

Clinical Communications

Frequent episodes of adult soybean allergy during and following the pollen season

Takafumi Minami, MD^{a,b}, Yuma Fukutomi, MD^a,
Akemi Saito, BSc^a, Kiyoshi Sekiya, MD^a,
Takahiro Tsuburai, MD^a, Masami Taniguchi, MD^a, and
Kazuo Akiyama, MD^a

Clinical Implication

- Soy-triggered allergic symptoms were most frequent during or after the pollen season. Patients with the pollen-food syndrome should be advised to be more careful about food intake especially during and after the pollen season.

TO THE EDITOR:

The pollen-food syndrome (PFS) is one of the most common forms of food allergy in adults and adolescents.¹ Allergic reactions to foods are explained by primary respiratory sensitization to pollen and IgE cross-reactivity between the pollen allergen and its homologous allergens in foods.^{2,3} In clinical practice, increased food-triggered allergic symptoms during or after the pollen season are observed in some patients with PFS,^{4,5} thought to be due to seasonal boosting of pollen-IgE levels. We consider that whether there is indeed a seasonal variation in food allergic symptoms is an important issue for the long-term management of patients with PFS. However, clinical evidence that supports seasonal variation has been quite limited so far, although there is one study that reports an increased clinical reactivity to apples during the birch pollen season.⁶ The aim of the present study was to clarify seasonal variation in severe allergic episodes of pollen-related food allergy. Here, we focused on the association between Betulaceae and Fagaceae pollen counts and increased episodes of severe allergic symptoms after soybean ingestion.

We performed a retrospective medical chart-based review on consecutive adult patients with soybean allergy who first visited the food allergy department of Sagami National Hospital between October 2008 and September 2013. Soybean allergy was defined as meeting two criteria: (1) positive case history of immediate allergic symptoms after ingestion of soy products and (2) positive skin prick test results to soybean extract (extract “edamame,” Torii, Tokyo, Japan) and/or the causative soy product. First, we screened 85 consecutive patients with soybean allergy after reviewing charts of all outpatients during the study period, and gathered detailed information on symptoms that occurred after soy intake, including the day, month, and year when they had symptoms. Although the most common symptoms of soy allergy are restricted to the oral cavity, the subjects studied here were limited to those who had experienced systemic allergic symptoms ($n = 26$) after soybean ingestion. Of these, 4 were excluded because data on the day, month, and year when they had symptoms were missing. Thus, 22 patients were finally included. The Ethics Committee of Sagami National Hospital approved the study protocol.

TABLE 1. Demographics and characteristics of patients with soybean allergy

Patients' characteristics	
Sex, n (%)	
Male	4 (18)
Female	18 (82)
Age at first episode (y), median (range)	49 (26-61)
Comorbidity, n (%)	
Allergic rhinitis	21 (96)
Asthma	3 (14)
Oral allergy symptoms other than soybean	14 (66)
Total IgE (kU/L), median (range)	155.5 (111.3-249.0)
Positivity for serum specific IgE (≥ 0.35 kU _A /L), n (%)	
Alder	22 (100)
Soybean	4 (19)
rBet v 1*	21 (100)
rGly m 4*	21 (100)
nGly m 5*	0 (0)
nGly m 6*	1 (5)
Causal soy products (total events = 33), n (%)	
Soymilk	21 (64)
Tofu	3 (9)
Bean sprouts	3 (9)
Roasted soybean	2 (6)
Dried tofu	1 (3)
Yuba	1 (3)
Fried tofu	1 (3)
Soy protein drink	1 (3)

*Serum samples for this measurement were available in 21 patients.

Levels of serum IgE antibodies specific for alder pollen, soybean extract, recombinant Bet v 1 (rBet v 1), rGly m 4, native Gly m 5 (nGly m 5), and nGly m 6 were determined using a commercially available ImmunoCAP system (Thermo Fisher Scientific, Uppsala, Sweden). A level of IgE antibody ≥ 0.35 kU_A/L was regarded as positive according to the manufacturers recommendation. Counts of airborne Betulaceae and Fagaceae pollen were recorded using a Durham gravity sampler on the roof of the Sagami National Hospital during the study period.

Demographic and clinical characteristics of the 22 patients studied are shown in Table 1. Twenty-one (96%) of them reported nasal allergic symptoms during the Betulaceae and Fagaceae pollen season (data not shown). They experienced a total of 33 episodes of systemic allergic symptoms after soy intake. We identified the timing of these episodes from the medical records. The most frequent offending soy product was soymilk ($n = 21$), followed by tofu ($n = 3$), and bean sprouts ($n = 3$), consistent with previous studies.⁷ Details of the 22 patients are shown in Table E1 of this article's Online Repository at www.jaci-inpractice.org. All patients were found to be sensitized to alder, the birch pollen major allergen, Bet v 1, and its homologous allergen in soy, rGly m 4. This indicates that all the patients can be regarded as having pollen-related soybean allergy.

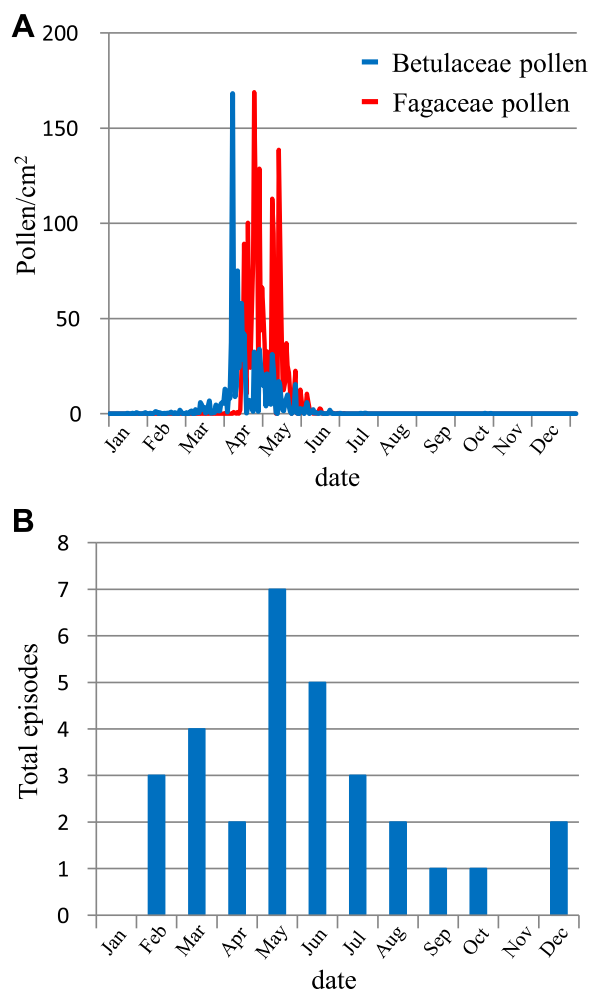


FIGURE 1. A, Daily birch and beech pollen levels (pollen/cm²) in 2011. B, Distribution of the numbers of episodes of systemic allergic symptoms in adults with soybean allergy.

As the patterns of pollen scattering were not significantly different between years, only the counts in are shown in Figure 1, A. High pollen concentrations were observed from March to May. The numbers of allergic episodes for all patients are summarized per month in Figure 1, B. There were statistically significant variations in the frequencies of soy allergic episodes between months ($P = .045$ using the Friedman test), which reached a peak in May, followed by June.

This study showed seasonal variation in systemic allergic symptoms after ingestion of soy products in patients with pollen-related soybean allergy. Soy allergic symptoms were most frequent during or after the relevant pollen season. To the best of our knowledge, this is the first report that documents seasonal variation in the frequency of soy-triggered allergic episodes among adult patients with pollen-related food allergy. Patients

with PFS should be advised to be more careful about food intake especially during and after the related pollen season.

We evaluated the seasonal variation in pollen-related food allergic symptoms by way of the example of soybean for 2 reasons. Although the most common foods responsible for PFS are fresh fruits such as apples and peaches, these are harvested seasonally, so that seasonal variation in the frequency of episodes of food allergy to them is also influenced by seasonality of intake. However, soy products such as soymilk are available all year, and thus seasonal limitation of availability is not an issue. Moreover, a second reason is that soy intake is more likely to induce episodic systemic symptoms than fresh fruits,^{2,8} which patients seem to remember more readily.

^aClinical Research Center for Allergy and Rheumatology, Sagami National Hospital, Sagami, Kanagawa, Japan

^bPresent address: Department of Respiratory Medicine and Allergology, Suita Municipal Hospital, 2-13-20 Katayamacho, Suita, Osaka 564-0082, Japan

This study was supported by a Health Labour Sciences Research Grant on allergic disease and immunology from the Ministry of Health, Labour and Welfare of Japan (grant number H23-Meneki-Wakate-021).

Conflicts of interest: T. Minami has received a Health Labour Sciences Research Grant on allergic disease and immunology from the Ministry of Health, Labour and Welfare of Japan. Y. Fukutomi has received a Health Labour Sciences Research Grant on allergic disease and immunology from the Ministry of Health, Labour and Welfare of Japan; and has received lecture fees from ThermoFisher Scientific. The rest of the authors declare that they have no relevant conflicts.

Received for publication September 13, 2014; revised November 4, 2014; accepted for publication November 10, 2014.

Available online ■ ■

Corresponding author: Takafumi Minami, MD, Clinical Research Center for Allergy and Rheumatology, Sagami National Hospital, 18-1 Sakuradai, Minami-ku, Sagami, Kanagawa 252-0392, Japan. E-mail: minami0008@mhp.suita.osaka.jp.

2213-2198

© 2015 American Academy of Allergy, Asthma & Immunology

<http://dx.doi.org/10.1016/j.jaip.2014.11.024>

REFERENCES

1. Sicherer SH. Clinical implications of cross-reactive food allergens. *J Allergy Clin Immunol* 2001;108:881-90.
2. Kleine-Tebbe J, Vogel L, Crowell DN, Hausteiner UF, Vieths S. Severe oral allergy syndrome and anaphylactic reactions caused by a Bet v 1-related PR-10 protein in soybean, SAM22. *J Allergy Clin Immunol* 2002;110:797-804.
3. Mittag D, Vieths S, Vogel L, Becker WM, Rihs HP, Helbling A, et al. Soybean allergy in patients allergic to birch pollen: clinical investigation and molecular characterization of allergens. *J Allergy Clin Immunol* 2004;113:148-54.
4. Asero R, Massironi F, Velati C. Detection of prognostic factors for oral allergy syndrome in patients with birch pollen hypersensitivity. *J Allergy Clin Immunol* 1996;97:611-6.
5. Kosma P, Sjolander S, Landgren E, Borres MP, Hedlin G. Severe reactions after the intake of soy drink in birch pollen-allergic children sensitized to Gly m 4. *Acta Paediatr* 2011;100:305-6.
6. Skamstrup Hansen K, Vieths S, Vestergaard H, Skov PS, Bindslev-Jensen C, Poulsen LK. Seasonal variation in food allergy to apple. *J Chromatogr B Biomed Sci Appl* 2001;756:19-32.
7. Fukutomi Y, Sjolander S, Nakazawa T, Borres MP, Ishii T, Nakayama S, et al. Clinical relevance of IgE to recombinant Gly m 4 in the diagnosis of adult soybean allergy. *J Allergy Clin Immunol* 2012;129:860-863.e3.
8. Berneder M, Bublin M, Hoffmann-Sommergruber K, Hawranek T, Lang R. Allergen chip diagnosis for soy-allergic patients: Gly m 4 as a marker for severe food-allergic reactions to soy. *Int Arch Allergy Immunol* 2013;161:229-33.

TABLE E1. Clinical characterization of patients with soy allergy

No.	Age (y)/sex	Total IgE (kU _A /L)	Skin prick test (mm)		ImmunoCAP (kU _A /L)						Number of episodes*	Causal soy product	Symptoms after soy ingestion	The day when they had symptoms
			Soybean	Soy milk	Alder	Soybean	rBet v 1	rGly m 4	nGly m 5	nGly m 6				
1	54/M	103	5.5	5.5	6.23	<0.35	ND	ND	ND	ND	1	Soy milk	OAS, AE, Dys, Pal, Co	May 2012
2	63/F	135	6	ND	11.2	<0.35	9.76	4.53	<0.35	<0.35	1	Soy milk	AE	February 2012
3	67/F	177	6	5	16.9	<0.35	22.2	5.32	<0.35	<0.35	1	Soy milk	AE, Dys	Unknown
											2	Dried tofu	AE, Dys, RC	April 2010
4	30/F	236	1	3	69.2	1.1	93.5	41.0	<0.35	<0.35	1	Roasted tofu	OAS, Co	December 2008
5	60/F	23.1	3.5	4	4.17	<0.35	4.80	1.03	<0.35	<0.35	1	Soy milk	OAS, RC, AE, Ur, Dys	June 2011
											2	Soy milk	OAS, RC, AE, Ur, Dys	March 2012
6	65/M	299	1	3	33.8	<0.35	45.2	2.05	<0.35	<0.35	1	Soy milk	OAS, AE, Dys, Re	Unknown
											2	Yuba	OAS, AE, Dys, Re	Unknown
											3	Tofu	OAS, AE, Dys, Re	June 2009
7	68/F	163	0	3	27.7	<0.35	29.9	8.52	<0.35	<0.35	1	Soy milk	OAS, AE, Re, Co, Dys	February 2009
8	41/F	1020	5	9	62.7	0.55	93.0	27.3	<0.35	<0.35	1	Tofu	OAS, Dys	June 2013
9	66/F	82.3	3	10	26.8	<0.35	34.7	7.02	<0.35	<0.35	1	Soy milk	AE, Re, Dys, Co, AP, RC, Vo, UC	May 2013
10	67/M	15.2	3.5	3.5	1.49	<0.35	1.85	0.79	<0.35	<0.35	1	Soy milk	OAS, Dys, AE, RC	July 2013
11	23/F	131	7.5	6	3.76	<0.35	5.64	3.66	<0.35	<0.35	1	Fried tofu	Dys, Co	February 2013
											2	Tofu	Co, Dys, Re	March 2013
12	70/F	62	2	2	10.1	<0.35	10.6	6.48	<0.35	<0.35	1	Soy milk	OAS, RC, Dys	August 2009
13	18/M	148	5	ND	24.8	<0.35	44.6	15.0	<0.35	<0.35	1	Soy milk	OAS, Dys, Wh	December 2011
14	51/F	114	5	ND	16.2	<0.35	15.8	6.48	<0.35	<0.35	1	Soy milk	RC, Re, Dys, AE	October 2012
15	35/F	24.7	3	2	1.31	<0.35	1.30	0.49	<0.35	<0.35	1	Soy milk	Dys, Ur, Pal, RC	May 2013
											2	Roasted soybean	Pal, Re	June 2013
16	62/F	288	7	ND	51.2	<0.35	52.5	5.89	<0.35	<0.35	1	Soy milk	OAS, Dys, AE, RC	April 2012
17	29/F	124	4	3	15.3	<0.35	14.3	4.04	<0.35	<0.35	1	Soy protein	OAS, RC, Dys, Ho	May 2013
18	60/F	205	7	3	33.1	<0.35	40.6	22.9	<0.35	<0.35	1	Soy milk	AE, Dys, Co, RC	May 2011
											2	Bean sprouts	AE, Re	June 2011
											3	Bean sprouts	AE, Re	July 2011
											4	Soy milk	AE	September 2011
19	42/F	183	3	ND	12.3	0.4	15.3	6.94	<0.35	<0.35	1	Soy milk	OAS, fatigue, Hy	May 2013
20	48/F	178	5	6	16.2	<0.35	12.5	1.31	<0.35	<0.35	1	Soy milk	OAS, AE, RC, Dys, Ho	May 2013
21	40/F	677	3	5	23.1	0.35	20.4	6.21	<0.35	<0.35	1	Soy milk	Ur, Hy	March 2009
											2	Soy milk	OAS, RC	March 2009
											3	Soy milk	AP, Di	August 2009
22	17/F	987	5	ND	3.79	1.07	3.54	1.96	<0.35	0.56	1	Bean sprouts	OAS, Re, Pal, AP, Di	July 2012

OAS, oral allergy syndrome; AE, angioedema; RC, rhinoconjunctivitis; Dys, dyspnea; AP, abdominal pain; AS, anaphylactic shock; Pal, palpitation; Co, cough; Wh, wheeze; Hy, Hypotonia; Ur, urticaria; Re, redness; Vo, vomiting; UC, unconsciousness; Di, diarrhea; Ho, Hoarseness; ND, Not done.

*Number of episodes of systemic allergic symptom after soy intake.