INTERNAL MEDICINE

□ ORIGINAL ARTICLE □

The Relationship between the Incidence of Summer-type Hypersensitivity Pneumonitis and Environmental Factors in Southern Tochigi Prefecture

Yuki Iijima, Yukihiko Sugiyama, Eri Suzuki, Masayuki Nakayama, Hideaki Yamasawa and Masashi Bando

Abstract

Objective Environmental and climatic changes have been occurring throughout the past 20 years in Japan. Correspondingly, the antigens that cause hypersensitivity pneumonitis might be changing. In an epidemiological survey of Japan in the 1980s, summer-type hypersensitivity pneumonitis (SHP) accounted for 74.4% of the cases of hypersensitivity pneumonitis. The epidemiological characteristics of this disease have not been reported since then. We investigated the annual changes in the number of cases of SHP and the factors affecting the results.

Methods Cases that were diagnosed as SHP were retrieved from the medical records of our institute between 1990 and 2015. The diagnostic criteria proposed by the Japanese Ministry of Health, Labour and Welfare in 1990 were applied to obtain the definite diagnosis.

Patients The study population included 25 diagnosed patients, including one intrafamilial case. The subjects were predominantly non-smoking women in their 50s and all lived in wooden houses that had been constructed more than 10 years previously.

Results The number of cases that were diagnosed as SHP tended to decrease during the study period. However, temporal increases tended to occur in years with increased rainfall and decreased daylight hours. No relationship appeared to exist between the number of cases and high temperatures or humidity levels.

Conclusion The incidence of SHP currently appears to be decreasing; however, the weather conditions in any given year might cause a temporal increase in the incidence rate.

Key words: Hypersensitivity pneumonitis, summer-type hypersensitivity pneumonitis

(Intern Med 56: 1023-1027, 2017)
(DOI: 10.2169/internalmedicine.56.6971)

Introduction

Summer-type hypersensitivity pneumonitis (SHP) can occur due to the repeated inhalation of *Trichosporon* species; this mostly occurs in wooden homes during periods of high temperature and humidity (1). The major causative antigen of hypersensitivity pneumonitis (HP) depends on the living environment. For example, in a nationwide epidemiological survey of chronic hypersensitivity pneumonitis (CHP) in Japan in the 2000s, the prevalence of isocyanate-induced HP and farmer's lung was found to be decreasing, while bird-related HP was increasing (2). However, the chronological changes in the incidence of SHP have not been reported; An epidemiological study on HP that was conducted in Japan in the 1980s showed that the proportion of SHP cases among HP cases was 74.4% (3). Furthermore, the Statistics Bureau of the Ministry of Internal Affairs and Communications stated that the prevalence of wooden homes decreased from 81.7% in 1968 to 58.9% in 2008 (4). SHP may be decreasing in line with these changes.

Jichi Medical University Hospital is a tertiary care center that covers the southern part of Tochigi Prefecture; many patients with pneumonia with an unclear etiology are referred

Division of Pulmonary Medicine, Department of Medicine, Jichi Medical University, Japan
Received for publication December 11, 2015; Accepted for publication August 25, 2016
Correspondence to Dr. Yuki Iijima, iijipulm@jichi.ac.jp

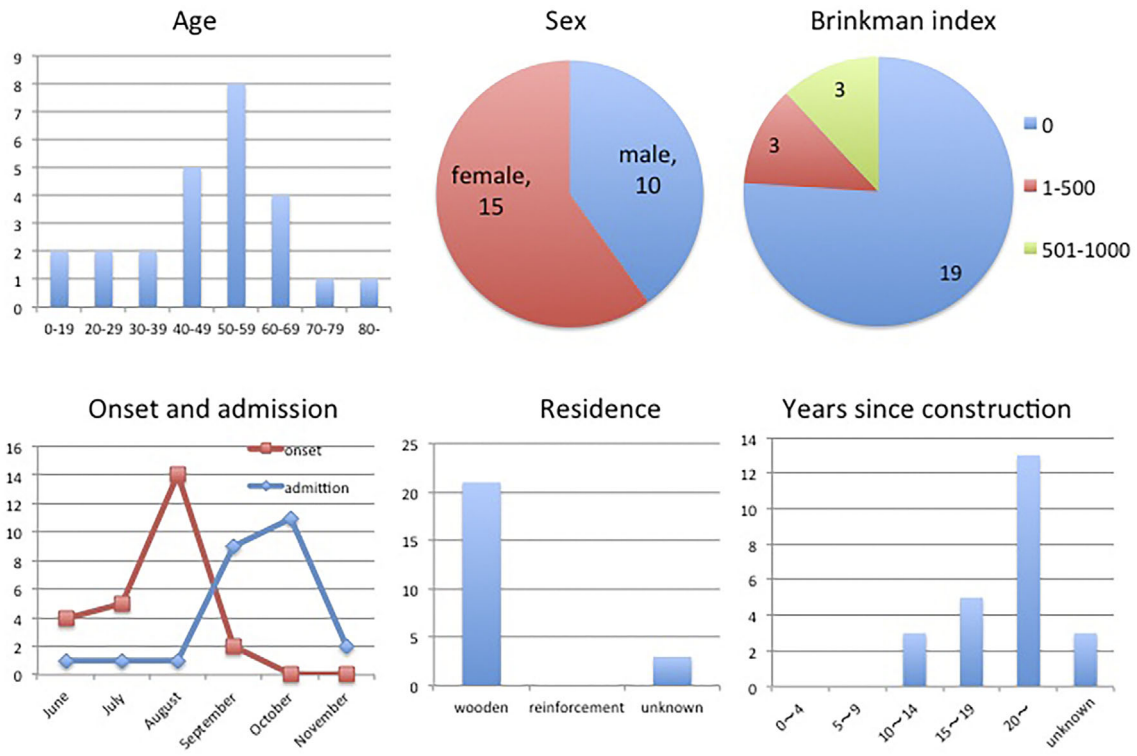

Figure 1. **The characteristics of the SHP patients.**

to this institution. In the present study, we investigated the annual changes in the number of cases of SHP and the background factors that affected the results in this local area.

Materials and Methods

Materials

We reviewed the medical records at our institute from 1990 to 2015 and found 25 eligible SHP cases. The diagnoses were defined by a modification of the criteria proposed by the Japanese Ministry of Health, Labour and Welfare in 1990 (5). SHP was defined on the basis of meeting I, II, III, and either IV or V of the following criteria: (I) chief complaints and CT findings that are compatible with HP; (II) the onset of symptoms during the summer season; (III) a serum sample that is positive for anti-*Trichosporon* antibodies; (IV) a positive environmental challenge test; (V) pathologically proven granuloma.

Methods

The age, sex, smoking history, month at the onset of symptoms, month at admittance, and residential circumstances were investigated. Yearly changes in the occurrence of SHP were also reviewed. Recurring cases were excluded because the study focused on primary SHP cases. Intrafamilial developments were treated as a single case during the investigation of residential circumstances and annual changes in the number of SHP cases. In addition, we investigated the relationship between the yearly incidence of SHP and environmental factors such as the daylight time, the amount of rainfall, the temperature, and the humidity. These data was obtained from the records of the Japan Meteorological Agency.

The study protocol was approved by the Ethics Committee of the Jichi Medical University (approval number A15-103).

Results

The baseline patient characteristics

Fig. 1 shows the characteristics of the cases that were diagnosed with SHP, which included 24 families and 25 patients. The most prevalent group was female patients of between 50 and 59 years of age. There were 19 non-smokers among the 25 patients, but even the smokers showed low Brinkman index values of <1,000. Although the onset of symptoms was highest in August, admittance to hospital tended to occur in September and October. The nature of the residence was unknown in three cases; all of the other subjects lived in wooden homes that had been built over 10 years previously.

Yearly changes

Fig. 2 shows the 5-yearly and annual changes in the number of cases. Seven patients were seen in the first 5 years of the 1990s; the number tended to decrease and only two patients were seen after 2010. Despite this decrease, a temporal increase was seen during 2006 during which four patients were diagnosed with SHP. It was suspected that climatic factors were involved in this temporal increase, thus

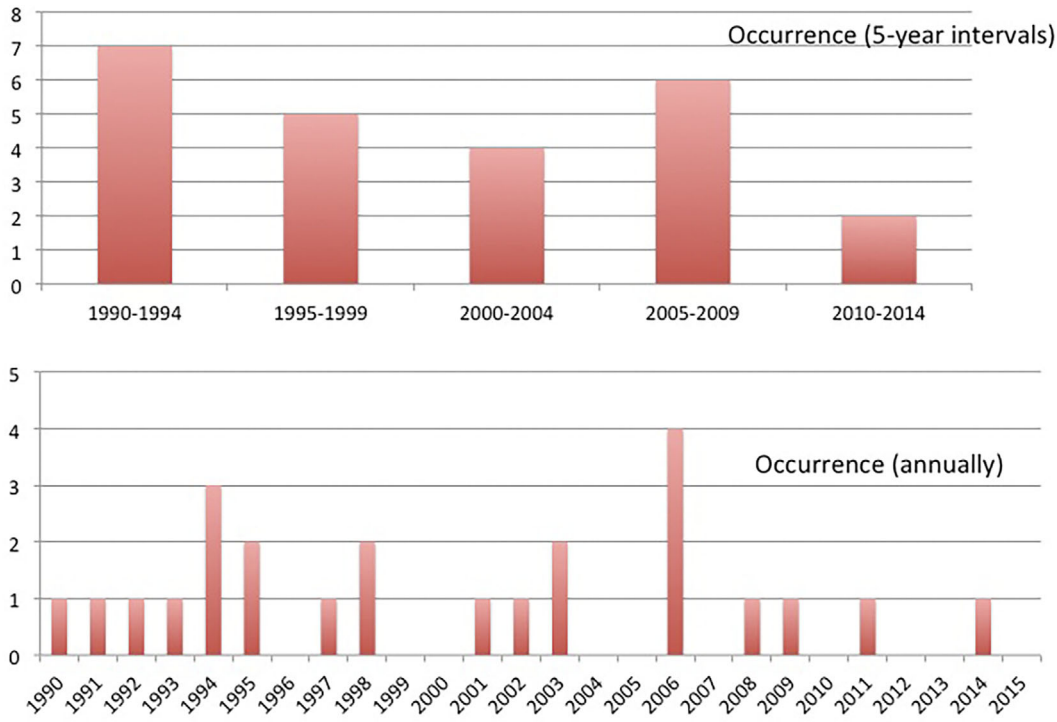

Figure 2. **The five-yearly and annual changes in the incidence of SHP. A chronological decrease was seen, while temporal increases occurred in 1998, 2003, and 2006.**

we investigated the records of the Japan Meteorological Agency and considered whether there was a possible relationship between the incidence of SHP and climatic factors. The climate records of Utsunomiya City in Tochigi Prefecture were considered as representative of the climatic factors in this region.

The relationship between the incidence of SHP and the climate

Fig. 3 shows the average amount of monthly rainfall, monthly daylight hours, and the amount of monthly rainfall divided by daylight hours (R/D ratio; rainfall/daylight ratio) from June to August each year and its correlation with the annual number of cases of SHP. With the exception of 1994, the R/D ratio in the years in which two or more cases were seen tended to be higher than that in the years when there were no cases.

Fig. 4 shows the maximum temperatures and average humidity from June to August; however, there was no apparent correlation between these data and the number of SHP cases.

Discussion

In the present study, SHP was more frequently diagnosed in middle-aged women and non-smokers. A previous study reported that SHP frequently occurs among women, especially homemakers who spend long periods at home exposed to *Trichosporon* antigens (1). Previous reports also suggested that cigarette smoking may disrupt the production of specific antibodies to the antigen, or lead to the dysfunctional production of cytokines by macrophages, which lowers the risk of SHP (6, 7). The characteristics of the patients in this study are correlated with these reports. Moreover, the onset of SHP symptoms generally occurred in August, which is in agreement with a previous report that showed that SHP occurs from June to August (1). There was a time lag between the onset of symptoms and hospital admission due to the fact that many of the SHP patients were referred to a pulmonologist after being diagnosed and treated for symptoms of cold or mycoplasmal pneumonia at a clinic. Furthermore, the nature of SHP, which tends to take an acute/subacute course and which slowly worsens, may have contributed to the time lag. With the exception of three patients, whose residential circumstances were unknown, all of the SHP patients lived in wooden houses that had been built more than 10 years previously. This type of environment enhances the proliferation of *Trichosporon*.

In the present study, the number of SHP cases tended to decrease from the second half of the 1990s. Ando et al. used a questionnaire to conduct an epidemiological survey of HP in Japan in 1991. Of the 835 cases of HP that were reported in the 1980s, 621 (74.4%) were diagnosed with SHP. Furthermore, Okamoto et al. reviewed 222 CHP cases at 22 institutes, and concluded that the proportion of bird-related HP cases was increasing and that isocyanate-induced HP and farmer's lung were decreasing. However, the subjects of the survey were CHP cases, and thus did not reflect the proportional changes in the number of SHP cases, a disease that tends to progress acutely or subacutely. The results of the present study, which suggest that the number of SHP cases tends to be decreasing, are therefore notable.

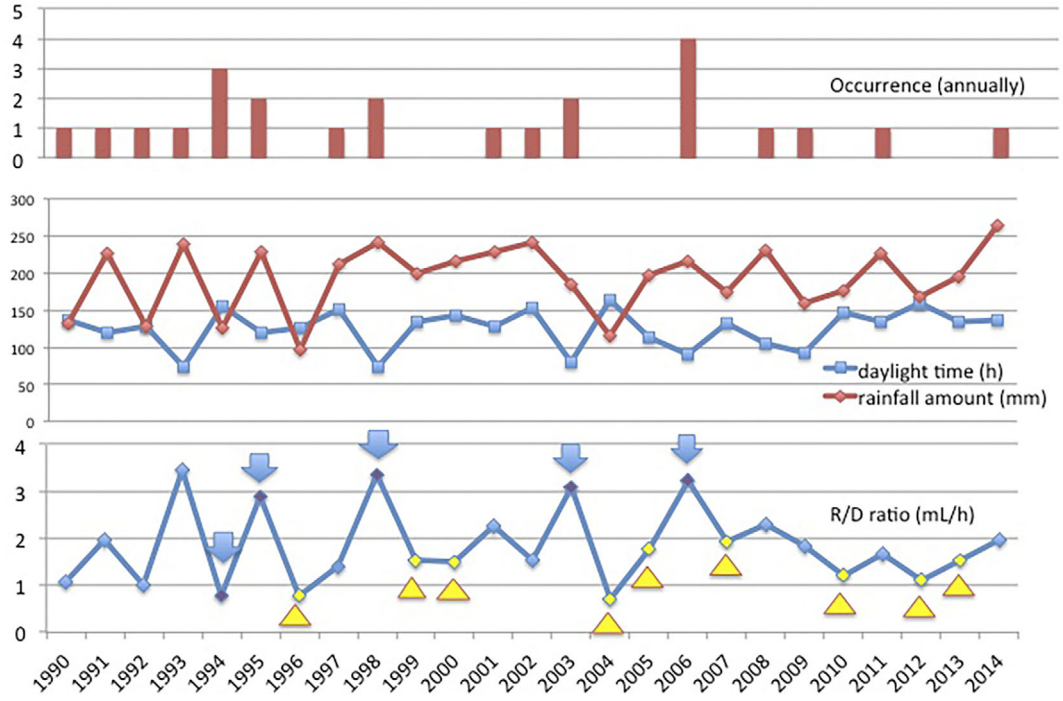

Figure 3. **The relationship between the incidence and the amount of rainfall, daylight hours, and the R/D ratio. These values were calculated based on the average monthly rainfall amount and the daylight hours from June to August. The R/D ratio tended to be high in the years of increased SHP incidence (arrows) and low in the years with no incidence (arrowheads).**

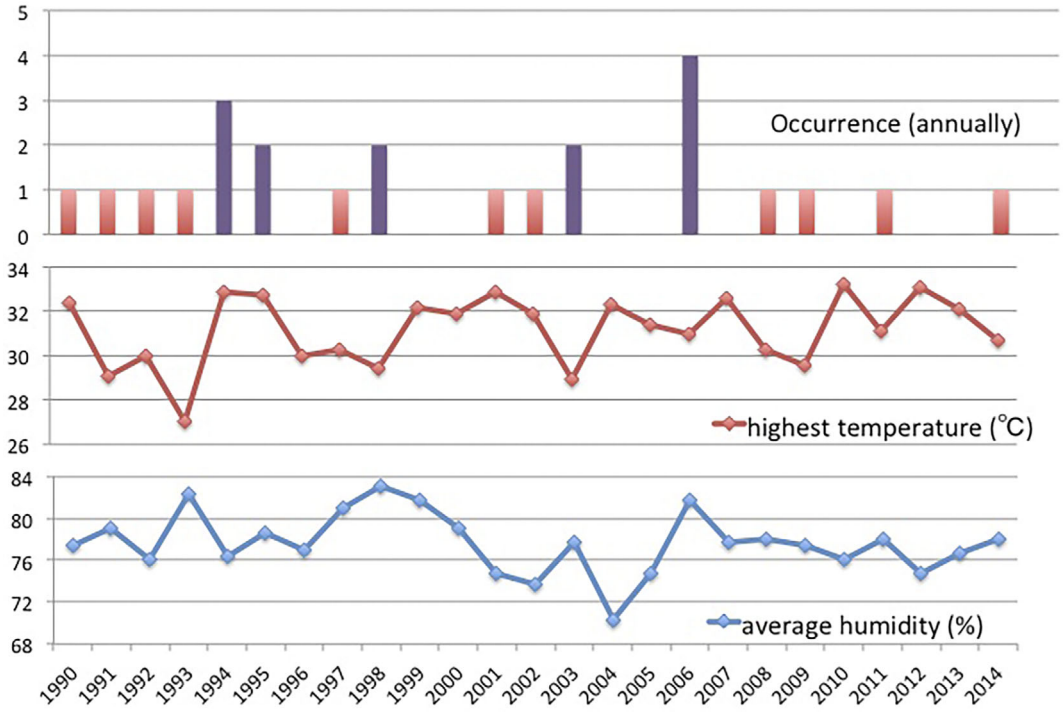

Figure 4. **The relationship between the incidence of SHP and the highest temperature or average humidity in the season. There does not appear to be any correlation between these factors and the incidence of SHP.**

The basis of this trend must be related to some factor that influences the incidence of SHP. It may be due to the HLA antigen, which is a host factor, or residential and/or climatic conditions, which are environmental factors. For example, some people do not develop SHP, even if they are exposed to the same amount of *Trichosporon* as those who develop

the disease, and it is suspected that the difference is influenced by HLA-DQ3 (8). However, we did not measure HLA antigen levels in the routine workup for SHP patients at our institute and since this study was retrospective, we could not investigate the HLA antigen status of our patients. In consideration of the residential conditions, Yoshida et al. insisted that damp places in the wood or tatami mats of the patients' homes played a significant part in the proliferation of *Trichosporon* (9). Most of the SHP patients in this study resided in wooden houses; thus, the recent decrease in the construction of wooden homes in Japan may be related to the decreasing trend in the incidence of SHP.

Despite the decreasing trend in the numbers of patients with SHP, there was a temporal increase during some of the recorded years. At our institute, the incidence of SHP was higher in years with greater rainfall and fewer daylight hours. *Trichosporon* would have proliferated in such conditions leading to an increased number of SHP patients. On the other hand, there was no clear relationship between the changes in the number of SHP cases and higher temperatures and humidity levels. This might be because the yearly changes in these parameters were small, which narrowed the difference between the years. As mentioned above, the incidence of SHP is decreasing because of changes in residential environments; in the future, it may become a disease of the past. However, as this disease still exists and its incidence could increase depending on the climate, respiratory physicians should keep the possibility of the disease in mind in the differential diagnosis, especially during the summer season in certain climates.

The present study is associated with some limitations. First, it was a retrospective study that was conducted at a single institute. However, Jichi Medical University Hospital is a unique tertiary care center in southern Tochigi Prefecture to which most undiagnosed pneumonia patients are referred. Thus, to some extent, the data of this study reflect the annual number of SHP cases in the region. Second, it is sometimes difficult to accurately assess the annual incidence because of the difficulty in evaluating whether the SHP patient is at the acute/subacute or chronic stage. However, most SHP cases have an acute/subacute course. Moreover, some pulmonologists insist that CHP patients should be classified into one of two subgroups: an acute-onset group, which progresses to fibrosis following repeated recurrence, and an insidious onset group, which progresses to fibrosis with repeated asymptomatic exposure. It is reported that many chronic cases of SHP take the former pattern (10). Hence, it is suspected that most SHP patients experience the most severe symptoms and require admittance during the first occurrence. Third, some patients showed respiratory symptoms prior to the month in which the R/D ratio was elevated. In such cases, the climatic conditions might not have affected the incidence of SHP, but could have subsequently affected the progression of the disease. Finally, the sample size was small because we limited the subjects to those who fit within a definite diagnostic group. In fact, the patients who were suspected of having SHP but who were not diagnosed, or those who were only diagnosed with home-related HP were not included in this study.

Conclusion

The incidence of SHP has shown a tendency to decrease over recent years. However, temporal increases may occur depending on the climate during a given year.

The authors state that they have no Conflict of Interest (COI).

References

1. Ando M, Arima K, Yoneda R, Tamura M. Japanese summer-type hypersensitivity pneumonitis. Geographic distribution, home environment, and clinical characteristics of 621 cases. Am Rev Respir Dis **144**: 765-769, 1991.
2. Okamoto T, Miyazaki Y, Ogura T, et al. A nationwide epidemiological survey of chronic hypersensitivity pneumonitis in Japan. Respir Investig **51**: 191-199, 2013.
3. Ando M, Konishi K, Yoneda R, Tamura M. Difference in the phenotypes of bronchoalveolar lavage lymphocytes in patients with summer-type hypersensitivity pneumonitis, farmer's lung, ventilation pneumonitis, and bird fancier's lung: report of a nation wide epidemiologic study in Japan. J Allergy Clin Immunol **87**: 1002-1009, 1991.
4. Ministry of Internal Affairs and Communications homepage. Available from: http://www.stat.go.jp/data/jyutaku/2008/nihon/2_1.htm
5. Yoneda R. A guideline and diagnostic criteria for hypersensitivity pneumonitis. Health, Labour and Welfare Grant-in-aid for Scientific Research, Diffuse Lung Diseases Research FY 1990 Research Report. 1990: 13-15.
6. Arima K, Ando M, Ito K, et al. Effect of cigarette smoking on the prevalence of summer-type hypersensitivity pneumonitis caused by *Trichosporon cutaneum*. Arch Environ Health **47**: 274-278, 1992.
7. Yamaguchi E, Okazaki N, Itoh A, Abe S, Kawakami Y, Okuyama H. Interleukin 1 production by alveolar macrophages is decreased in smokers. Am Rev Respir Dis **140**: 397-402, 1989.
8. Ando M, Hirayama K, Soda K, Okubo R, Araki S, Sasazuki T. HLA-DQw3 in Japanese summer-type hypersensitivity pneumonitis induced by *Trichosporon cutaneum*. Am Rev Respir Dis **140**: 948-950, 1989.
9. Yoshida K, Ando M, Sakata T, Araki S. Prevention of summer-type hypersensitivity pneumonitis: effect of elimination of *Trichosporon cutaneum* from the patients' homes. Arch Environ Health **44**: 317-322, 1989.
10. Yoshizawa Y, Ohtani Y, Hayakawa H, Sato A, Suga M, Ando M. Chronic hypersensitivity pneumonitis in Japan: a nationwide epidemiologic survey. J Allergy Clin Immunol **103**: 315-320, 1999.