

Psyllium hypersensitivity

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Background: Psyllium-containing laxatives are used by 4 million Americans daily. Dietary supplements for the management of hypercholesterolemia and for prevention of colon cancer make up additional uses of this plant fiber.

Objective: To assess a patient in an HMO practice with allergic cutaneous and respiratory findings associated with chronic psyllium ingestion and review information on psyllium hypersensitivity.

Methods: Clinical and laboratory evaluation of the patient and literature review through MEDLINE.

Results: Two years after initiating regular psyllium-containing laxative use a 40-year-old woman presented with a pruritic macular, papular, and urticarial rash involving the entire body including the palms, soles, and oropharynx sparing only the face. There was an associated sensation of chest and throat tightness and lip swelling. The signs and symptoms resolved upon discontinuance of the psyllium and recurred immediately after the patient initiated a challenge test. The total serum IgE was elevated and the modified RAST for psyllium-specific IgE was positive (*Plantago ovata* antigen).

Conclusions: The allergens in psyllium appear to be protein in nature and derived from the inner seed endospore and embryo rather than from the husk itself. The patient described herein was sensitized and challenged via ingestion.

INTRODUCTION

Psyllium is a natural plant product that commands a major over-the-counter market as a bulk laxative. Allergy to psyllium is recognized both in workers who prepare and dispense the product and in those who use it therapeutically. Herein a patient in an HMO practice who manifested allergy to ingested psyllium is reported and the literature on psyllium hypersensitivities is summarized from a computerized search of MEDLINE (National Library of Medicine, Bethesda, MD) 1980 to present.

CASE REPORT

A 40-year-old woman, a bank employee, was seen in allergy consultation for a generalized rash of 3 weeks' duration.

The patient had been taking a psyllium husk-containing laxative

three times weekly for several years following a delivery-related rectal injury. Three weeks before the appearance of the rash, the rectal scar was revised under general anaesthesia, at which time she was given a single intravenous injection of an unknown antibiotic. One week before the onset of the rash she sought dental care for a "migraine" at which time no dental pathology was found; however, erythromycin was prescribed and taken for two days.

One week later the rash appeared which she described as intermittent in occurrence with a burning or itching quality. The rash was accompanied by a tight sensation in the chest with wheezing and occasional facial or lip swelling lasting several hours. After 1 week she consulted a dermatologist who noted urticaria of the arms and legs. Hydroxyzine was prescribed and ameliorated the pruritus. Three brief courses of prednisone had been given without resolution of the rash.

The patient suspected that the rash might be related to her laxative and accordingly she discontinued it.

One week later she challenged herself with a dose of the psyllium laxative and within 15 minutes experienced swelling of her lips and a sensation of her throat closing as well as a flaring of the rash. She went to an emergency facility where epinephrine was administered with some relief; however a second injection was required the following day.

Past history revealed symptoms of mild seasonal rhinitis, a two stage breast reduction and silicone augmentation 15 years previously, and hepatitis A. There was no history of asthma, drug allergy or occupational contact with psyllium. The patient's mother was diagnosed as having scleroderma.

At allergy consultation a diffuse symmetrical rash was present involving the entire body including the palms and soles but sparing the face. The rash was erythematous and consisted of small (<5 mm) circular nonconfluent erythematous macules, several of which had a multiforme "target" appearance. The lesions on the back were slightly papular. The oropharynx also was involved with similar lesions.

A total serum IgE was 675 IU/mL (normal <180 IU/mL), which was considered compatible with her seasonal rhinitis. A modified RAST using *Plantago ovata* antigen (Unilab Corp, Sacramento, CA) was reported as class 3 positive, (3669 counts/min, normal <750 counts/min). No commercial extract for skin testing was available. The following tests were negative or within normal limits: complete blood count with differential, total eosinophil count, sedimentation rate, RPR, ASO titer, ANA, rheumatoid factor, hepatitis screen, coccidioidomycosis serology, chest radiograph, and sinus radiographs. Biopsy of a skin lesion was interpreted

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as showing "nonspecific dermatitis."

With strict psyllium avoidance the rash resolved over the ensuing 3 months and has not recurred.

In this patient the untoward reaction complex consisted of a pruritic macular, papular and urticarial rash involving the trunk, extremities, palms and soles and the oropharynx. There was lip swelling and a sensation of throat tightness.

The evidence that this was caused by her psyllium-containing laxative was the presence of high titer IgE specific for psyllium detected by a modified RAST. A physician-directed challenge test was deemed unnecessary as the patient had already performed this confirmatory procedure on her own initiative.

DISCUSSION

Psyllium is derived from the seed husk of *Plantago ovata* and *P. psyllium*. The psyllium in most of the bulk laxatives, such as used by the patient reported here, is from *P. ovata*. The various *Plantago* are cultivated in the Mediterranean areas and the Indian subcontinent as important export crops.¹ Several species of *Plantago* were cultivated in Arizona but the venture proved economically unfeasible because of frost and grasshopper predation.^{1,2} *P. psyllium* grows wild on southwestern deserts in the US.³ Indigenous plantain (*P. lanceolata*) in the United States is familiar to the allergist as a hay fever-causing weed.

The *Plantago* seed is composed of the outer mucilaginous husk surrounding the endosperm within which is the embryo.⁴ The outer husk, which is the source of psyllium, is separated by grinding of the whole seed and processed for medicinal use while the inner endosperm and embryo are used as animal feed. The laxative property of psyllium derives from its highly hydrophilic soluble polysaccharide structure, which results in increased bulk upon imbibing water.

It is estimated that psyllium-con-

taining laxatives are used daily by 4 million Americans. Recently, the hypocholesterolemic effect of psyllium has been described.⁵ Psyllium alone or mixed with other water-soluble dietary fibers produces a modest but significant fall in total serum cholesterol and in low density lipoprotein cholesterol.⁶ This effect is achieved without the considerable cost and side-effects of other lipid lowering agents. Also there is epidemiologic evidence that dietary plant fiber decreases the incidence of colon cancer.⁷ These additional potential health benefits may further increase the use of this relatively benign plant derivative.

Besides over-the-counter laxatives, such as Metamucil (Procter & Gamble, Cincinnati, OH) and Perdiem Fiber (Rhône-Poulenc Rorer Pharmaceuticals, Inc., Collegeville, PA), psyllium has been available in the recent past in a variety of other forms including ready-to-eat cereals and dietary supplements. These are labeled variously as containing high potency psyllium seed husk, finely ground psyllium husk, psyllium seed powder, and natural psyllium powder. In general these products are packaged without any health warnings although one exception is Fiber Plan (Shaklee, USA Inc. San Francisco, CA) which states "Note: This product contains psyllium which can cause allergic reactions."

Psyllium is recognized as a significant occupational allergen for pharmaceutical workers preparing and processing the seed husk and health-care workers dispensing it.⁸⁻¹⁰ Dispensing requires measuring of the powder or pouring premeasured packets into containers and adding liquid. The powdered husks are readily aerosolized and consequent sensitization is believed to be by the respiratory route. Reactions have included asthma, anaphylaxis and rashes, some of which are urticarial. Several cases of anaphylactic reactions in workplaces have been reported in the past two decades from the US^{8,9} and abroad.¹⁰ In addition,

anaphylaxis has been reported in individuals who ate psyllium-enriched cereal.^{11,12} In each of these cases the skin test and/or RAST to psyllium was positive. After a strongly positive skin test, one patient experienced itching and redness of her face and eyes.¹²

James et al¹³ contacted 20 of 24 women who had reported to the manufacturer systemic symptoms following ingestion of a psyllium supplemented cereal. In each case some form of medical therapy had been required. Symptoms included wheezing, throat and chest tightness, and urticaria occurring within 30 minutes of eating no more than one cup of the cereal. Eighteen of these 20 women were deemed atopic. All but three had had prior workplace psyllium exposure either as a dust or as an ingested laxative or cereal. Nine of the 20 recalled nausea and abdominal cramping following ingestion of the psyllium. Eleven of the 20 had previously dispensed psyllium during the course of their occupation as nurses and had experienced mild allergic symptoms from this activity. All 20 women had IgE antibodies to various psyllium proteins in this retrospective study. Sera from these subjects reacted to *P. ovata* but not to *P. lanceolata* (plantain).

Sensitization, as evidenced by skin test or in vitro tests, have been reported in 3.0% to 26% of psyllium workers.¹⁴⁻¹⁶ In one survey, 18% of workers reported symptoms associated with their job-related exposure.¹⁷ The frequency with which these workers become sensitized, presumably by respiratory exposure, suggests that those who become allergic to ingested laxatives or cereals may actually acquire their hypersensitivity from small aerosols produced during the mixing or pouring of the powdered products.

Challenges have been carried out in small series of affected workers. Four of five nurses, all with asthma symptoms and rhinoconjunctivitis as well as positive skin tests and

RASTs had hyperresponsiveness to methacholine challenge suggesting an innate bronchospastic tendency. These five nurses were then challenged with psyllium inhalation and reacted with significant bronchospasm. One of them required intubation.¹⁸ Bardy et al¹⁶ examined pharmaceutical workers before and during their work with psyllium with peak flow and methacholine challenge monitoring. Eighteen of those with positive methacholine challenges were then challenged with psyllium and five had immediate bronchoconstriction.

Ingestion of psyllium-containing cereals and laxatives can cause mild gastrointestinal symptoms, as was noted in a study on its use as an hypocholesterolemic agent.⁶ In these cases the mechanism of the intolerance was not investigated; thus, it is not known whether the side effect was immunologically or pharmacologically mediated. Of possible relevance is a patient who presented only with 17% eosinophilia¹⁹ which resolved when a psyllium laxative was discontinued and recurred upon challenge. Possibly the full spectrum of manifestations resulting from psyllium allergy remains to be defined.

Recent attempts have been made to identify the responsible allergen or allergens in psyllium. Arlian et al⁴ have examined various *P. ovata* seed extracts by several immunoelectrophoresis procedures using sera from 11 psyllium RAST positive individuals. In this study commercial grade husks (95% pure), Freon-purified husks (99% pure), endosperm and embryo were examined. The protein concentrations of these four preparations were 2.7%, 0.6%, 24%, and 41.2%, respectively. Common IgE binding proteins were found in all four preparations, with the smallest quantity in the Freon-purified husks. In addition, upon microscopic examination of commercial grade psyllium, white flakes consistent with endosperm particles and brownish gran-

ules consistent with pieces of embryo were observed. It was concluded that the allergenic components in psyllium husk are protein in nature and are derived from the endosperm and embryo. On the basis of these results the authors suggest that more highly purified psyllium preparations might have a lower incidence of sensitization. Noteworthy is that a revised formulation of psyllium-enriched Heart-Wise cereal (Kellogg Co., Battle Creek, MI) containing more highly purified psyllium appeared to produce fewer side effects while it was available.¹³

It should be pointed out that not all of the untoward effects of psyllium are immunologic in origin. Doses of unsoaked seeds have caused intestinal obstruction.¹ Also powdered or chewed *Plantago* seeds can cause deposition of pigment in the renal tubule cells with consequent functional impairment.¹

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