13	5/36	0.458
Japanese cedar or cypress (+ ^a /–)	13/4	16/25	0.020*
Pulmonary function test			
% Predicted FVC (%)	99.6 $\pm$ 12.1	103.3 $\pm$ 15.3	0.274
% Predicted FEV ₁ (%)	91.0 $\pm$ 21.6	87.9 $\pm$ 17.8	0.318
FEV ₁ /FVC (%)	75.0 $\pm$ 14.8	69.0 $\pm$ 10.1	0.061
FEV ₁ /FVC < 70% (+/–)	5/12	22/19	0.148
FeNO level (ppb)	78.9 $\pm$ 104.8	57.1 $\pm$ 58.7	0.474
Rescue use of systemic CS for the past one year (+/–)	8/9	8/33	0.033 [†]

Data are shown as geometric mean $\pm$ standard deviation.

BMI: body mass index; WBC: white blood cell; FVC: forced vital capacity; FEV₁: forced expiratory volume in one second, FEV₁/FVC: forced expiratory volume one second percent; FeNO: fractional exhaled nitric oxide; CS: corticosteroids.

* Indicates values of $p < 0.05$.

^a Indicates serum specific IgE level ≥ 0.70 UA/mL.

measured serum IgE specific for house dust mite, weed, Poaceae, dog, cat, and mold. The number of subjects with positive house dust mite-specific IgE showed a trend toward higher levels in the worsened group than in the stable group (9/17 [52.9%] and 11/41 [19.0%], respectively, $p=0.073$; Fisher's exact test), whereas no differences were observed in other antigen-specific IgE levels between both groups. We used multivariate logistic regression modeling to calculate odds ratios and 95% confidential intervals after controlling for potential confounders (Table 2). Dependent variables showing significant associations with symptom changes in September and October 2013 were Japanese cedar- and Japanese

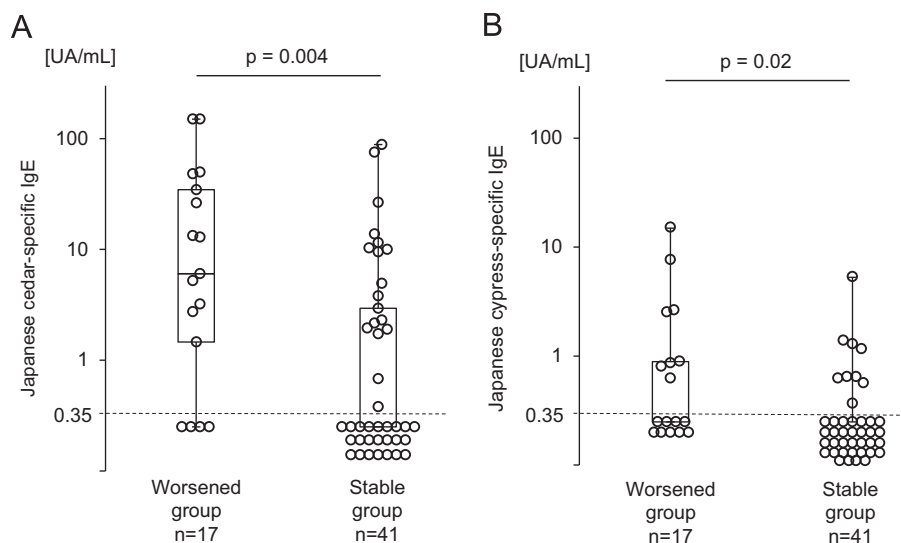


Fig. 1 – Comparison of antigen-specific IgE levels in the serum between the worsened and stable groups. In our study, the measurable range of each serum antigen-specific IgE level was >0.35 UA/mL. Comparisons were made using Mann-Whitney U test. (A) Japanese cedar-specific serum IgE levels in the worsened group were significantly higher than those in the stable group ($p=0.004$). (B) Japanese cypress-specific serum IgE levels in the worsened group were significantly higher than those in the stable group ($p=0.02$).

Table 2 – Multiple logistic regression analysis: factors associated with a worsening of symptoms related to the approach of a typhoon.

Factor	Odds ratio (95% CI ^a)	p Value
log ₁₀ (serum total IgE level)	2.101 (0.642–6.881)	0.220
Mite-specific IgE (+) ^b	1.074 (0.228–5.070)	0.928
Japanese cedar or cypress-specific IgE (+) ^b	5.374 (1.168–24.725)	0.031*
Rescue use of systemic CS ^c for the past one year	4.391 (1.021–18.890)	0.047*

^a Confidential interval.
^b Serum specific IgE level ≥ 0.70 UA/mL.
^c Corticosteroids.
 * Indicates values of $p < 0.05$.

cypress-specific serum IgE levels, and use of systemic corticosteroids as rescue medication over the past year.

4. Discussion

In our study, 17 out of 58 (29.3%) asthmatic subjects who were undergoing treatment noted symptom changes during typhoon season in Japan. Moreover, serum levels of total IgE and IgE specific for Japanese cedar and Japanese cypress were significantly higher in the worsened group than in the stable group. Pollinosis, which is caused by Japanese cedar pollen, is one of the most common allergic respiratory diseases in Japan [5]. The major allergen of Japanese cedar and Japanese cypress pollens was identified as having common antigenicity [6]. Our results suggest that elevated levels of IgE specific for Japanese cedar or cypress are associated with worsening of symptoms related to the approach of typhoons. In Japan, most Japanese cedar pollen is released

between February and April, and the allergy season extends from the end of winter through spring. Japanese cypress pollen is dispersed in April and May, after dispersal of Japanese cedar pollen. Since small amounts of Japanese cedar pollen are detectable during autumn [7], pollen from Japanese cedars during this time may be associated with worsening of asthma symptoms during typhoon season. Of related significance are studies that reported an association between thunderstorms and allergic asthma outbreaks in subjects with pollen allergies [3,8]. It has been demonstrated that changes in weather, such as rain or humidity, may induce hydration and, occasionally, fragmentation of pollen grains that generate atmospheric biological aerosol carrying allergens [9]. Similar mechanisms have also been suggested as causes for our present study results. Japanese cedar pollen, which contains 2 allergens (Cry j 1 and Cry j 2), belongs to a group of particles that are too large to reach the lower airway. Miki-Hiroshige et al. suggested that the orbicules of Japanese cedar pollen contain allergenic protein [10]. They reported that orbicules have a diameter approximately 430 nm and can easily reach sensitive patient tissue. These particles may be resuspended in the atmosphere after rainfall and could cause asthma to worsen. In Japan, the mean global temperature has significantly increased over the past 100 years and hot summers affect the ability of Japanese cedar trees to form flower buds and increase pollen production. Seasonal allergic rhinitis caused by Japanese cedar pollen is now considered a national affliction [11]. Furthermore, global warming will also cause an increase in the frequency of extreme weather phenomena, such as typhoons and tropical storms. For these reasons, it is important for physicians to be cognizant of worsening asthma during future typhoon seasons.

Additionally, a greater number of asthmatics in the worsened group used systemic corticosteroids at least once between November 2012 and August 2013 (typhoon

offseason). There is a possibility that asthmatics in the worsened group may be unable to control their asthma all year round.

There are some limitations associated with our study. Firstly, the definition of “worsening asthma” was based on each subject’s memories and reports. In order to diagnose worsening asthma in a prospective study accurately, using objective parameters, such as peak flow monitoring, pulmonary function test and an asthma questionnaire may be necessary. Secondly, we could not measure concentration of airborne pollen grains on days when typhoons passed through Fukushima and we did not explore subject behavior of the worsened group, such as staying indoors with the window open or going outdoors, on days when typhoons struck Fukushima; such data may help prove our hypothesis.

5. Conclusion

In conclusion, our results suggest that Japanese cedar and cypress pollen allergies, as well as insufficient control of asthma year round, are factors associated with worsening asthma symptoms during typhoon season in Japan.

Author contributions

Conception and design: SS, JS, YS, MU, AF. Analysis and interpretation: YS, XT, RT, KM, TN. Preparation of manuscript: SS, YT, MM.

Conflict of interest

The authors have no conflicts of interest.

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