CASE REPORT

Coexistence of two types of allergic hypersensitivity to drugs

Joanna Glück, Barbara Rymarczyk, Barbara Rogala

Department of Internal Diseases, Allergology and Clinical Immunology, Medical University of Silesia, Zabrze, Poland

KEY WORDS

allergic hypersensitivity to drugs, fluoroquinolones, povidone-iodine (PVP-I)

ABSTRACT

Hypersensitivity to drugs is a complex diagnostic challenge. Detailed medical history remains the mainstay of drug hypersensitivity evaluation, which further determines diagnostic procedures, especially the types of skin tests to be performed. The current paper presents the case of a female patient with coexisting features of supposed immunoglobulin E (IgE) dependent allergic hypersensitivity to fluoroquinolones and those of non-IgE dependent allergic hypersensitivity to povidone-iodine. Hypersensitivity was diagnosed based on the appropriately selected skin tests.

INTRODUCTION Hypersensitivity to drugs is an important issue in day-to-day medical practice. Appropriate management of suspected drug hypersensitivity is even more difficult because available diagnostic methods are of limited specificity, sensitivity, and predictive-value. Detailed analysis of the patient's history is the basis for drug hypersensitivity evaluation and determines further diagnostic procedures, especially the types of skin tests to be performed. We present the case of a female patient with features of immunoglobulin E (IgE) dependent allergic hypersensitivity to fluoroquinolones, most probably coexisting with those of non-IgE dependent allergic hypersensitivity to povidone-iodine (PVP-I).

CASE REPORT A 42-year-old woman was referred to the hospital with a suspicion of PVP-I and fluoroquinolone hypersensitivity. In October 2006, the patient underwent the right upper eyelid chalazion removal. The ophthalmologist administered prophylactic treatment with local, 0.3% ofloxacin solution (Floxal®, Mann) eye drops. As a result of ocular drug instilling, palpebral edema and cheekbone skin itching associated with lacrimation, sneezing, and nasal secretion occurred. The patient used 10 mg/d cetirizine (Zyrtec UCB®) and the symptoms resolved quickly.

In December 2006, the patient was prescribed tablets of PVP-I a iodinated disinfectant intravaginally (Polseptol®, GlaxoSmithKline SA Poland). Several hours after the administration of the first tablet, generalized itching, erythema, edema, and micropapular confluent lesions occurred and persisted for a few days. Two days after the onset of symptoms, the patient took cetirizine (Zyrtec UCB®), and as there was no improvement, clemastin (Clemastinum®, Polfa Warszawa) was administered. The symptoms gradually resolved within 4–5 days.

Regarding previous diseases, at the age of 4, the patient underwent appendicitis surgery. At the age of 32, she was admitted to the department of dermatology and venereology at the city hospital, with the diagnosis of allergic dermatitis and facial edema, oral and vaginal candidasis, severe dental caries. The patient was diagnosed with chronic allergic rhinitis. She reported excessive reactivity to chemicals and cosmetics (Nivea cream – local edema). A family history revealed contact allergy in the patient's mother.

On physical examination the patient was normal. Additional tests showed thyroid insufficiency (free thyroxine 4–0.9 ng/dl, normal values: 0.99–1,7; thyroid stimulating hormone – 5.86 μIU/ml, normal values: 0.27–4.2).

The following baseline diagnosis was made on the basis of the patient's history:

1 IgE dependent allergic hypersensitivity to fluoroquinolones

2 non-IgE dependent allergic hypersensitivity to PVP-I

3 abnormal thyroid function.

Correspondence to:
Joanna Glück, MD, PhD, Katedra i Klinika Chorób Wewnętrznych, Alergologii i Immunologii Klinicznej, Śląski Uniwersytet Medyczny, ul. 3 Maja 13–15, 41-800 Zabrze, Poland, phone/fax: + 48-32-271-81-10, e-mail: joagluck@mp.pl

Received: August 8, 2008.
Revision accepted: September 1, 2008.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2009; 119 (6): 418-421
Translated by Elżbieta Cybulska, MD

The following diagnostic tests were scheduled: skin prick tests with common environmental allergens, total IgE plasma level assessment, patch tests with a standard set of contact allergens (European standard), prick tests with undiluted parenteral fluoroquinolone preparation, intracutaneous tests with the same fluoroquinolone preparation starting at the dilution of 1:1000, and patch tests with a PVP-I preparation. Further endocrinological evaluation was also planned.

Considering the patient's history (persistent allergic rhinitis diagnosed in 1997), prick tests with common environmental allergens were performed (Allergopharma, Germany). Negative results were obtained for all tested allergens, i.e. pollen, weeds, grass, grain, mold, *Dermatophagoides pteronyssinus* and *Dermatophagoides farina*e. Contact tests with a set of standard Hal Allergy allergens were performed. Moderate hypersensitivity to wool alcohols (30%) was observed. The total IgE level was measured using an immunoenzymatic assay (Allergopharma) and the result was 74 kU/l. A skin prick test with a parenteral solution of undiluted ciprofloxacin showed a positive result: an 8 mm wheal and an 18 mm erythema.

Patch tests with PVP-I were installed with white soft paraffin as the vehicle, which also served as negative control. The tests were performed in IQ chambers (Chemotechnique Diagnostic, Malmö, Sweden). There were no hypersensitivity features in an open patch test (20-minute occlusion); in a patch test with 24 hour occlusion time, flare and a wheal were observed after 48 hours (recorded with a visual analog scale according to Darsow).

Ultrasound was performed due to suspected thyroid abnormalities and demonstrated increased thyroid echogenicity, its dimensions being slightly above normal. The consultant endocrinologist diagnosed subclinical hypothyroidism, and considering episodic sinus tachycardia, he recommended low-dose (25 μg/d) thyroid hormone substitution.

Finally, the patient was diagnosed with IgE-mediated allergic hypersensitivity to fluoroquinolones, non-IgE- mediated allergic hypersensitivity to PVP-I and subclinical hypothyroidism. Further management included restrictions on the use of fluoroquinolone and iodinated disinfectants. Care was recommended when using different iodine preparations. Low-dose thyroid hormone substitution was initiated.

DISCUSSION The present case relates to two types of allergic hypersensitivity to two different drug classes coexisting in the same individual: the IgE-mediated allergic hypersensitivity to fluoroquinolones and the non-IgE dependent allergic hypersensitivity to PVP-I. The patient reported conflicting data on signs and symptoms associated with the use of the medications tested and this was analyzed in this case report. Ocular administration of fluoroquinolones caused symptoms typical of IgE- mediated allergic conjunctivitis and rhinitis. The symptoms including lacrimation, sneezing, nasal discharge, and skin itching were sensitive to antihistamines. Local (intravaginal) use of PVP-I produced symptoms indicative of non-IgE-mediated allergic hypersensitivity reactions. Medical history was the basis for diagnostic procedures conducted in line with the recommendations of the European Academy of Allergology and Clinical Immunology interest group on drug hypersensitivity (European Network for Drug Allergy – ENDA).[1]

According to ENDA guidelines, prick and intradermal tests are done when anaphylactic symptoms, bronchial constriction, conjunctivitis, rhinitis and/or urticaria or angioneurotic edema occur. Patch tests are performed in the case of acute generalized exanthematous pustulosis, contact dermatitis, drug-induced skin eczema, fixed erythema, photoallergic reactions, leukocytoclastic vasculitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis. Therefore, a skin prick test was performed to diagnose suspected allergic hypersensitivity to fluoroquinolone, and patch tests were used in diagnostic evaluation of PVP-I allergic hypersensitivity. The skin prick test was performed using an undiluted fluoroquinolone preparation for parenteral use. The subsequent diagnostic evaluation stages included intracutaneous tests performed at gradually increasing dilutions (starting with dilution of 1:1000), and an oral provocation test. Because of a clearly positive result of the skin prick test, no further evaluation was required and hypersensitivity to this drug class was diagnosed.

Allergic hypersensitivity to fluoroquinolones is an important medical issue, especially that this antibiotic class is administered increasingly more often and is not uncommon in the first-line treatment. The frequent use of this antimicrobial drug class is associated with increasing bacterial resistance to their effect on the one hand, and with allergic hypersensitivity reaction on the other.

Fluoroquinolones have been used since the 1980s, and because of their wide antibacterial spectrum they are particularly effective for microorganism resistance to other antibiotics, and also for confirmed hypersensitivity reactions to other chemotherapeutic agents, e.g. β-lactams because of the absence of cross-reactivity.

Fluoroquinolones may cause a wide range of hypersensitivity reactions, including IgE dependent allergic reactions, urticaria, angioneurotic edema, itch, anaphylactic shock and other anaphylactic reactions, as well as the symptoms of non-IgE-mediated allergic hypersensitivity reactions such as maculopapular rash, drug-induced fever, erythema nodosum, or acute generalized exanthematic pustulosis. It has been estimated that allergic hypersensitivity reactions occur in 2–3% of individuals treated with fluoroquinolones.[2] Similarly to other antibiotics and chemotherapeutic agents, AIDS patients are particularly predisposed to allergic hypersensitivity to fluoroquinolones.[3]

Davila et al., who used prick and intracutaneous tests, histamine release test, the radio-allergosorbent test, and oral provocation in diagnosing allergic hypersensitivity to drugs, assessed cross-reactivity between fluoroquinolones of different generations.[4] They demonstrated an important role of cross reactions between individual drugs, and at the same time recommended avoidance of any drug of the fluoroquinolone class should allergic hypersensitivity to one of its preparations occur. Cross-reactivity to various fluoroquinolone derivatives has also been confirmed by other authors.[5] Therefore, we used a different fluoroquinolone derivative, ciprofloxacin, and based on a positive result of the skin prick test with this drug avoidance of all fluoroquinolones was recommended. Of note, if fluoroquinolone use is absolutely necessary in an individual with known allergic hypersensitivity, an attempt to induce a state of temporary tolerance might be undertaken. The efficacy of this approach has been reported.[6] However, having previously analyzed the possibility of alternative antimicrobial agent administration, it is necessary to assess the risk-benefit ratio of such procedure.

Allergic hypersensitivity to iodinated disinfectants including PVP-I is another clinically interesting issue. Iodinated agents have been used as antiseptics and disinfectants for centuries. They are available as aqueous and alcoholic solutions, aerosols, ointments and ready-made dressings. Because of its high effectiveness in combating microorganisms and its weak irritating properties, the PVP-I solution is the most commonly used one. However, this agent may cause local skin irritations, though less severe than those caused by aqueous iodine solutions. PVP-I disintegrates as it touches the skin or the mucous membranes, and releases iodine, which has an antibacterial effect on the Gram-positive and Gram-negative bacteria, mycobacteria, viruses, fungi, yeasts, and protozoans. In the reported case, the local use of a PVP-I agent (Polseptol®) on vaginal mucous membranes resulted in generalized skin lesions, indicating an allergic mechanism (lesion generalization), and not uniquely a consequence of irritation. A patch test with the use of a PVP-I solution in white soft paraffin confirmed the baseline diagnosis of hypersensitivity reaction to this antiseptic agent. However, there is a possibility of obtaining a false positive test result. In a study on a group of 500 individuals, in 14 (2.8%) subjects the patch test result with the use of 1% aqueous PVP-I solution was positive, but only in 2 (0.4%) subjects cutaneous lesions were present in an open-label test with a drug concentration of 10%.[7]

The lack of standardization of PVP-I prick tests is undoubtedly a serious problem. Since a marked individual variability has been demonstrated in the tests, it is necessary to correlate the diagnostic test results with clinical data.[8] Thus, it is vital to consider the probability of an irritant reaction rather than allergic hypersensitivity. Non-IgE-mediated PVP-I allergic hypersensitivity reactions are not rare; however, sporadically, IgE-mediated allergic hypersensitivity reactions can be observed. A case of anaphylactic shock in reaction to intravaginal PVP-I administration has been reported.

The most important conclusions that can be drawn from the presented case are listed below.

1 With the suspicion of drug hypersensitivity it is necessary to choose the appropriate diagnostic test based on clinical signs and symptoms.

2 Local (ocular, intravaginal) drug administration may cause generalized allergic hypersensitivity reactions.

3 Drug hypersensitivity reactions may be accompanied by thyroid disorders.

REFERENCES

1 Brockow K, Romano A, Blanca M, et al. General considerations for skin tests procedures in the diagnosis of drug hypersensitivity. Allergy. 2002; 57: 45-51.

2 Schmid DA, Depta JP, Pichler WJ. T cell-mediated hypersensitivity to quinolones: mechanisms and cross-reactivity. Clin Exp Allergy. 2006; 36: 56-69.

3 Al-Hedaithy MA, Noreddin AM. Hypersensitivity anaphylactoid reaction to pefloksacin in a patients with AIDS. Ann Pharmacotherapy. 196; 30: 612-614.

4 Davila I, Diez ML, Quirce S, et al. Cross-reactivity between quinolones. Report of three cases. Allergy. 1993; 48: 388-390.

5 Gonzales I, Lobera T, Blanco A, del Pozo MD. Immediate hypersensitivity to quinolones: moxifloxacin cross-reactivity. J Investig Allergol Clin Immunol. 2005; 15: 146-149.

6 Bircher AJ, Rutishauser M. Oral „desensitization" of maculopapular exanthema from ciprofloxacin. Allergy. 1997; 52: 1246-1248.

7 Lee S, Ziai H, Maibach H. Allergic contact dermatitis from iodine preparations: a conundrum. Contact dermatitis. 2005; 52: 184-187.

8 Adachi A, Fukunaga A, Hayashi K, et al. Anaphylaxis to polivinylopyrrolidone after vaginal application of povidone-iodine. Contact Dermatitis. 2003; 48: 133-136.

Współistnienie dwóch różnych rodzajów nadwrażliwości alergicznej na leki

Joanna Glück, Barbara Rymarczyk, Barbara Rogala

Katedra i Klinika Chorób Wewnętrznych, Alergologii i Immunologii Klinicznej, Śląski Uniwersytet Medyczny, Zabrze

SŁOWA KLUCZOWE

fluorochinolony, jodopowidon, nadwrażliwość alergiczna na leki

STRESZCZENIE

Nadwrażliwość na leki jest trudnym problemem diagnostycznym. Podstawą jej diagnostyki pozostaje szczegółowo zebrany wywiad, który decyduje o dalszym postępowaniu diagnostycznym, a zwłaszcza o rodzaju wykonywanych testów skórnych. Opisany przypadek dotyczy chorej, u której występowały równocześnie cechy nadwrażliwości alergicznej prawdopodobnie zależnej od immunoglobuliny E (IgE) na fluorochinolony i nadwrażliwości alergicznej niezależnej od IgE na jodopowidon. Rozpoznanie nadwrażliwości ustalono na podstawie wyników odpowiednio dobranych testów skórnych.

Adres do korespondencji:
dr med. Joanna Glück, Katedra i Klinika Chorób Wewnętrznych, Alergologii i Immunologii Klinicznej, Śląski Uniwersytet Medyczny, ul. 3 Maja 13–15, 41-800 Zabrze, tel./fax: 032-271-81-10, e-mail: joagluck@mp.pl
Praca wpłynęła: 04.08.2008.
Przyjęta do druku: 01.09.2008.
Nie zgłoszono sprzeczności interesów.
Pol Arch Med Wewn. 2009; 119 (6): 418-421