

Lupine-induced anaphylaxis

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Background: Legumes are one of the most common foods causing allergic reactions in children and adults. Cross-reacting antibodies are frequently demonstrated in this family but the real clinical cross-reactivity is uncommon.

Objective: To report a case of lupine-induced anaphylaxis and to elucidate in vivo and in vitro cross-reactivity with some legumes.

Methods: Skin prick test (SPT) with some legumes were performed. Cap-IgE, ELISA-IgE, and immunoblotting were carried out. Open oral challenges with some legumes were performed. Cross-reactivity was studied by ELISA and immunoblotting inhibition.

Results: The results demonstrated type-I hypersensitivity reactions with lupine and some other legumes. Cap-IgE with peanut was positive but the SPT and ELISA-IgE were negative and the patient tolerated a peanut challenge. ELISA inhibition revealed a partial inhibition (62%) using lupine as the solid phase. Partial inhibition was demonstrated by immunoblotting inhibition. Open oral challenge with peanut and green bean were negative but positive with pea.

Conclusion: We present a lupine sensitized patient with positive SPT and in vitro cross-reactivity with other legumes. Clinical cross-reactivity progressively developed over a 5-year period. Discrepancies were found between the clinical aspect and in vitro study of peanut allergy. Factors determining the wide variability in cross-reactivity among individuals are still obscure.

Ann Allergy Asthma Immunol 1999;83:406-408.

INTRODUCTION

Seeds from the legume family, such as peanut and soybean, are consumed in considerable quantities by humans because of their low price and high protein content.¹ This phenomenon is probably responsible for the increased development of food allergies and fatal anaphylactic reactions reported.² Peanuts are one of the most common foods causing allergic reactions in children³ and adults⁴ in the USA. Peanut allergy is characterized by severe symptoms and by a high prevalence of symptoms on minimal contact.⁵

Lupine (*Lupine albus*), another member of the legume family, is cultivated all over the world. It is less popular but is used for flour for bread,⁶

cookies,⁷ pasta⁸ and milk substitutes,⁹ and sometimes as a snack.⁹

Multiple food allergy within the legume family has been suggested to be common based on in vitro cross reactivity studies by some authors.^{10,11} Studies based on oral challenge, however, have reduced the rate of cross-sensitivity to 5% of patients.¹²

We report an anaphylactic episode after ingestion of lupine seeds in a patient previously sensitized to other legumes with tolerance to peanut.

CASE REPORT

A 38-year-old atopic woman presented with diffuse urticaria, angioedema on her hands and face, dysphagia, chest tightness, shortness of breath, and throat swelling immediately after the ingestion of three lupine seeds in 1996. It was the first time she had eaten this legume.

In her past medical history, this patient suffered several episodes of palmar itching erythema and facial angio-

edema in 1992. Three of these episodes were related to the ingestion of chickpea. She affirmed tolerance of all other legumes including peanut. She had a positive skin prick test (SPT) to chickpea and was diagnosed with chickpea allergy and was advised to exclude all legumes from the diet. Nevertheless, she continued eating lentils, white and green bean, pea and peanut with no reactions. Some time after, in 1995, she started to have wheals and throat swelling each time she ate lentils and white beans. She abandoned their consumption but continued eating peanuts and occasionally peas with no reactions. More recently, the patient had an urticarial episode following the ingestion of an unusual kind of green bean called "garrafó." At present she tolerates peanut. She has never eaten soybean or chickling.

Skin prick test with commercial extracts (LETI, Madrid, Spain) to chickpea, white bean, pea, lentil, and soybean were positive yet negative to peanut, chickling, and green bean (Table 1). Skin prick test with lupine extract prepared at our laboratory (0.3 mg/mL) produced a wheal of 16 × 12 mm with two pseudopoda, ocular itching, and palmar erythema.

Total IgE was 11.7 kU/L (CAP-system, Pharmacia-Upjohn, Uppsala, Sweden). Assays for specific IgE antibodies (CAP-system, Pharmacia-Upjohn, Uppsala, Sweden) were positive to all legumes except green bean (Table 1). An ELISA assay was designed for specific IgE to legumes and demonstrated antibodies to lupine, chickpea, white bean, and lentil. ELISA inhibition assay, using lupine as the solid phase, revealed an 83% inhibition with chickpea, 86% with white bean, 62% with peanut, 32% with lentil, and 27% with pea (Table 1).

Proteins of lupine extract were resolved in a 12.5% SDS-PAGE and

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Received for publication August 31, 1998.

Accepted for publication in revised form June 11, 1999.

Table 1. In Vivo and in Vitro Results with Some Legumes

Food	Prick Test 1996	IgE* kU/L			ELISA 1997	Inhib 1/1† Lup/Food	Symptoms/year	Challenge 1997
		1992	1996	1997				
Chickpea	+	ND	2.36	3.46	+	83%	U/A/1992	ND
Lupine	+	ND	ND	ND	+	94%	Ana/1996	ND
White bean	+	1.3	2.71	2.94	+	86%	Ana/1995	ND
Pea	+	2.6	3.89	3.9	—	27%	T/1996	RC
Soybean	+	2.2	6.54	4.11	ND	ND	NE	ND
Peanut	—	<0.35	1.18	1.2	—	62%	T/1997	T
Lentil	+	ND	3.69	4.1	+	32.5%	Ana/1995	ND
Chickling	—	ND	2.37	1.23	ND	ND	NE	ND
Green bean	—	ND	ND	<0.35	ND	ND	T/1997	T

* Specific IgE by Cap-Pharmacia.

† ELISA inhibition assay using lupine as the solid phase.

U/A: urticaria-angioedema. Ana: anaphylaxis. RC: rhinoconjunctivitis. T: tolerated. NE: not eaten. ND: not done.

transferred electrophoretically to a polyvinylidene fluoride microporous membrane (Immobilon-P Transfer Membrane, Millipore Co, MA, USA). Eight IgE-binding components were detected between 12.5 to 61 kD (Fig 1). An immunoblotting inhibition study was done with chickpea, peanut, and white bean. These legumes partially inhibited bands corresponding to proteins from 26.5 to 61 kD.

After written informed consent, the patient underwent an open oral challenge with some legumes to which the patient was apparently tolerant. The patient tolerated up to 8 g of peanut and green bean but, 10 minutes after pea ingestion, she developed ocular itching, rhinorrhea, sneezing, watery eyes, and palm-plantar itching.

DISCUSSION

Allergists often recommend restriction of all members of a food family when a patient is allergic to one of its members. The recommendation differs, however, in every food family and it must be based on oral challenge because often the overall accuracy of skin prick test and of specific IgE measurement is poor.¹³ Food allergy diagnosis is not questioned when it is supported by a clear history of anaphylaxis or a positive blind oral food challenge. Although sometimes difficult, avoidance of the causative food is the only effective treatment of food hypersensitivity.¹⁴

Legume allergy is a well described entity. The majority of allergic reactions are believed to be IgE-mediated, mast cell-dependent, immediate hypersensitivity reactions.¹⁵ IgE-mediated in vitro cross-reactivity within the legume botanical family is frequent but the clinical relevance of this is not so common.¹² In fact, most peanut-allergic patients tolerate other legumes.

Clinical hypersensitivity to one legume does not warrant dietary elimination of all legumes¹² even if skin prick-testing and peanut-specific IgE levels are positive. Positive skin prick-testing and specific IgE do not predict symptoms in 100% of patients and their level is not proportional to clinical severity.⁵

Lupine allergy is still rare but it is an important issue due to its progressive

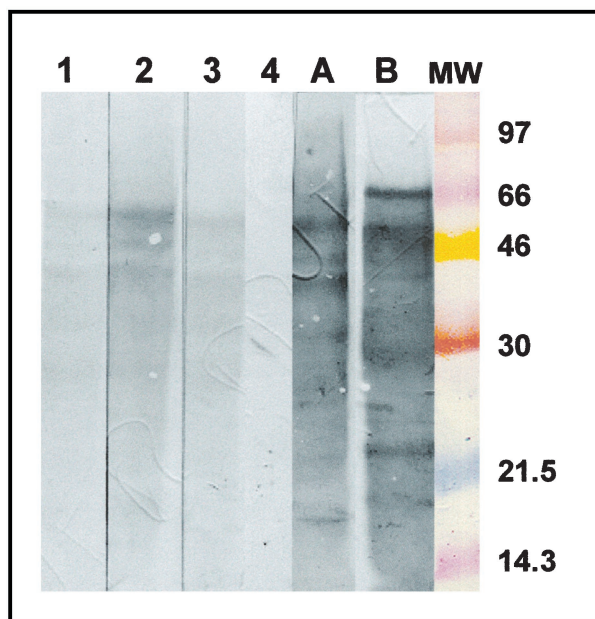


Figure 1. Immunoblot inhibition with some legumes: Lane 1: Partial inhibition with chickpea. Lane 2: Partial inhibition with peanut. Lane 3: Partial inhibition with white bean. Lane 4: Total inhibition with lupine extract. (A) Immunoblot demonstrating serum-specific IgE against lupine proteins ranging from 12.5 to 61 kD. (B) Amido-black staining demonstrating protein profile of lupine extract. (MW) Molecular weights markers.

appearance as foods for human consumption.⁸ To our knowledge, only one case of urticaria-angioedema has been described,¹⁶ three oral allergy syndromes,¹⁷ and a contact urticaria¹⁸ induced by *Lupinus albus*.

We describe a legume-sensitized patient who developed one episode of anaphylaxis after the first ingestion of lupine seed. The patient's clinical history and in vivo and in vitro tests demonstrated an IgE-mediated mechanism. Furthermore, we presented a clinical and in vitro cross-reactivity study for some legumes. In our patient, specific IgE was detected by Cap and/or ELISA with all legumes except green bean. Cross-reactivity was shown by ELISA-inhibition and immunoblotting among all legumes; however, with peanut there were discrepancies between the clinical aspect and in vitro study.

Legume sensitization appears to be a dynamic process in this patient. Her symptoms started with only one legume (chickpea) and she progressively developed a multiple legume sensitization (lentil, white bean, lupine, and pea). If oral challenges had been carried out in 1992, they would probably not have predicted clinical sensitivity to all the other members of the family to which the patient reacted 5 years later. She only developed clinical allergy to these later on. It is also possible, but difficult to predict, that she will develop peanut and green bean clinical sensitivity in the future. The progressive increase in symptoms with previous subclinical sensitization suggests that a legume-free diet might be recommendable.

Hefle et al reported five of seven peanut-sensitive patients to have a positive RAST and skin prick test with lupine extract. All five patients had clinical symptoms with green pea.¹⁶ Hefle et al, however, did not carry out oral challenges with lupine so we do not know their lupine tolerance. In our patient, lupine and pea allergy coexist but until now she continues with peanut tolerance. Romano et al described

three cases of oral allergy syndrome induced by *Lupinus albus* with previous symptoms with peanut.¹⁷ We found a peanut-specific IgE by Cap and 62% inhibition to a study of lupine-sensitive IgE binding by ELISA, but open challenge resulted into negative reaction. From a clinical viewpoint, the number of people with specific IgE in SPT or serologic testing without clinical symptoms who can transform into symptomatic patients is not known. Bernhisel-Broadbent, et al found that most children with severe anaphylactic reactions to peanut tolerate other legumes,¹² but we cannot predict whether this tolerance will stay or for how long. The factors determining the allergenicity of molecules and, therefore, the wide variability of individual cross-reactivity are still obscure. In the future, this will determine the action of allergists in relation to allergies to foodstuff families. In the absence of severe reactions the final diagnosis should be based on oral challenge studies.

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