

Chronic generalized pruritus caused by nitrate intolerance

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For years, a number of studies have suggested that many patients with chronic urticaria have symptoms caused by the ingestion of food additives. Because few of these studies were properly controlled, most such reports remain unproved or anecdotal.¹ In this article, a case of chronic pruritus caused by intolerance to a single food additive diagnosed by rigorously controlled methods is reported.

CASE REPORT

A 28-year-old woman was referred to this allergy center because of a 4-year history of persistent generalized pruritus without any visible rash that was markedly enhanced after taking warm showers or baths. For this reason, the patient was receiving long-term antihistamine treatment (terfenadine, 120 mg daily). Physical urticarias such as cholinergic or aquagenic urticarias were ruled out, because the woman had never had urticaria (except for a single occasion following ciprofloxacin treatment 2 years before); moreover, neither exercise nor contact with cold water enhanced the pruritus.² She did not use other drugs and did not note any clear relationship between symptoms and specific food intake. The woman had seen several dermatologists who excluded infestations such as pediculosis or scabies and did not find any skin abnormality. Laboratory analyses including complete blood cell counts, erythrocyte sedimentation rate, blood glucose levels, urinalysis, liver function tests, thyroid function tests, thyroglobulin and thyroperoxidase antibodies, renal function tests, and stool tests for ova and parasites had been carried out several times during the past 2 years, and results were always normal. Findings of a chest roentgenogram were normal. A family history of atopic diseases was noted, but the patient had never had eczema or respiratory allergy.

METHODS

Results of skin prick tests with a large panel of commercial food extracts (Dome-Hollister/Stier 1:20 wt/vol) were negative, as were skin prick tests with airborne allergens. The intradermal injection of autologous serum did not elicit any wheal and flare reaction.³ An elimination diet (free of food additives) was started; on the fifth day of the diet, the pruritus completely disappeared, and the woman could stop taking antihistamines. After 1 month of an additive-free diet, during which the patient remained symptom-free, an open challenge (unrestricted diet for 15 days) was carried out. After some days, this open challenge caused a gradual relapse of pruritus that lasted throughout the entire open-challenge period. The additive-free diet was resumed and, again, symptoms totally disappeared

TABLE I. Food additives used in challenge tests

Additive	Dose (mg)
Tartrazine (E 102)	10
Erythrosine (E 127)	10
Sodium metabisulfite (E 223)	25
Sodium benzoate (E 211)	100
Sodium glutamate (E 621)	100
Sodium nitrate (E 251)	10
Sorbic acid (E 200)	100
Butylated hydroxyanisole (E 320)	10
Talc (Placebo)	

after 4 to 5 days. After 3 weeks without symptoms, double-blind placebo-controlled peroral challenges with food additives were carried out. The patient continued the elimination diet throughout the entire challenge period.

Additives used and doses given are shown in Table I. All preparations were given in opaque capsules (prepared by the local hospital pharmacy) in a randomized sequence. Talc capsules were used as a placebo. To enhance the study design and to eliminate bias, multiple placebos were used.¹ Because of possible delayed reactions, consecutive substances were challenged 1 week apart. The patient remained at the allergy center under controlled conditions for at least 2 hours after each challenge and gave an informed written consent before starting oral provocations.

RESULTS

Sixty minutes after the ingestion of sodium nitrate, 10 mg, the patient reported generalized pruritus that worsened during the following 30 minutes and disappeared after the intravenous administration of an antihistamine (chlorphenamine, 10 mg). None of the other substances nor the placebos induced any symptoms. Nitrate intolerance was diagnosed.

DISCUSSION

Itching patients without an apparent skin eruption pose a diagnostic challenge.⁴ Hyperthyroidism, lymphomas, infestations and parasitoses, hematologic diseases such as polycythemia vera, and hepatic diseases must be considered in the differential diagnosis.⁴ All of these conditions were excluded by proper laboratory and radiographic investigations, and chronic pruritus was eventually found to be caused by intolerance to a food additive.

Despite their widespread use as preservatives and as flavoring and coloring agents in processed meats (eg, salami and frankfurters), nitrates and nitrites have been rarely associated with adverse pseudoallergic reactions: a total of 11 cases of nitrate-dependent chronic urticaria are reported in the literature.⁵⁻⁷ This patient showed a

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J Allergy Clin Immunol 1999;104:1110-1.

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0091-6749/99 \$8.00 + 0 1/54/101541

more subtle form of intolerance characterized by chronic generalized pruritus without any visible rash. A nonspecific response to challenge tests seems unlikely for the following reasons: (1) the patient did not show any reactivity to placebos or substances other than sodium nitrate; (2) the administration of sodium nitrate exactly reproduced the clinical symptoms present during the past 4 years; and (3) the study design (double-blind and multiple placebos) should have minimized possible bias. As in other cases of other food additive intolerance, pathogenetic mechanisms remain elusive. This case suggests that food additive intolerance should be included in the differential diagnosis of patients with chronic persistent pruritus of unknown origin.

I thank the nurses of the allergy center—Stefania Arienti, Ombretta Dolcino, and Aurelio Tirloni—for their cooperation in carrying out the double-blind challenges.

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