

CASE REPORT/OPIS PRZYPADKU

Local allergic rhinitis or local allergic conjunctivitis?

Lokalny alergiczny nieżyt nosa czy lokalne alergiczne zapalenie spojówek

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ABSTRACT

Differential diagnosis of the local allergic reaction is mainly based on conjunctival, nasal and bronchial provocation tests, which, in theory, may lead to further treatment. The most common local response can be observed in the nasal mucosa. In the long run, it may manifest itself by coexisting local reactions in other areas such as the eye and/or bronchial tree. In a 45-year-old patient who has been experiencing health problems typical for grass/grain allergy for nearly 10 years, two challenges were carried out, i.e. nasal and conjunctival provocation tests, and the latter elicited a highly positive response to the applied allergen compared to the intranasal route. When there are clinical discrepancies in the local allergic reaction, allergen provocation tests should be considered in the differential diagnosis and, when the results are negative, conjunctival challenge should be considered as well.

KEY WORDS

allergy, conjunctival allergen challenge, local allergic conjunctivitis, local allergic rhinitis, nasal allergen challenge, differential diagnosis.

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INTRODUCTION

The local allergic reaction (LAR) is characterized by a local inflammatory response (sIgE antibody production) mediated by Th2 lymphocytes without the presence of sIgE on either the mast cells of the skin or in the serum,

without systemic atopy [1, 2]. In practice, it means that in patients diagnosed with LAR (as opposed to those undergoing differential diagnosis of allergy by performing skin tests, sIgE), the allergen challenge is the only method that can determine the final diagnosis of local response (in addition to history and physical examination) [3].

Depending on the location of the response, conjunctival, nasal and bronchial provocation can be distinguished, along with the basophil activation test (BAT) (a so-called *challenge in a test tube*). They are performed in a hospital/office/laboratory setting and simulate the natural response of the organism to the administered allergen at each level of response. The nasal allergen challenge is particularly informative because not only the response from the provoked organ can be observed, but also because of the contribution of other organs/systems to the local immune response (nasal challenge may provoke a response from the eye and the lower respiratory tract) [4, 5]. This applies to both patients with general allergy (atopy) as well as to those with localized allergy (entopy) [1]. The standardized conjunctival provocation test is also crucial in the diagnosis of LAR with increasing doses of allergen administered to the conjunctivae according to the standardized test protocol. In those two types of tests, accompanying symptoms can be observed from other organs, e.g. nasal challenge can provoke itching, tears and redness of the eye, and when the eye is challenged, it can elicit nose itching, sneezing, watery secretion, and nasal congestion. The specificity and sensitivity of both tests are estimated to be very high [6], reaching on average 98% and 83%, respectively [7, 8].

It seems that LAR should be given priority over the response from each individual system or organ, i.e. local allergic rhinitis, local conjunctivitis, and local asthma [9, 10]. While interpreting the word *locally* in a literal sense, we focus on a response that is not general but rather limited to a certain area, which in the case of long-term observations [9] seems reasonable from a methodological and clinical point of view. However, there is evidence that isolated responses can be transferred to other organs and systems. It is particularly important in situations where, as with LAR and conjunctivitis, symptoms can overlap due to close proximity and affinity and they can be thought of selectively rather than as a group of local diseases or so-called multimorbidity [9, 10]. Similarly, according to the common theory of *one system, two diseases*, the coexistence of LAR and local asthma is important [9]. In each of the previously listed diseases, there is a local allergic reaction which, over many years, may also lead to a systemic response (atopy) [9].

CASE REPORT

A 45-year-old man presented to the Allergology Clinic in Warsaw because of the symptoms of allergy, which lasted for almost 10 years, including tears, itching of the eye and nose, runny nose and postnasal drip, which increased significantly in May, June and the first half of July. The history was positive with genetic predisposition as

his mother had allergy. In childhood, the patient received medications for asthma.

CLINICAL INFORMATION

On physical examination, the patient was evaluated to be in good health. On anterior rhinoscopy, swollen and pale bluish mucosa with watery secretion was observed. Further tests including the nitrogen oxide concentration in the air exhaled from the lower respiratory tract (22 ppb (EV (NOEx) 46 ml/s; VNO exhale 56 nl/min; pres. NO 12 cm H₂O; Conf. index 94%) and spirometry (FEV%VCmax 97% (37th percentile); FEV1 89%, FVCex 95%, PEF 97%) also showed no significant abnormalities. The nasal cytology results were as follows: columnar cells 71.2%, goblet cells 1.6%, basal cells 9.4%, squamous cells 4.1%, neutrophils 9.4%, eosinophils 14.3%. In the differential diagnosis of rhinitis, skin tests were performed (positive control – histamine 3/25, negative control – 0/0) and sIgE levels were tested, which clearly showed no sensitization to common environmental allergens including grass and grain pollen. Due to the discrepancy between the patient's history and the test results (negative skin tests and sIgE levels), it was decided to perform the nasal allergen challenge. This work has been financed by The importance of environmental factors in the allergization of patients with allergic rhinitis (National Science Centre N N402 5208 39). The study was approved by the Bioethics Committee at the Medical University of Warsaw (KB/79/2019).

ALLERGEN CHALLENGE

The observation of the nasal allergen challenge test according to the EAACI standard [4, 5] was limited to the early phase of the allergic reaction. The study was evaluated in three stages: after local acclimatization, administration of the control solution, and after local application of the allergen. At each stage, including the first stage, the objective nasal patency was assessed using acoustic rhinometry (Rhino, Provita Strzelce Opolskie) and a subjective scoring system (Total Nasal Score) after local acclimatization. In the second stage, 0.02 ml of the control solution was administered intranasally (0.9% NaCl + Phenol to both nostrils with the standardized atomizer), in which lyophilized grass/grain allergen was dissolved (at the next stage of the test). No significant increase in relative reactivity of the nasal mucosa to the control solution was observed, and hence the grass/grain allergen solution (5 000 SBU/ml, Allergopharma) was administered after a 15-minute delay. After another 15 min, the objective evaluation was made using acoustic rhinometry, which showed slight differences in the

TABLE 1. Acoustic rhinometry in the nasal provocation test

Nasal cavity	Area			Distance		
	First exam	Second exam	Third exam	First exam	Second exam	Third exam
Right side nasal cavity:						
MCA	0.83	0.91	0.94	1.24	1.23	1.28
First minimum	0.83	0.91	0.94	1.24	1.23	1.28
Second minimum	3.42	3.85	3.71	3.89	4.01	4.36
Volume (0–5)	11.94	11.8	11.0	–	–	–
Left side nasal cavity:						
MCA	0.71	0.69	0.51	1.71	1.70	2.19
First minimum	0.71	0.69	0.51	1.71	1.70	2.19
Second minimum	0.57	0.55	0.49	2.25	2.21	2.22
Volume (0–5)	9.07	9.05	9.01	–	–	–

reactivity of the nasal mucosa to the given allergen (Table 1).

On evaluation of subjective changes, minor discomfort was observed in the form of nasal pruritus (0.2/1 point) and moderate nasal congestion (0.4/2 point). As far as other extra-nasal symptoms were concerned, the itching of the corner of the eye (1/2 point) and mild na-

sal congestion (0.8/2 point) were observed. After visiting the doctor, i.e. the allergist, and due to continuing discrepancy between the clinical presentation and the result of the challenge (associated with eye symptoms), the conjunctival challenge was organized, similar to that with Allergopharma mixture of allergens. According to the commonly accepted diagnostic approach, the test was



FIGURE 1. The eye's response to the conjunctival challenge with the grass/grain pollen allergen: **A** – conjunctival challenge response to 500 SBE/ml, **B** – the response of the conjunctival challenge to the concentration of 1600 SBE/ml

a titration challenge starting with the smallest dose of 5 SBE/ml, through 50 SBE/ml, 160 SBE/ml, 500 SBE/ml, 1600 SBE/ml to the largest dose of 5000 SBE/ml (Allergopharma, Figure 1) The allergen was given alternately to the right and left corners of the eye with a standardized eye dropper at 15-minute intervals between doses. The response of the eye was evaluated by subjective assessment (Abelson's score: eye itching, redness, nasal symptoms).

The allergen administration preceded the administration of the control solution (0.9% NaCl + Phenol) to the conjunctiva on both sides. At the concentration of 500 SBE/ml, eye itching and lachrymation were observed (1/3 point), while at the dose of 1600 SBE/ml the itching (3/3 point) was accompanied by eye redness (2/3 point). At this stage, the conjunctival challenge was completed. During the provocation test, nasal symptoms occurred such as itching, watery secretion and congestion. As a result of the provocation tests, local conjunctivitis and rhinitis were diagnosed in the patient secondary to an allergy to grass and grain allergens. Shortly before and during the pollen season for grass, the patient received pharmacological treatment including second-generation oral antihistamine – bilastine (Clatra) at a dose of 20 mg daily, combined with antihistamine medicine in a single spray (25 µg of mometasone furoate and 600 µg of olopatadine, Ryaltris) at two doses to each nasal opening twice daily, and in the presence of eye symptoms – olopatadine (Opatanol) in eye drops of 1 mg/ml, one drop to each eye twice daily. The treatment fully controlled the symptoms

of allergic conjunctivitis and rhinitis. Furthermore, since the only causal treatment for allergic rhinitis, conjunctivitis and LAR is allergen-specific immunotherapy and the fact that it also helps prevent the development of new allergies and asthma, we are considering to use this therapy in our patient.

DISCUSSION

This is the first case report discussing the need for a broader differential diagnosis of LAR, which is mainly associated with LAR and is expanded with a provocation test other than nasal challenge, which included conjunctival allergen challenge in our patient (Figure 2) [1–3].

The hypothetical reliance on the result of the nasal challenge, as in our case report, carries a potential risk of not recognizing LAR. In the literature, local conjunctivitis is described as secondary to the underlying disease such as LAR rather than an isolated disease [9]. In patients with LAR, conjunctivitis is common at a rate of 48.8–64.5% of the patients vs. those with allergic rhinitis 61–61.9% of the total studied population [9, 11]. There is also evidence that, over time, in patients diagnosed with LAR including the eye involvement, the quality of life deteriorates; those patients are more likely to take medications to alleviate their symptoms and, what is important, other diseases develop in the course of LAR over time (such as food allergy, allergy to nonsteroidal anti-inflammatory drugs, atopic dermatitis or hives) [9, 11]. What is important, a prospec-

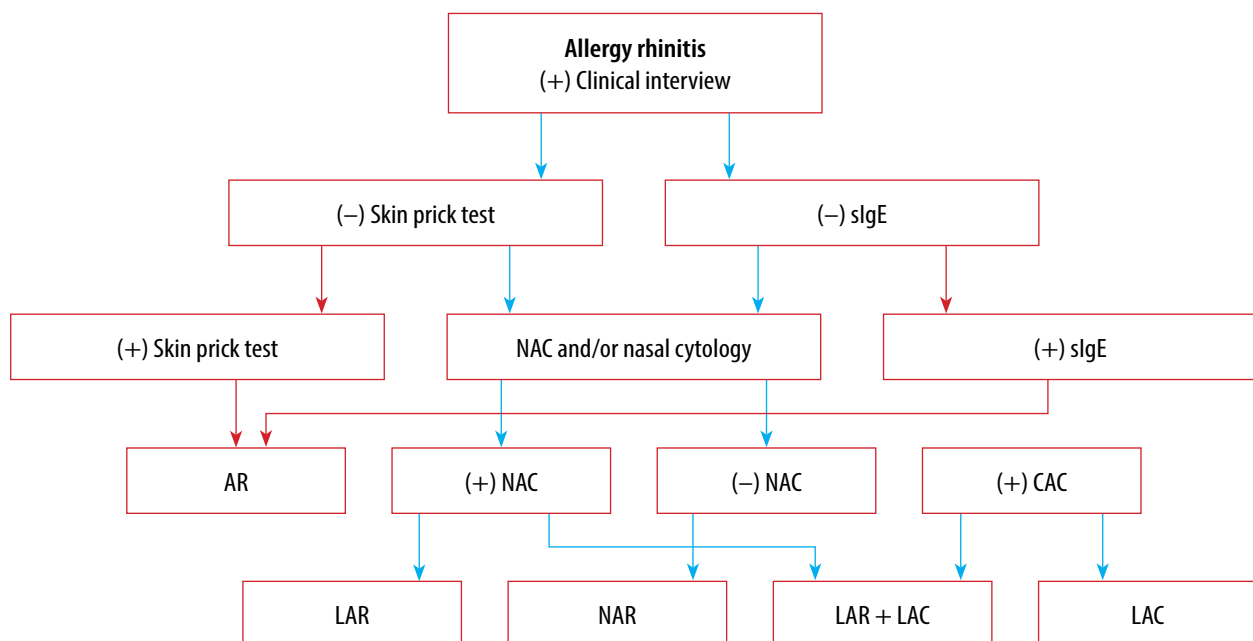


FIGURE 2. The modified algorithm for the diagnosis of conjunctivitis in a group of patients with a local allergic response [1–3]

AR – allergic rhinitis, NAC – nasal allergen challenge, LAR – local allergic rhinitis, NAR – non-allergic rhinitis, CAC – conjunctival allergen challenge, LAC – local allergic conjunctivitis.

tive study showed that LAR has a low conversion rate of local allergic reactions to systemic atopy (positive skin prick test and/or sIgE), which proves a distinct and specific clinical presentation of this disease. In addition, those patients tolerate antihistamine therapy, nasal glucocorticosteroids and immunotherapy with satisfactory clinical effects [9]. Therefore, there is further supporting evidence that differential diagnosis in LAR should include widely available tests.

In the literature, it has been noted that patients with LAR report symptoms associated with conjunctivitis [9], more frequently relating to seasonal vs. year-round allergens. The cause-effect relationship is thought to be the naso-conjunctival reflex vs. the actual allergic reaction [1, 3]. Our case study shows that the symptoms associated with the nasal allergen challenge were mainly limited to the so-called *extranasal symptoms*, including symptoms typical for conjunctivitis. Moreover, the second challenge that was conjunctival (following nasal) was suggestive of a highly positive result. This case is somewhat a confirmation of an isolated eye response coexisting with LAR. On the other hand, local allergic conjunctivitis may be accompanied by other conditions, which can be diagnosed in patients with entopy. Similar to allergic rhinitis, it can be a consequence of the so-called *local allergic march*.

CONCLUSIONS

Our case study demonstrates that it is necessary to think about the LAR more broadly. Extending the diagnostic workup at the stage of nasal congestion differential by using widely available methods including the nasal or conjunctival allergen challenge is an important reference point for further research in this area.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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