

Brief report

Food-dependent and food-exacerbated symptomatic dermographism: New variants of symptomatic dermographism

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Background: Symptomatic dermographism (SD) is the most common form of chronic inducible urticaria. The criterion standard for diagnosing SD and disease activity assessment in SD is provocation testing. As of now, if and what cofactors have an impact on provocation test results is unknown.

Objective: We sought to determine whether the induction of signs and symptoms of SD is affected by the intake of food.

Methods: We performed standardized skin provocation testing with a dermographometer (FricTest) before and after the intake of food. Patients were off antihistamine treatment for at least 3 days before testing. In total, 17 patients were tested after not having eaten for at least 4 hours (preprandial) on one volar forearm and 60 minutes after a carbohydrate-rich meal (postprandial) on the other. FricTest responses (wheals, itch) at trigger thresholds were assessed at 5 and 30 seconds as well as at 1, 2, 5, and 10 minutes.

Results: We identified 7 patients with SD who showed faster onset of FricTest-induced whealing and/or lower trigger thresholds after the intake of food, that is, food-exacerbated SD. In 5 other patients, FricTest provocation testing resulted in a positive response only after the intake of food, but not before. Three of these 5 patients with food-dependent SD had comorbid chronic spontaneous urticaria and 1 had cholinergic urticaria.

Conclusions: We describe 2 previously unknown subtypes of SD, food-exacerbated SD and food-dependent SD. The prevalence and underlying pathomechanisms of food-exacerbated SD and food-dependent SD need to be investigated, and the impact of food intake on other forms of chronic inducible urticaria should be explored. (J Allergy Clin Immunol 2021;■■■:■■■-■■■.)

Key words: Symptomatic dermographism, chronic inducible urticaria, food intake, preprandial, postprandial

INTRODUCTION

Symptomatic dermographism (SD) is the most common subtype of chronic inducible urticaria (CIndU).¹ SD is characterized by the development of itchy and/or burning wheals that result from scratching, rubbing, or mild pressure on the skin, and it can be difficult to treat.² In SD, provocation testing with dermographometers such as FricTest is the criterion standard approach for establishing the diagnosis and for assessing disease activity by measuring trigger thresholds.³ FricTest allows for provocation testing with 4 trigger strengths, where the absence of wheal responses to all (–) excludes SD, whereas whealing to 1 (+), 2 or 3 (++, +++), and 4 triggers (+++++) reflects low, moderate, and high SD disease activity, respectively. Here, we report 2 novel variants of SD, food-dependent SD (FD-SD), in 5 patients who tested positive for FricTest only after the intake of food, and food-exacerbated SD (FE-SD), in 7 patients who showed decreased whealing thresholds in FricTest provocation testing after the intake of food.

RESULTS AND DISCUSSION

Our study and discovery of these new SD variants was prompted by the case of a 25-year-old female patient with SD (patient no. 1 in Table I), who reported increased itching and scratching-induced whealing shortly after eating, independent of the type of food eaten. Preprandial provocation testing with FricTest showed onset of whealing after 1 minute, in response to 2 of 4 trigger strengths (++), and wheals for all 4 trigger strengths after 10 minutes (++++). Provocation testing with FricTest 60 minutes after the intake of food showed quicker onset of whealing, after only 5 seconds (++) and, again, wheals for all 4 trigger strengths after 10 minutes (++++). The patient had no history of comorbid disease, including other skin conditions and food allergy, and skin prick testing results with 7 different foods such as wheat, hazelnut, milk, egg yolk, egg white, tomato, and

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Data availability: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Abbreviations used

CIndU: Chronic inducible urticaria
 FD-SD: Food-dependent SD
 FE-SD: Food-exacerbated SD
 SD: Symptomatic dermographism

beef were all negative. This interesting observation had us hypothesize that the intake of food may reduce trigger thresholds and exaggerate disease activity in further patients with SD.

To test this hypothesis, we subjected 16 additional patients with SD to standardized preprandial and postprandial provocation testing. All patients rested for at least 15 minutes and abstained from the use of antihistamines and drinking alcohol for 72 hours before provocation testing, on one volar forearm, after not having eaten for at least 6 hours. Patients then had a carbohydrate-rich and spice-free meal (sandwich, bagel, pastry or cake) and were tested with FricTest on the other forearm 60 minutes thereafter. FricTest responses were documented after 5 and 30 seconds as well as after 1, 2, 5, and 10 minutes, as negative (–) or positive (+ to + + + +, depending on the number of trigger strengths that produced an itchy wheal). All provocation tests were done by the same investigator at the same time of the day, between 11:00 am and 01:00 pm. With this protocol, we identified 6 additional patients with SD who showed faster onset of whealing and/or lower trigger thresholds after the intake of food (Table I). The same protocol was also performed by another investigator in 5 of these patients to assess the reproducibility of the results, and we found that the results were similar and independent of the investigator. Differences between preprandial and postprandial time to onset of whealing in response to FricTest provocation testing were substantial in some patients. Patient number 4, for example, showed onset of postprandial whealing after 2 minutes as compared with 10 minutes after preprandial provocation testing. We consider our 7 patients with increased whealing responses after the intake of food to have FE-SD.

Our findings prompted the question whether there are patients who develop the signs and symptoms of SD only after the intake

of food. To answer this question, we applied the same protocol as described. We identified 5 patients with negative and positive FricTest provocation test results before and after the intake of food, respectively (Table II). Three of these 5 patients had comorbid chronic spontaneous urticaria and 1 had cholinergic urticaria. We consider our 5 patients with positive whealing responses to provocation testing only after the intake of food to have FD-SD.

To our knowledge, this is the first report of FE-SD or any form of food-exacerbated CIndU, and also the first report of FD-SD. Food-dependent CIndU has recently been described in a patient with cold urticaria.⁴ In this patient, preprandial cold provocation testing result was negative. After a food challenge, multiple itchy wheals developed in response to cold provocation testing, at the provocation site as well as on the trunk and upper torso of the patient.⁴ The patient was diagnosed with food-dependent cold urticaria. This patient is different from our patients with food-dependent SD in that eating of only certain foods, not food intake per se, lead to positive postprandial provocation test results.

The underlying mechanisms of FE-SD and FD-SD are currently unclear and need to be investigated. Some of the current hypotheses include a role for alterations in plasma osmolality and pH after food intake, altered activities of enzymes in the skin, redistribution of blood flow, altered gastrointestinal permeability and epitope recognition, facilitation of allergen binding, and neurogenic mechanisms.⁵ Increased central parasympathetic activity in the postprandial state⁶ may result in lowering of mast cell degranulation thresholds or directly activate mast cells, through muscarinic receptors, as has been shown in the gastrointestinal system.⁷ What also needs to be investigated further is the prevalence of FE-SD and FD-SD. In the present study, we investigated 17 consecutive patients with SD, and 7 and 5 of them had FE-SD and FD-SD, respectively, suggesting a high prevalence. Larger and multicenter studies are needed to explore this further and should also assess other subtypes of CIndU for subpopulations of patients with food-dependent or food-exacerbated signs and symptoms. Also, our findings make it possible that factors other than the intake of food, such as stress or infections, may alter trigger thresholds and disease activity in patients with SD and other CIndUs.

TABLE I. Patients with FE-SD

No.	Age (y)	Sex	SD duration (mo)	Comorbid CU	IgE (IU/mL)	State	FricTest results					
							5 s	30 s	1 min	2 min	5 min	10 min
1*	25	F	72	CSU	165	Preprandial	–	–	++	++	+++	++++
						Postprandial	++	++	++	+++	++++	++++
2	18	F	3	CSU	53	Preprandial	–	–	–	–	+	++
						Postprandial	–	–	–	–	++	+++
3*	48	F	216	CSU	651	Preprandial	–	–	+	++	+++	++++
						Postprandial	–	–	++	+++	++++	++++
4	25	M	24	CholU	201	Preprandial	–	–	–	–	–	+
						Postprandial	–	–	–	+	+	+
5	17	F	4	CSU	24	Preprandial	–	–	–	–	+	+
						Postprandial	–	–	–	+	+	+
6	42	M	72	CSU	32	Preprandial	–	–	–	+	++	+++
						Postprandial	–	–	–	++	+++	+++
7	17	F	4	CSU	15	Preprandial	–	–	–	+	++++	++++
						Postprandial	–	–	–	+++	++++	++++

Patients were tested with FricTest after not having eaten for at least 6 hours (preprandial) and 60 minutes after having a carbohydrate-rich and spice-free meal (postprandial). CholU, Cholinergic urticaria; CSU, chronic spontaneous urticaria; F, female; IgE, baseline total IgE level (IU/mL); M, male.

All patients were asked whether they had observed, before testing, that eating makes their SD worse, and only 2 of 7 patients () with FE-SD confirmed that this was the case.

TABLE II. Patients with FD-SD

No.	Age (y)	Sex	SD duration (mo)	Comorbid CU	IgE (IU/mL)	State	FricTest results					
							5 s	30 s	1 min	2 min	5 min	10 min
8	23	F	36	CSU	386	Preprandial	—	—	—	—	—	—
						Postprandial	—	—	—	+	++	++
9	16	F	2	—*	14	Preprandial	—	—	—	—	—	—
						Postprandial	—	—	—	+	++	++
10	25	F	36	CSU	27	Preprandial	—	—	—	—	—	—
						Postprandial	—	—	—	—	+	+
11	15	M	3	CSU, CholU	12	Preprandial	—	—	—	—	—	—
						Postprandial	—	—	—	—	+	+
12†	21	F	6	CSU	47	Preprandial	—	—	—	—	—	—
						Postprandial	—	—	—	—	—	+

Patients were tested with FricTest after not having eaten for at least 6 hours (preprandial) and 60 minutes after having a carbohydrate-rich and spice-free meal (postprandial). *CholU*, Cholinergic urticaria; *CSU*, chronic spontaneous urticaria; *F*, female; *IgE*, baseline total IgE level (IU/mL); *M*, male.

*This patient presented with a 2-month history of unexplained pruritus and was subjected, empty stomach, to FricTest provocation testing, the result for which was negative. The test was repeated after the patient had a meal and the result was positive, twice, with the test being performed by independent investigators.

†All patients were asked whether they had observed, before testing, that eating is required for them to experience the signs and symptoms of their SD, and only 1 of 5 patients (†) with FD-SD confirmed that this was the case.

In summary, we demonstrated that the intake of food can be a relevant cofactor in SD. Our findings may help clinicians to better standardize FricTest provocation testing in their daily clinical practice and to identify patients with FE-SD and FD-SD, which, in turn, may help their patients to better manage their disease. Further studies are needed to characterize the prevalence of FE-SD and FD-SD and their real-life impact on affected patients.

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Clinical implications: We define SD in patients who develop postprandial SD symptoms in the absence of preprandial symptoms as FD-SD, and in patients with postprandial exacerbation of SD as FE-SD.

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