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A case of anaphylaxis to Pollinex® Quattro MPL-4

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Key words

Anaphylaxis; subcutaneous allergen immunotherapy (SCIT); allergoid; monophosphoryl lipid A

Summary

We described the first case reported in literature of anaphylactic shock after administration of pollen extract vaccine chemically modified (allergoid) adsorbed onto L-Tyrosine depot adjuvanted with monophosphoryl lipid A (Pollinex® Quattro MPL-4).

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Introduction

Subcutaneous allergen immunotherapy (SCIT) is an approved efficacious treatment for respiratory allergy, confirmed by WHO Position Paper (1).

The incidence of fatal reactions, as reported in an American study, in twelve years of surveillance (1990-2001) is 3.4 per year (41 fatal immunotherapy reactions in 12 years). In particular, the fatality rate is estimated at 1 per 2.5 million injections approximately, according to the incidence rates reported by Lockey et al. and Reid et al. (2). An Italian prospective study conducted on 1738 subjects for a total of 60785 injections over a mean immunotherapy duration of 3 years (3) suggests that SCIT is safe, since systemic reactions occurred only in 3.6% of patients and 0.15% of injections, with only one grade 4 reaction per > 2000 courses.

Sublingual immunotherapy (SLIT) is generally considered to have a better safety profile: most reactions are local and transient and usually do not lead to interruption or cessation of treatment. Calderon et al. estimated that the incidence of SLIT-induced anaphylaxis is 1 case per 100 million SLIT administrations or per 526000 treatment years, no reaction observed was fatal (4).

Modified vaccines with pollen allergoid (chemically modified allergen with a lowered recognition by IgE allergen-specific antibodies) have been developed in order to make immunotherapy more effective, reduce side effects and improve compliance.

Allergy Pollinex® Quattro MPL-4 is a pollen extract vaccine (chemically modified by glutaraldehyde) adsorbed onto L-tyrosine with addition of the immunostimulatory adjuvant monophosphoryl lipid A (MPL). 4

MPL is a detoxified, attenuated form of the lipid A component of the lipopolysaccharide of *Salmonella Minnesota,* a Toll-like receptor 4 agonist.

The inclusion of MPL reduces the number of required injections (only 4) for effective SCIT and improves compliance (5).

In vitro studies on peripheral blood mononuclear cells from patients with seasonal allergic rhinitis to grass pollen showed that MPL added to grass pollen extract resulted in the suppression of allergen-induced peripheral Th2 cell responses, in favour a protective Th1 response (6).
Several studies demonstrated its clinical efficacy, safety, tolerability (7,8,9,10), improvement of patient's symptoms and combined medication/symptom scores (8,5).
In addition, this treatment is usually well tolerated. Local reactions, such as redness and swelling in injection site, are the most common reported symptoms. Systemic reactions are rare and mild (5).
For example, Crivellaro et all (11) reported in their study that only 1.37% of patients (510 in total) experienced an adverse systemic reaction (SR): all SRs were delayed (> 30 minutes), at grade 1 or 2; epinephrine was not required for any of the reactions, all resolved spontaneously or after administration of oral antihistamine.
No report of anaphylaxis is described in literature with this vaccine.

Case Description

We report the first case of anaphylaxis after administration of Pollinex® Quattro MPL.
A 50-year-old Caucasian male with a history of asthma and rhinitis since 1992, sensitized to grass, ragweed and birch, usually controlled his symptoms with frequent administration of inhaled salbutamol or disodium cromoglycate and oral antihistamine.
In February 2012 he started SCIT with Pollinex® Quattro MPL for grass pollen (concentrations at the end of the therapeutic cycle are of 21.5 mcg/ml and 13.64 mcg/ml for the major allergens, Phl p 1 and Phl p 5).
His clinical history presented arterial hypertension in therapy with beta-blocker, that was pre-emptively substituted with an angiotensin-II receptor blocker (olmesartan) before the start of the immunotherapy.
The patient, in good health, tolerated the first three injections (300, 800 and 2000 standardized unit SU). However, 10 minutes after the fourth administration (2000 SU), that had been properly executed, he presented palpebral swelling, conjunctivitis, rhinitis, asthma with serrated bronchospasm, hypotension (PA 70/60). The patient was initially treated with oral antihistamine and methylprednisolone IV but since the symptoms were fast-growing, he was administered twice with epinephrine 0.3 cc IM and beta agonist inhaler, and treatment with hydrocortisone was repeated. No biphasic anaphylaxis was observed.

Discussion

This case documents that although an allergoid, Pollinex® Quattro MPL is not risk free from systemic reaction. It is very important to underline that anaphylaxis must be treated immediately with an intramuscular injection of epinephrine, as death can occur within minutes. All anaphylaxis guidelines recommend prompt intramuscular injection of epinephrine, although they differ with regard to the importance of H1-antihistamines, H2-antihistamines, corticosteroids, and bronchodilators other than epinephrine (12).
Information should be collected on the role of potential amplifying factors and co-factors, such as concurrent use of beta-blockers or other medication (ACE inhibitors, FANS), viral infection, fever, emotional stress, disruption of routine, premenstrual status in females, and exercise (12).
Although ARBs are associated with a lower anaphylactic risk than angiotensin-converting enzyme (ACE) inhibitors (13), in our report we cannot exclude that this drug played a facilitating role.

Disclosure

The manuscript has not been published elsewhere and it's not under consideration elsewhere. The authors disclose any financial or personal relationship which could result in a conflict of interest.

References

1. Bousquet J, Lockey R, Malling HJ. WHO Position Paper Allergen Immunotherapy: Therapeutic Vaccines for Allergic Diseases. Allergy. 1998; Suppl 44:1-42.
2. Bernstein DI, Wanner M, Borish L, Liss GM. Twelve-year survey of fatal reactions to allergen injections and skin testing: 1990-2001. J Allergy Clin Immunol. 2004;113:1129-36.
3. Schiappoli M, Ridolo E, Senna G, Alesina R, Antonicelli L, Asero R, Costantino MT, Longo R, Musarra A, Nettis E, Crivellaro M, Savi E, Massolo A, Passalacqua. A prospective Italian survey on the safety of subcutaneous immunotherapy for respiratory allergy. Clin Exp Allergy. 2009;39:1569-1574.
4. Calderon M.A., Simons FE, Malling HJ, Lockey RF, Moingeon P, Demoly P. Sublingual allergen immunotherapy: mode of action and its relationship with the safety profile. Allergy. 2012;67:302-311.
5. Patel P, Salapatek AM. Pollinex Quattro: a novel and well-tolerated, ultra short-course allergy vaccine. Expert Rev Vaccines. 2006;5:617-629.
6. Puggioni F, Durham SR, Francis JN. Monophosphoryl lipid A (MPL) promotes allergen-induced immune deviation in favour of Th1 responses. Allergy. 2005;60:678-684.
7. Drachenberg KJ, Heinzkill M, Urban E, Woroniecki SR. Efficacy and tolerability of short-term immunotherapy with pollen allergoids adjuvanted by monophosphoryl lipid A (MPL) for children and adolescents. Allergol Immunopathol. 2003;31:270-7.
8. Drachenberg KJ, Wheeler AVV, Stuebner P, Horak F. A well-tolerated grass pollen-specific allergy vaccine containing a novel adjuvant, monophosphoryl lipid A, reduces allergic symptoms after only four preseasonal injections. Allergy. 2001;498-505.
9. Mc Cormack PL, Wagstaff AJ. Ultra short course seasonal allergy vaccine (Pollinex® Quattro). Drugs. 2006;66:931-8.
10. Rosewich M, Schulze J, Fischer von Weikersthal-Drachenberg KJ, Zielen S. Ultra-short course Immunotherapy in children and ad-

olescent during a 3-yrs post-marketing surveillance study. Pediatr Allergy immunol. 2010;21:e185-e9.
11. Crivellaro M, Senna GE, Pappacoda A, Vanzelli R, Spacal B, Marchi G, Recchia G, Makatsori M. Safety of ultrashort-term sit with pollen allergoids adjuvanted by monophosphoryl lipid A: a prospective italian survey. Eur Ann Allergy Clin Immunol. 2011;43:58-60.
12. Simons FE, Ardusso LR, Bilò MB, El-Gamal YM, Ledford DK, Ring J, Sanchez-Borges M, Senna GE, Sheikh A, Thong BY. World Allergy Organization anaphylaxis guidelines: summary. J Allergy Clin Immunol. 2011;127:587-593.
13. Ruëff F, Przybilla B, Biló MB, Müller U, Scheipl F, Aberer W, Birnbaum J, Bodzenta-Lukaszyk A, Bonifazi F, Bucher C, Campi P, Darsow U, Egger C, Haeberli G, Hawranek T, Körner M, Kucharewicz I, Küchenhoff H, Lang R, Quercia O, Reider N, Severino M, Sticherling M, Sturm GJ, Wüthrich B. Predictors of severe systemic anaphylactic reactions in patients with Hymenoptera venom allergy: Importance of baseline serum tryptase–a study of the European Academy of Allergology and Clinical Immunology Interest Group on Insect Venom Hypersensitivity. J Allergy Clin Immunol. 2009;124:1047-54.