Compound Allergy to an Antihemorrhoidal Ointment Demonstrated by the Repeated Open Application Test

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Key words: Allergic contact dermatitis. Antihemorrhoidal ointment. Compound allergy. Patch test. Repeated open application test (ROAT).

Palabras clave: Dermatitis alérgica de contacto. Pomada antihemorroidal. Alergia por componentes. Pruebas epicutáneas. Prueba abierta de aplicación repetida (ROAT).

The most commonly used topical pharmacologic agents for symptomatic management of hemorrhoids include vasoconstrictors, astringents, anesthetics, keratolytics, corticosteroids, and antipruritic agents. Some of these drugs have been involved in contact dermatitis [1-7].

A 57-year-old woman presented with a pruritic, sharply demarcated, erythematous rash on the anogenital area that spread within 2-3 days to the trunk, neck, forearms, groins, and upper inner aspect of the thighs. The rash began 3 to 4 days after application of an antihemorrhoidal ointment (Ruscus Llorens, Llorens, Barcelona, Spain) containing ruscogenin, prednisolone, cinchocaine, menthol, zinc oxide, and excipients (a mixture of parabens [methyl, ethyl, and butyl], polyethylene glycol, and cetyl alcohol). Avoidance of the antihemorrhoidal ointment and treatment with topical and oral corticosteroids and oral antihistamines improved the lesions within 2 weeks. The patient denied previous exposure to the ointment and had no history of atopy or contact dermatitis. One month after the reaction, the patient tolerated varicose vein cream containing *Ruscus aculeatus* (its primary active ingredients are ruscogenins), *Melilotus officinalis*, zinc oxide, the paraben mixture (methyl, ethyl, and butyl), and sodium edetate.

Six weeks later, we performed patch tests using the Spanish Contact Dermatitis Research Group standard series and corticosteroid series, the antihemorrhoidal ointment as is, and all the individual components to which the patient had not been exposed after the reaction (ie, ruscogenin 30% pet and 30% eth, prednisolone 1% pet, cinchocaine 5% pet, menthol 2% pet, polyethylene glycol 4% pet, and cetyl alcohol 5% pet). These concentrations were higher than in the ointment. Readings at 48 hours, 96 hours, and 1 week were negative for all of them. A repeated open application test (ROAT) was performed on the flexor forearm with the ointment as is and its individual components (2 daily applications for 7 days). Negative results were obtained with the individual components, but the result for the ointment was positive on the third day: erythema, papules, infiltration, and pruritus appeared on the application area, although they all resolved within 7 days (Figure). The results of the same test performed on 5 control patients proved negative.

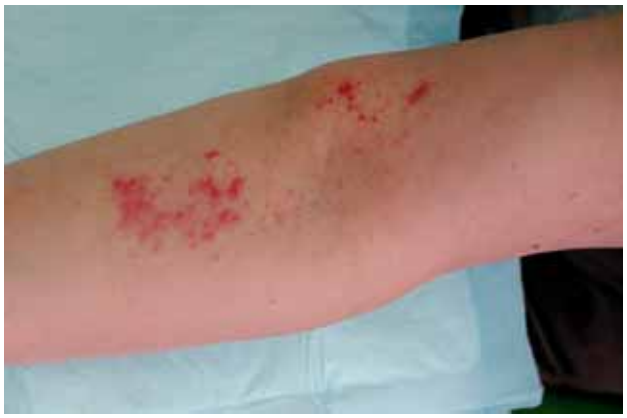

Figure. Repeated open application test with the ointment as is on the third day.

We report a case of generalized contact dermatitis due to an antihemorrhoidal ointment demonstrated by ROAT. Only the whole preparation caused the reaction, whereas the results of testing its individual ingredients were negative. The positive patch test results to a commercial product and negative results to its individual ingredients could indicate that the patient experienced a compound allergy. In some cases, a chemical interaction has been demonstrated between the ingredients within the whole preparation to form a new allergen, and in others, the authors suggest enhanced delivery of the allergen via the original preparation rather than the patch test vehicle [8]. We ruled out alternative explanations such as contamination of the ointment, an irritant reaction, or an insufficient concentration of individual ingredients for patch testing. The negative results of the patch test with the ointment applied on the back, and the positive results of the ROAT with the ointment applied on the forearm could be explained by the fact that the first test does not reproduce the clinical exposure (multiple applications). In addition, it is difficult to reproduce the particular anatomical and pathological conditions of the anogenital area (ie, sweating, friction, pressure, damaged skin), which could increase skin penetration and the sensitizing capacity of pharmaceutical products [9]. Therefore, patch testing on the back may give false-negative results, especially when the product is applied to sites such as the anogenital area. Diagnosis of allergic contact dermatitis in these cases can be confirmed by ROAT with the preparations used by the patient and their individual ingredients.

In conclusion, we report the first case of systemic contact

dermatitis due to a compound allergic reaction to Ruscus Llorens ointment diagnosed by ROAT test.

These data were presented in part in abstract and poster form at the XXVII Congress of the EAACI, Barcelona, June 7-11, 2008.

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References

1. Proske S, Uter W, Schnuch A, Hartschuh W. Severe allergic contact dermatitis with generalized spread due to bufexamac presenting as the "baboon" syndrome. Dtsch Med Wochenschr. 2003;128:545-7.
2. Reyes JJ, Fariña MC. Allergic contact dermatitis due to trimebutine. Contact Dermatitis. 2001;45:164.
3. Tanaka S, Otsuki T, Matsumoto Y, Hayakawa R, Sugiura M. Allergic contact dermatitis from enoxolone. Contact Dermatitis. 2001;44:192.
4. Lodi A, Ambonati M, Coassini A, Kouhdari Z, Palvarini M, Crosti C. Contact allergy to 'caines' caused by anti-hemorrhoidal ointments. Contact Dermatitis. 1999;41:221-2.
5. González-Mahave I, Lobera T, Blasco A, del Pozo MD. Allergic contact dermatitis caused by cinchocaine. Contact Dermatitis. 2008;58:55-8.
6. Sánchez-Pérez J, Abajo P, Córdoba S, García-Díez A. Allergic contact dermatitis from sodium metabisulfite in an antihemorrhoidal cream. Contact Dermatitis. 2000;42:176-7.
7. Ramírez-Hernández M, García-Sellés J, Mérida-Fernández C, Martínez-Escribano JA. Allergic contact dermatitis to ruscogenins. Contact Dermatitis. 2006;54:60.
8. Bashir SJ, Maibach HI. Compound allergy. An overview. Contact Dermatitis. 1997;36:179-83.
9. Nakada T, Hostynek JJ, Maibach HI.Use tests: ROAT (repeated open application test)/PUT (provocative use test): an overview. Contact Dermatitis. 2000;43:1-3.

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Photoallergic Contact Dermatitis Due to Isoamyl-p-Methoxycinnamate

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Key words: Photoallergic contact dermatitis. Photopatch test. Sunscreens. Isoamyl-p-methoxycinnamate.

Palabras clave: Dermatitis de contacto fotoalérgica. Fotoparche. Crema solar. Isoamyl-p-methoxycinnamate.

Despite the huge increase in the use of sunscreens during recent years and the addition of ultraviolet (UV) filters to cosmetic products such as moisturizers and lipsticks, photoallergic contact dermatitis to these agents remains rare [1]. However, sunscreens have emerged as the most frequent cause of photoallergic reactions [2].

We report a case of photoallergic contact dermatitis to a UV filter, isoamyl-p-methoxycinnamate.

A 34-year-old woman attended the allergy unit after 2 episodes of dermatitis during the previous 2 months. She experienced a symmetrical eczematous eruption on the face, neck, V-area of the upper chest, dorsum of the hands, forearms, and legs after application of sunscreen and exposure to the sun. She had no personal or family history of atopy. She was successfully treated with a reducing course of oral prednisone and topical hydrocortisone ointment for 3 weeks.

Patch tests were performed using the standard series of the Spanish Contact Dermatitis Research Group (www.aedv.es/res.asp). She was also tested with the photopatch series of the Spanish Photobiology Group [3], the sunscreen chemical series of the European Task Force for Photopatch Testing [4], and her own sunscreen. The methodology followed was that of the European protocol [4]. The only positive reactions were to isoamyl-p-methoxycinnamate and the patient's own sunscreen, both of which occurred at D4 (+++) (Table). Her sunscreen contained isoamyl-p-methoxycinnamate. Unirradiated and irradiated controls were negative.

Table. Positive Results of Photopatch Testing in an Irradiated Set

Agent	D2 Pre-irradiation	D2 Postirradiation	D4 Postirradiation
Isoamyl-p-methoxycinnamate	–	–	+++
Patient's own sunscreen	–	–	+++

A variety of topical agents have been associated with photoallergic contact dermatitis [5]. Antibacterial and antifungal agents were the first described. In the 1960s and 1970s, the most sensitizing substances were salicylanilides, and in the 1970s and 1980s fragrances such as musk ambrette were prevalent causes. Both were withdrawn. More recently, active agents in sunscreens have been important causes of photoallergic contact dermatitis [6]. The most common UV filter photoallergens are benzophenones and p-aminobenzoic acid [1].

In recent years cinnamates have emerged as an alternative to p-aminobenzoic acid and benzophenones in Europe, the United States, Japan, and Australia [6]. The cinnamates are primarily UV-B absorbers. Given their poor water solubility, they are often used in sunscreens marketed as waterproof. Whereas allergy to cinnamate sunscreen ingredients is uncommon, cross-reactivity with flavorings and fragrances that include balsam of Peru, coca leaves, cinnamic acid, cinnamic aldehyde, and cinnamon oils is more significant [7].

We report a case of photoallergic contact dermatitis to isoamyl-p-methoxycinnamate. The prevalence of this condition may increase as sunscreen use becomes more widespread. The pattern of reactions to active sunscreen agents is also changing, and proper identification of the sunscreen allergen is very important. Photopatch test series should be regularly reviewed and updated.

References

1. Darvay A, White IR, Rycroft RJ, Jones AB, Hawk JL, McFadden JP. Photoallergic contact dermatitis is uncommon. Br J Dermatol.2001 Oct;145(4):97-601.
2. Fotiades J, Soter NA, Lim HJ. Results of evaluation of 203 patients for photosensitivity in a 7.3 year period. J Am Acad Dermatol.1995;33:597-602.
3. de la Cuadra Oyanguren J, Pérez Ferriols A, Lecha Carrelero M, Giménez Arnau AM, Fernández Redondo V, Ortiz de Frutos FJ, Silvestre Salvador JF, Serra Baldrich E. Resultados y evaluacion del fotoparche en España: hacia una nueva batería estándar de fotoalergenos. Actas Dermosifilograf. 2007;98:96-101.
4. Bruynzeel DP, Ferguson J, Andersen K, Gonçalo M, English J, Goosens A, Holzle E, Ibbotson SH, Lecha M, Lehmann P, Leonard F, Moseley H, Pigatto P, Tanew A. Photopatch testing: a consensus methodology for Europe. J Eur Acad Dermatol Venereol. 2004 Nov;18(6):679-82.
5. Cook N, Freeman S. Report of 19 cases of photoallergic contact dermatitis to sunscreens seen at the Skin and Cancer Foundation. Australasian Journal of Dermatology. 2001;42:257-9.
6. Schauder S, Ippen H. Contact and photocontact sensitivity to sunscreens. Review of a 15-year experience and of the literature. Contact Dermatitis.1997;37:221-32.
7. Fisher AA. Sunscreen dermatitis: Part II: the cinnamates. Cutis.1992;50:253-4.

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Successful Treatment of Allergic Bronchopulmonary Candidiasis With a Recombinant Anti–Immunoglobulin E Antibody

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Key words: Allergic bronchopulmonary aspergillosis. Allergic bronchopulmonary candidiasis. Allergic bronchopulmonary mycoses. Omalizumab.

Palabras clave: Aspergilosis broncopulmonar alérgica. Candidiasis broncopulmonar alérgica. Micosis broncopulmonar alérgica. Omalizumab.

Allergic bronchopulmonary aspergillosis (ABPA) was first described in 1952 [1]. Since then, other fungi that produce diseases with similar presentations to ABPA have been described. These diseases are known as allergic bronchopulmonary mycoses (ABPM). *Candida albicans* has been reported as a causative agent in ABPM [2-5].

Traditionally, the treatment of ABPM has been based on corticosteroids and, occasionally, antifungal drugs. We present a case of allergic bronchopulmonary candidiasis (ABPC) that was successfully treated with a recombinant anti–immunoglobulin (Ig) E antibody (omalizumab).

A 59-year-old man first attended our pneumology unit in 2005 with dyspnea on moderate exertion, purulent sputum, and nocturnal wheezing. Spirometry prior to initiation of treatment showed a forced vital capacity (FVC) of 2600 mL (61%) and a forced expiratory volume in 1 second (FEV_1) of 1540 mL (45%) with a positive bronchodilator test result. Short-acting and long-acting $ß_2$-agonists, leukotriene receptor antagonists, and corticosteroids (inhaled and oral) were prescribed. Despite this treatment, he was hospitalized 3 times in 2 years due to acute exacerbations of his symptoms and developed pulmonary infiltrates and peripheral bronchiectasia. After a 2-year follow-up, he was diagnosed with severe, persistent, and corticosteroid-dependent asthma. At this time, spirometry showed an FVC of 3250 mL (84%) and an FEV_1 of 2490 mL (74%). Therefore, omalizumab was added to his treatment regimen. He was also referred to the allergy unit for an allergologic work-up. After in vivo and in vitro tests, the patient met the criteria for ABPC [5] (Table). Furthermore, a significant improvement in respiratory symptoms and pulmonary function (FVC, 4070 mL [97.5%]; FEV_1, 2730 mL [82.5%]) was observed when omalizumab was administered. Oral corticosteroids were no longer necessary after 3 months under recombinant anti-IgE antibody therapy.

When pulmonary infiltrates co-occur with purulent sputum in patients with severe asthma, ABPM should be suspected. Isolation of the fungus is necessary to confirm the diagnosis of ABPM. *C albicans* is frequently recovered from bronchial

Table. Clinical, Imaging, and Laboratory Findings

Diagnostic Criteria[a]	Case
Asthma[b]	Yes
Peripheral blood eosinophilia	1000/μL (reference range, 800-1200)[c]
Skin test reactivity[d] to *C albicans*	
Skin prick test	Positive
Intradermal test (immediate and delayed)	Positive
Elevated total IgE levels	531 IU/mL
Presence of serum IgE antibody to *C albicans*	2.1 kU_A/L[e]
Precipitating antibody to *C albicans*	Positive
Isolation of *C albicans*	*C albicans* in induced sputum
Recurrent pulmonary infiltrates	Yes
Bronchiectasia	Peripheral
Exclusion of ABPA as diagnostic consideration	Negative in vivo and in vitro tests

Abbreviations: ABPA, allergic bronchopulmonary aspergillosis; Ig, immunoglobulin.
[a] Modified from Lee TM et al [4].
[b] According to the criteria of the Global Initiative for Asthma 2006. Basal spirometry prior to initiation of treatment: forced vital capacity of 2600 mL (61%) and forced expiratory volume in 1 second of 1540 mL (45%) with bronchodilator test >12% and 200 mL.
[c] Mean of 7 determinations performed when free of oral corticosteroids, from 2005 to 2008.
[d] According to Dreborg S [9].
[e] Mean value of serum specific immunoglobulin E from a pool of 5 patients who were allergic to *C albicans* was 0.41 kU_A/L (range, 0.1-3.06/kU_A/L).

specimens and erroneously classified as a contaminant. Nevertheless, it has been cultured under sterile conditions at autopsy, thus suggesting true bronchial colonization [6]. Although not as common as ABPA, cases of ABPC have also been reported [2-5].

There is evidence that appropriate management of ABPA may limit the extent of pulmonary damage and improve pulmonary physiology [7]; therefore, other allergic bronchopulmonary mycoses could also benefit from the same management. Treatment has traditionally been based on corticosteroids and, occasionally, itraconazole as a corticosteroid-sparing therapy or in patients with a slow response to corticosteroids.

Omalizumab is a recombinant DNA–derived humanized IgG1 monoclonal antibody that selectively binds to human IgE. It inhibits binding of IgE to the high-affinity IgE receptor on the surface of mast cells and basophils, thus limiting the degree of release of mediators and downregulating the presence of FcεRI on the surface of these cells. Omalizumab is indicated for adults with moderate to severe persistent asthma and positive skin test results or in vitro reactivity to perennial aeroallergens and whose symptoms are inadequately controlled with inhaled corticosteroids. Efficacy after treatment with recombinant anti-IgE antibodies has been reported in ABPA [8], but there are no data regarding its efficacy in other ABPM.

We present a case of ABPC. To the best of our knowledge, this is the first report of ABPC successfully treated with omalizumab. Although this drug's indications are currently limited to moderate to severe persistent asthma, omalizumab and other anti-IgE antibodies could play an increasingly important role in high-affinity IgE receptor diseases.

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References

1. Hinson KF, Moon AJ, Plummer NS. Broncho-pulmonary aspergillosis: a review and report of eight new cases. Thorax. 1952;7:317-33.
2. Matsumoto H, Niimi A, Suzuki K, Kawai M, Matsui Y, Amitani R. Allergic granulomatous angiitis (Churg-Strauss syndrome) associated with allergic bronchopulmonary candidiasis. Respiration. 2000;67:577-9.
3. Pinson P, Van der Straeten M. Fibrotic stage of allergic bronchopulmonary candidiasis. Chest. 1991;100:565-7.
4. Lee TM, Greenberger PA, Oh S, Patterson R, Roberts M, Liotta JL. Allergic bronchopulmonary candidiasis: case report and suggested diagnostic criteria. J Allergy Clin Immunol. 1987;80:816-20.
5. Akiyama K, Mathison DA, Riker JB, Greenberger PA, Patterson R. Allergic bronchopulmonary candidiasis. Chest. 1984;85:699-701.
6. Mullins J, Seaton A. Fungal spores in lung and sputum. Clin Allergy. 1987;8:525-33.
7. Lee TM, Greenberger PA, Patterson R, Roberts M, Liotta JL. Stage V (fibrotic) allergic bronchopulmonary aspergillosis: a review of 17 cases followed from diagnosis. Arch Intern Med. 1987;147:319-23.
8. van der Ent CK, Hoekstra H, Rijkers GT. Successful treatment of allergic bronchopulmonary aspergillosis with recombinant anti-IgE antibody. Thorax. 2007;62(3):276-7.
9. Dreborg S. Standardization of allergenic preparations by in vitro and in vivo methods. Position paper: Allergen standardization and skin testing. The European Academy of Allergology and Clinical Immunology. Allergy. 1993;48:63-70.

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Use of a Short Messaging Service System to Provide Information About Airborne Pollen Concentrations and Forecasts

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Key words: Aerobiology. Allergy. Forecast. Pollen. Short messaging service (SMS).

Palabras clave: Aerobiología. Alergia. Pronóstico. Polen. SMS (Servicio de mensajes cortos).

Table. Results of a Questionnaire Answered by 132 Patients to Assess Their Knowledge of Pollen Information Systems and Interest in Receiving Pollen Information Via SMS

Knowledge of pollen information systems	80 (60%)
Knowledge of a website that provides pollen information	22 (17%)
Knowledge of pollen information sent via SMS	20 (15%)
Interest in receiving pollen information via SMS	118 (90%)
– Weekly	47 (36%)
– Monthly	30 (23%)
– Daily	22 (17%)
– Fortnightly	19 (15%)
– Only in the spring	75 (57%)
– Throughout the year	37 (28%)

Abbreviation: SMS, short messaging service.

Information on airborne pollen concentrations is invaluable for the diagnosis and treatment of allergic diseases. Patients who are allergic to pollen can also benefit from this information, especially if they can get an up-to-date or early prognostic estimate of pollen concentrations.

Almost the whole population of our Autonomous Community owns a mobile telephone. Hence, information disseminated via this medium has the potential to reach the entire interested population. In this sense, the short messaging service (SMS) system may be an appropriate method of providing data on the pollen concentrations and forecasts. We currently obtain this information from the following sources: 1) a fixed Burkard volumetric trap, which continuously analyzes the atmosphere; 2) 2 portable Burkard volumetric traps that take specific samples at solar noon; 3) phenological observations of the plants that are the principal sources of pollen; 4) daily meteorological data; and 5) comparison with data from previous years since 1993. The resultant information provides a model or pattern for each pollen type [1].

The information obtained is disseminated through the research group's website, *http://www.aerouex.es*, and during 2007 and 2008 it was also distributed weekly via SMS without charge to people who had registered on the website. The message sent included concentrations of total pollen and of the 3 to 4 most abundant pollen types, indicating current intensity and the forecast for the following days.

Between February and March 2008, a survey was conducted among patients from the Allergology Department of the Infanta Cristina University Hospital in Badajoz to assess the level of interest in pollen information and in the possibility of receiving this information via SMS (Table).

Between 2007 and 2008, we sent 12 200 SMS, for which demand increased steadily. At the end of June 2008, there were 878 registered users, of whom 85% had provided their mobile telephone number to receive the SMS. The greatest increments in registrations were observed after local press reports about the system.

The usefulness of information on pollen concentrations is widely accepted by allergologists. Furthermore, SMS is increasingly used in medicine with various objectives: monitoring and treatment of certain diseases, as reminders of medical appointments, or to provide information to family about hospitalized patients. It has been proven to reduce health care costs and improve patient quality of life [2-9]. However, we were unable to find data in the literature on the use of SMS as a means of providing information to allergic patients. Although information on pollen concentrations is also provided via Internet in many countries, in Spain, only half the population have access to this medium in some Autonomous Communities [10].

The cost of sending messages to mobile phones can be borne institutionally or by the person interested in receiving them. Indeed, it could be argued that institutional involvement would be justified if the information provided a social or economic benefit. One option would be to offer the information to interested parties at a reasonable price. We continue to offer our information free of charge in 2009, and we provide the possibility of receiving the information on demand by sending an SMS to the number 5399 with the word *polen* in the text. This information is updated daily in spring, and weekly for the rest of the year.

In our opinion, SMS is an excellent channel for keeping allergic patients informed about pollen concentrations. We found that the service was well accepted, although the benefits and effectiveness should be evaluated using satisfaction questionnaires and/or assessment of how the patient controls the illness.

These data were presented in part in abstract and poster form at the XXVII Congress of the EAACI, Barcelona, June 7-11, 2008.

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References

1. Chappard C, Bonnevial J, Colson M, Mathern G, Emonot A. Forecast of pollination dates and relation to onset of allergic pathology. Aerobiologia. 2004;20:35-42.

2. Lee HR, Yoo SK, Jung SM, Kwon NY, Hong CS. A Web-based mobile asthma management system. J Telemed Telecare. 2005;11:56-9.
3. Yoon KH, Kim HS. A short message service by cellular phone in type 2 diabetic patients for 12 months. Diabetes Res Clin Pract. 2008;79:256-61.
4. Robinson S, Perkins S, Bauer S, Hammond N, Treasure J, Schmidt U. Aftercare intervention through text messaging in the treatment of bulimia nervosa--feasibility pilot. Int J Eat Disord. 2006;39:633-8.
5. Fjeldsoe BS, Marshall AL, Miller YD. Behavior change interventions delivered by mobile telephone short-message service. Am J Prev Med. 2009;36:165-73.
6. Neville RG, Reed C, Boswell B, Sergeant P, Sullivan T, Sullivan FM. Early experience of the use of short message service (SMS) technology in routine clinical care. Inform Prim Care. 2008;16:203-11.
7. Jareethum R, Titapant V, Chantra T, Sommai V, Chuenwattana P, Jirawan C. Satisfaction of healthy pregnant women receiving short message service via mobile phone for prenatal support: A randomized controlled trial. J Med Assoc Thai. 2008;91:458-63.
8. Downer SR, Meara JG, Da Costa AC, Sethuraman K. SMS text messaging improves outpatient attendance. Aust Health Rev. 2006;30:389-96.
9. Huang F, Liu SC, Shih SM, Tao YH, Wu JY, Jeng SY, Chang P. A Web-based short messaging service system to enhance family-centered surgical patient care. Stud Health Technol Inform. 2006;122:163-6.
10. AIMC (Asociación para la Investigación de Medios de Comunicación) Audiencia de Internet, Octubre/Noviembre 2008. Available from: www.aimc.es/aimc.php

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Immediate Hypersensitivity to Latex in the Absence of Demonstrable Specific Immunoglobulin E

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Key words: Latex. Allergy. Glove use test. Basophil activation test.

Palabras clave: Látex. Alergia. Test del guante. Test de activación de basófilos.

Allergy to natural rubber latex (NRL) is commonly encountered in the allergy clinic. Diagnosis is based on a strong history of type I hypersensitivity reaction after contact with NRL and supported by the results of skin prick testing (SPT), serum specific immunoglobulin E (SSIgE), and/or the basophil activation test (BAT). Reported sensitivity and specificity rates vary depending upon the extract or kit used, and it is unusual in clinical practice for all the diagnostic tests to be negative in the presence of a strong clinical history. The combined sensitivity and specificity of the diagnostic tests mentioned above has not been reported. BAT showed a sensitivity of 100% in a small group of clinically reactive patients with no specific IgE demonstrable by SPT or SSIgE [1]. In cases where the diagnostic tests are not confirmatory, provocation testing with NRL gloves has been recommended [2], despite the potential risk of anaphylaxis. We use a locally modified glove use test (Figure).

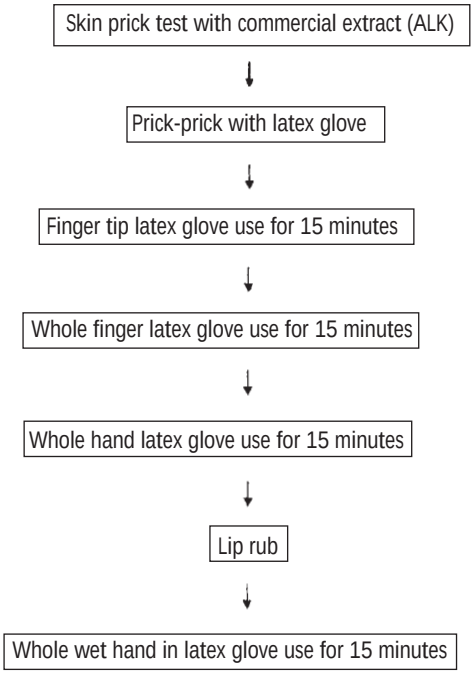

Figure. Natural rubber latex graded challenge.

To highlight the difficulties in diagnosing NRL allergy, we report 2 patients with a strong history of immediate hypersensitivity reactions to latex in the absence of demonstrable SSIgE (Pharmacia CAP, Phadia Ltd, Milton Keynes, UK), negative SPT (ALK-Abello Ltd, Hungerford, UK), negative prick-prick test with an NRL glove, and, in 1 patient, negative BAT.

A 53-year-old female health care assistant presented with a 5-year history of pruritis and erythema developing within minutes of contact with an NRL glove. She also experienced proximal urticaria and, on 2 occasions, shortness of breath and tightness of the throat. The patient had a history of grass pollen allergy and epilepsy. Application of the glove use test

on wet hands induced intense pruritis and erythema almost immediately, and this extended to the forearm when the test was terminated. The BAT result was positive for expression of CD63.

A 27-year-old female shop assistant had a history of recurrent local irritation and swelling after contact with a condom. Following normal vaginal delivery in an obstetric unit where no NRL avoidance measures were taken, she developed significant inflammation in her genitalia requiring a prolonged stay in hospital. She also had a history of mild asthma and chronic idiopathic urticaria, which was in remission at the time. Application of the glove use test produced no symptoms, although rubbing the mucosa of the lip with the NRL glove resulted in pronounced swelling. The BAT was negative for expression of CD63.

This report demonstrates that immediate hypersensitivity to latex can occur in the absence of demonstrable specific IgE and a negative BAT result. Interestingly, neither case showed a positive response to prick-prick skin testing despite a positive result with provocation testing using the same glove. One possible explanation for this discrepancy is that non-IgE–mediated mechanisms may be involved, although it is more likely that conventional diagnostic methodologies were not sensitive enough to detect specific IgE. It is plausible that specific IgE in these patients is directed against an epitope that was either not present at a sufficient concentration or was absent or denatured in the SPT extract and in vitro tests. Chromatographic studies to separate the NRL proteins in the glove may be used to identify undetermined latex antigens in such circumstances. This could pave the way for the development of additional diagnostic approaches; however, such studies are outside the remit of our clinical service.

Improved diagnostic testing is necessary because of the small yet real risk of anaphylaxis associated with provocation testing, which should only be undertaken when the history is suggestive and diagnostic test results are indeterminate. An accurate diagnosis of latex allergy is paramount, since it has important health, occupational, and medicolegal implications.

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References

1. Nettis E, Colanardi MC, Dambra PP, Capuzzimati L, Loria MP, Ferrannini A, Vacca A and Tursi A. Flow cytometric basophil activation test: detection of CD63 expression as a useful aid to diagnosis of latex allergy. Ann Allergy Asthma Immunol. 2006 Nov; 97:715-16.
2. Hamilton RG, Peterson EL and Ownby DR. Clinical and laboratory-based methods in the diagnosis of natural rubber latex allergy. J Allergy Clin Immunol. 2002 Aug; 110(2):S47-56.

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Anaphylaxis to Mango Fruit and Cross-reactivity With *Artemisia vulgaris* Pollen

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Palabras clave: Anafilaxia. *Artemisia vulgaris*. Reactividad cruzada. Mango. Síndrome polen-frutas.

Anaphylactic reactions to mango fruit (*Mangifera indica*) are extremely rare, with only 8 cases reported worldwide [1-7].

Mango allergy may occur in isolation or in association with pollen or latex allergy [5,8]. One study [9] demonstrated that allergens weighing 40, 43, and 67 kDa in mango fruit extract were responsible for cross-reactivity to Artemisia pollen, birch pollen, celery, and carrot. Another 14-kDa allergen was also identified in mango, with cross-reactivity to celery and birch pollen, but not to *Artemisia*.

We report the case of a 39-year-old woman who had an anaphylactic reaction immediately after ingestion of fruit salad containing fresh mango, strawberry, kiwi, orange, and pineapple. She experienced oral allergy syndrome, pruritus of the palms, facial angioedema, hoarseness, nausea, vomiting, and respiratory distress. She had previously eaten all these fruits, except mango, with no allergy symptoms. She was admitted to the emergency department, where she received adrenaline and corticosteroids, and her clinical condition improved. She subsequently ate all the culprit fruits except mango, with no reaction. She had allergic rhinitis with sensitization to house dust mites and *Artemisia vulgaris* pollen, but no history of asthma, urticaria, or food or latex allergy. She denied allergy symptoms to other foods, including celery, carrot, anise, cashew, and pistachio nuts.

Skin prick tests (SPT) with commercial extracts and prick-to-prick tests (SPPT) with fresh fruit were performed. The results were considered positive if the wheal had a mean

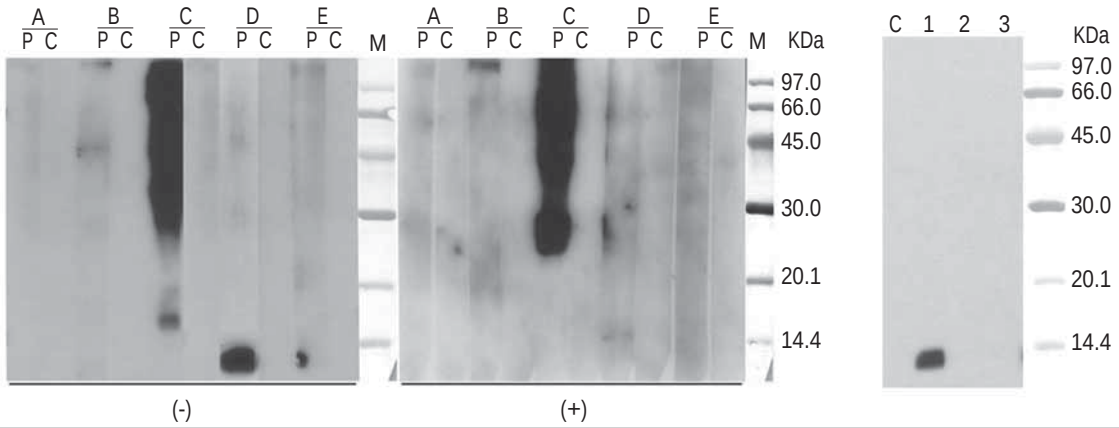

Figure. Left: SDS-PAGE immunoblotting results for extracts from *Lolium perenne* pollen (A), *Olea europaea* pollen (B), *Artemisia vulgaris* pollen (C), mango pulp (D), *Betula verrucosa* pollen (E). Lane P, patient's serum; lane C, control serum (pool of sera from non atopic subjects); lane M, molecular mass marker. (-) samples without 2-mercaptoethanol (nonreducing electrophoretic conditions), (+) samples with 2-mercaptoethanol (reducing electrophoretic conditions). Right: SDS-PAGE immunoblotting-inhibition results with mango pulp extract in the solid phase. Lane C, control serum (pool of sera from non atopic subjects); lane 1, patient's serum; lane 2, patient's serum previously incubated with mango pulp extract (homolog inhibition and positive control of inhibition); lane 3, patient serum previously incubated with *Artemisia vulgaris* pollen extract; lane M, molecular mass marker. SDS-PAGE indicates sodium dodecyl sulfate polyacrylamide gel electrophoresis.

diameter ≥3 mm. SPT results were positive for mango (5 mm) and negative for strawberry, kiwi, orange, and latex. The results of SPPT with fresh fruit were positive for mango (7 mm) and negative for strawberry, kiwi, orange, and pineapple.

The serum specific immunoglobulin (Ig) E level to mango pulp was 5.96 kU_A/L and to the other fruits it was <0.35 kU_A/L (Unicap, Phadia, Uppsala, Sweden). Specific IgE levels to pollens were as follows: *Artemisia vulgaris* >100 kU_A/L, *Lolium perenne* 0.8 kU_A/L, *Olea europaea* 0.4 kU_A/L, and *Betula verrucosa* <0.35 kU_A/L.

We considered 2 hypotheses: co-sensitization to mango fruit and *Artemisia* pollen or cross-reactivity between them. A sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) immunoblotting assay was carried out under reducing and nonreducing conditions. The *Artemisia* pollen extract immunoblot under nonreducing conditions showed a broad IgE-binding area in the high molecular weight zone and a 17-kDa IgE-binding band. Under reducing conditions, the same broad high molecular weight area and a 25-28–kDa IgE-binding band were detected. The mango extract revealed a 13-kDa IgE-binding band under nonreducing conditions and a very faint 15-kDa band under reducing conditions. No IgE-binding bands were detected with extracts from *Lolium, Olea*, or *Betula* pollens. It is possible that the 15-kDa and 13-kDa bands that appeared in the mango extract under reducing and nonreducing conditions could represent different electrophoretic behaviors of the same protein, whose tertiary structure is altered by the reducing treatment. Cross-reactivity was assessed and confirmed by immunoblotting-inhibition assay using mango fruit in the solid phase. When the patient's serum was preincubated with *Artemisia vulgaris* pollen extract, no IgE-binding band was detected in mango fruit.

The patient was therefore diagnosed with mango fruit allergy, in the context of a pollen-fruit (*Artemisia*-mango) allergy syndrome manifesting as an anaphylactic reaction. She was informed about dietary restrictions and prescribed self-injectable adrenaline. The immunological study identified a 13-kDa protein from mango fruit involved in this cross-reactivity.

In regions such as southern Europe, where *Artemisia* pollen sensitization is prevalent [10], doctors must be aware of the potential role of cross-reactivity between this pollen and mango fruit in severe allergic reactions.

References

1. Rubin JM, Shapiro J, Muehlbauer P, Grolnick M. Shock reaction following ingestion of mango. JAMA. 1965;193:397-8.
2. Dang RW, Bell DB. Anaphylactic reaction to the ingestion of mango. Case report. Hawaii Med J. 1967;27(2):149-50.
3. Miell J, Papouchado M, Marshall AJ. Anaphylactic reaction after eating a mango. BMJ. 1988 Dec 24-31;297(6664):1639-40.
4. Armentia A, Sanchis E, Mendez J, Frutos J, De la Fuente R, Sánchez P. Anafilaxia por ingesta de mango. Alergol Inmunol Clin. 1994;7:105.
5. Duque S, Fernandez-Pellon L, Rodriguez F. Mango allergy in a latex-sensitized patient. Allergy. 1999;54(9):1004-5.
6. Hegde VL, Venkatesh YP. Anaphylaxis following ingestion of mango fruit. J Investig Allergol Clin Immunol. 2007;17(5):341-4.
7. Renner R, Hipler C, Treudler R, Harth W, Süß A, Simon JC. Identification of a 27 kDa protein in patients with anaphylactic reactions to mango. J Investig Allergol Clin Immunol. 2008;18(6):476-81.
8. Brehler R, Theissen U, Mohr C, Luger T. "Latex-fruit syndrome": frequency of cross-reacting IgE antibodies. Allergy. 1997;52:404-10.
9. Paschke A, Kinder H, Zunker K, Wigotzki M, Steinhart H, Weßbecher R, Vieluf I. Characterization of cross-reacting allergens in mango fruit. Allergy. 2001;56:237-42.

10. Spieksma FThM, von Wahl PG. Allergenic significance of Artemisia (mugwort) pollen. In: D'Amato G, Spieksma FThM, Bonini S, editors. Allergenic pollen and pollinosis in Europe. Oxford: Blackwell Sc Publ; l991. p. 121-4.

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ERRATUM

Isolated Growth Hormone Deficiency in a Patient with Immunoglobulin Class Switch Recombination Deficiency

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