

Hypereosinophilia, neurologic, and gastrointestinal symptoms after bee-pollen ingestion

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A patient developed hypereosinophilia (13,440 cells per cubic millimeter) 6 weeks after beginning the ingestion of bee pollen. Symptoms included generalized malaise, headache, nausea, abdominal pain diarrhea, generalized pruritus, and decreased memory. Evaluation revealed no other known cause for the patient's hypereosinophilia, which resolved after bee-pollen ingestion was stopped. The product contained a mixture of entomophilous and anemophilous pollens to which the patient was skin test positive. An open challenge with the bee pollen later reproduced the presenting symptoms with a concomitant rise of the eosinophil count from 207 to 890 cells per cubic millimeter. The patient has since remained well avoiding bee pollen. This study strongly suggests that hypereosinophilia with attendant pathophysiologic disturbances may be an adverse reaction to bee-pollen ingestion in atopic individuals. (J ALLERGY CLIN IMMUNOL 1989;83:793-6.)

Throughout history there has been a great desire to find a panacea for health, strength, and virility. Claims of improved health and cured disease after bee-pollen ingestion have made this therapy popular in segments of the public. Honeybee collected or entomophilous pollens are not generally considered to elicit rise to allergic difficulties.¹ Jackson et al.² concluded that pollen eaten in even large quantities was not harmful to humans. However, in 1979, Cohen et al.³ reported three cases of anaphylaxis after bee-pollen ingestion. Nonetheless, users still undertake pollen therapy without awareness of any potential dangers that may ensue. We present the evaluation of one patient who developed hypereosinophilia and systemic symptomatology after bee-pollen ingestion.

CASE REPORT

G. B., a 37-year-old white woman, purchased bee pollen from a local health food store with the intent of increasing her energy. Approximately 3 weeks after she began in-

Abbreviations used

HES: Hypereosinophilic syndrome
MBP: Major basic protein

gesting the bee pollen, she developed general malaise, headache, nausea, abdominal pain, diarrhea, myalgia, and generalized pruritus associated with an evanescent maculopapular rash. The symptoms progressed in severity during the next 3 weeks while she continued to take the bee pollen. Disorientation and decreased memory prompted a visit to her physician, and hypereosinophilia was discovered, with a maximum total eosinophil count of 13,400 cells per cubic millimeter obtained. At this time, she denied any history of foreign travel, fever, chills, weight loss, or ingestion of any medication. After admission at her community hospital in October 1986, initial evaluation revealed a normal physical examination and the following normal studies: urinalysis, blood chemistries (SMAC 18), antinuclear antibody, rheumatoid factor, chest x-ray, upper gastrointestinal series, barium enema, abdominal ultrasound, and lumbar puncture for cerebrospinal fluid. IgE was 35.6 IU/ml (normal, 0 to 180). Complete blood cell count on initial visit while she was still taking bee pollen revealed a hemoglobin of 12.2 gm/dl, white blood cell count of 19,200 cells per cubic millimeter, with 11% neutrophils, 19% lymphocytes, and 70% eosinophils.

The patient was transferred to Fitzsimons Army Medical Center for further evaluation. Six days after bee pollen was stopped, a complete blood cell count revealed a hemoglobin of 11.1 gm/dl, mean corpuscular volume of 91 μm^3 , erythrocyte sedimentation rate of 15, platelet count of 313,000,

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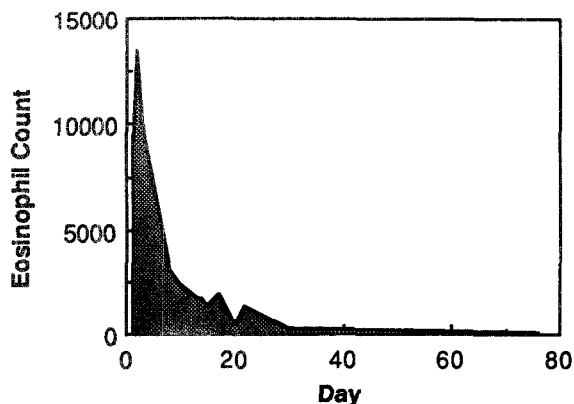


FIG. 1. Serial eosinophil counts demonstrated a precipitous drop after bee-pollen ingestion was stopped on day 1.

and white blood cell count of 9500 cells per cubic millimeter, with 19% neutrophils, 40% lymphocytes, 5% monocytes, 1% basophils, and 32% eosinophils. Bone marrow aspirate and biopsy specimen revealed large number of mature eosinophils, but no other abnormalities were noted.

The patient's symptoms and eosinophilia resolved spontaneously during the 2-week period after bee-pollen ingestion was stopped (Fig. 1). A prick skin test with the patient's bee pollen elicited rise to a 3+ reaction; this testing was attended by a feeling of malaise in the patient associated with an increase in her absolute eosinophil count from 1342 to 1872 15 hours later. Despite a negative personal and family history of atopy, the patient had 3 to 4+ reactions to intradermal skin tests to common inhalant pollens: oak, mountain cedar, elm, June grass, Bermuda grass, Johnson grass, burning bush, giant ragweed, and sage. Skin tests to Hymenoptera venoms were negative. She was discharged in November 1986 and remained asymptomatic while she avoided bee-pollen ingestion. Absolute eosinophil counts ranged from 124 to 312.

Bee-pollen challenge

The patient was readmitted to Fitzsimons Army Medical Center in January 1987 for an open oral bee-pollen challenge, at which time her baseline eosinophil count was 474. Objective measures, such as recurrence of eosinophilia or demonstrable rash, were considered a positive result, with purely subjective symptoms considered negative. Bee pollen was reinstituted at one teaspoon twice daily. After 2 days of receiving bee pollen, she remained asymptomatic, and the eosinophil count was 207. The dosage was increased to two teaspoons twice daily, and after a cumulative dose of six teaspoons, she complained of general malaise and nasal congestion. Stomach ache and diarrhea appeared after a total of eight teaspoons, and the eosinophil count rose to 586. After 10 teaspoons, she experienced generalized pruritus with an eosinophil count of 890. Her symptoms continued to escalate with continued ingestion, but the eosinophil count did not increase further. The challenge was stopped after a cumulative dose of 18 teaspoons (administered dur-

ing 6 days) because of the patient's inability to tolerate further symptoms. Six random endoscopic biopsy specimens from stomach and duodenum at this juncture failed to reveal eosinophilic infiltration. Resolution of symptoms occurred 36 hours after the termination of the challenge. The bee-pollen challenge and results are depicted in Fig. 2. The patient has remained asymptomatic in the year after the challenge with continued avoidance of bee pollen.

Bee-pollen identification

The incriminated bee pollen contained granules of various color, representing different pollens. These were identified as sage, ragweed, goldenrod, lilac, clover, daisy, sunflower, and chenopod/amaranth pollens. The patient was skin tested to these individual pollens and responded with a 3 to 4+ reaction to prick or intradermal skin tests to all these pollens. Based on this identification, commercially available bee pollen for ingestion may contain not just pollens of insect-pollinated plants, but highly allergenic air-dispersed pollens as well.

DISCUSSION

In a review of clinical studies, Jackson et al.² believed that orally administered bee pollen demonstrated promise of diminishing sensitivities to airborne pollen. Cohen et al.,³ however, reported three patients who experienced anaphylaxis after bee-pollen ingestion. They postulated as well that atopic individuals may suffer anaphylaxis from ingestion of food stuffs that cross-react with pollens to which they are sensitive. Mansfield and Goldstein⁴ reported a severe anaphylactic reaction after ingesting bee pollen by a patient for self-treatment of hay fever. The incriminated bee pollen contained a large quantity of mesquite pollen, an important aeroallergen in the patient's area and to which he was markedly sensitive. Pieroni et al.⁵ reported refractory worsening of asthma in a patient 1 week after instituting bee-pollen ingestion. Our patient is different from the previous studies of immediate anaphylactic reactions.

This case illustrates that a potentially serious adverse reaction, hypereosinophilia associated with gastrointestinal and neurologic dysfunction, can result from the ingestion of bee pollen obtained in health food stores. Despite a negative personal and family history for atopy, the patient reacted to extracts of various common grasses, trees, and weeds; she also reacted on skin testing to the bee-pollen mix, as well as the individual pollens. The potential for significant antigen exposure is present with this form of bee pollen because each granule may contain up to 500,000 pollen grains.³ This chronic antigenic load during a period of 6 weeks could have resulted in the eosinophilia, rash, and functional disturbances observed.

Considering that most of the patient's initial symp-

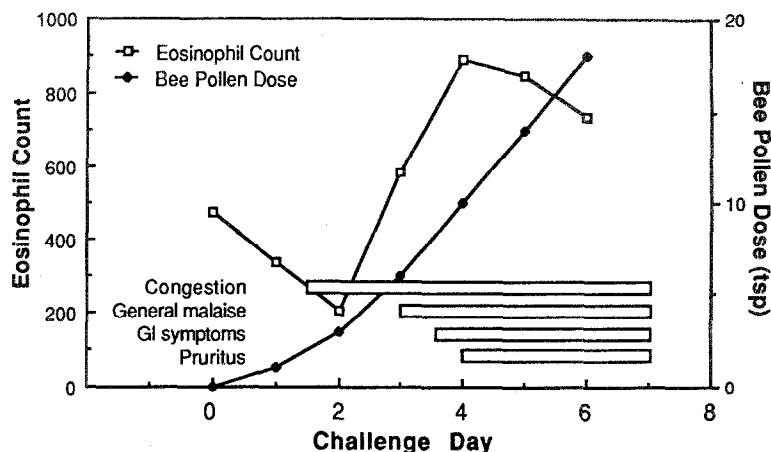


FIG. 2. Bee-pollen challenge, first dose administered on day 1. Horizontal bars indicate onset of specific symptoms.

toms were of a subjective nature, the validity of an open challenge may be argued. A double-blind challenge would have been more difficult to administer and would have incurred more time in the hospital, which was not feasible for this patient living far away from the medical facility. Additionally, ethical considerations over possible harm from a blinded trial were raised. Since an objective rise in eosinophil count, and not only the appearance of subjective symptoms, was considered a positive challenge, the use of the open trial appears defensible.

The chronology of the initial exposure and its resolution plus the greater than fourfold rise in the eosinophil count with the challenge support the contention that the hypereosinophilia was caused by the bee-pollen ingestion and that the reappearance of symptoms was based on more than the patient's expectations. The presence of eosinophils in the gastric biopsy specimen would have provided further evidence, but the absence of eosinophils was perhaps not unexpected. The short duration of the reinstitution of bee-pollen ingestion may have been inadequate to allow time for sufficient eosinophilic infiltration in random mucosal biopsy specimens. Additionally, eosinophils may not be easily demonstrated, even at sites of presumed injury. In the article by Davies et al.⁶ of cardiovascular features of patients with eosinophilic endomyocardial disease, degranulated eosinophils were observed in cardiac biopsy specimens from only five of the 11 patients. This could be due to the difficulty of identifying degranulated eosinophils or these effector cells having already departed the site of inflammation. MBP has been immunofluorescently demonstrated in skin lesions devoid of eosinophils.⁷

The difference in antigenic load and duration of exposure probably accounts for the differences in

magnitude of eosinophilia between the hospital challenge and her ingestions at home. During her initial ingestion period, she consumed 39 teaspoons of bee pollen during 6 weeks. At this time her eosinophil count was 13,440. During the hospital challenge, 10 teaspoons of bee pollen were administered during the first 4 days. The eosinophil count at this time was 890. In the study by Ottesen and Weller⁸ of eosinophilia after treatment of patients with schistosomiasis and filariasis, it was demonstrated that the magnitude of an individual's acute eosinophilic response bore a direct relationship to the antigenic load presented. They suggested that the increase in numbers of circulating eosinophils reflected active eosinophilopoiesis, since the eosinophilic responses took several days to develop and then 1 or more weeks to peak.

The variety of systemic symptoms expressed by this patient with bee-pollen ingestion is very similar to the diversity of presenting symptoms described in HES.⁹ Generalized pruritus with or without rash and neurologic abnormalities occur in >50% of patients with HES. The presumed mechanism of injury would be the generalized release from the degranulating circulating eosinophils of such toxic substances as MBP, eosinophil cationic protein, or eosinophil-derived neurotoxin. The direct toxicity of these proteins on a variety of cell types has been demonstrated.¹⁰ Alternately, damage to vascular endothelium with resultant microthrombi, as has been reported in HES, could result in ischemic dysfunction in any part of the circulation. This mechanism could account for transient disturbances, such as observed in this patient. Such processes are speculative and remain to be documented in future cases. Unfortunately, serum from this patient's initial presentation was not available to analyze retrospectively for the presence of MBP. In-

terestingly, gastrointestinal complaints of diarrhea, abdominal pain, and nausea have been reported during the initiation of oral immunotherapy.¹¹⁻¹³ However, hypereosinophilia has not been described.

Analysis of the bee-pollen mixture that our patient had been ingesting revealed it to contain many highly allergenic airborne pollens. Physicians should acquaint themselves with the potential hazards of bee-pollen ingestion, especially in atopic individuals, and educate their patients and the lay public on the possible dangers that can result from the use of so-called "health foods."

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