Allergic rhinitis and the weeds pollen sensitization – clinical case presentation

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Abstract

Allergic diseases and among them the allergic rhinitis have become a major healthcare concern due to their increasing prevalence. We present the case of a young woman with moderate/severe allergic rhinitis with moderate sensitization to cat dander and intense sensitization to weeds pollen. We discuss the diagnostic features for allergic rhinitis, the general conditions leading to the pollen sensitization, especially from weeds with emphasis on ragweed (Ambrosia sp.) pollen, as well as the impact on human health and economic aspects. Therapeutic measures are also presented.

Allergic diseases have become a major healthcare concern due to their increasing prevalence that remains largely unexplained (10,25,26).

Allergic rhinitis is a symptomatic disorder of the nose induced after allergen exposure by an immunoglobulin E (IgE)-mediated inflammation of the membranes lining the nose (10). It was defined in 1929 (22): “The three cardinal symptoms in nasal reactions occurring in allergy are sneezing, nasal obstruction and mucous discharge”.

The clinical case

We present the case of a young woman (L.V., 31 years old) who was examined in a private outpatient clinic in March 2016. The patient experienced severe nasal pruritus, intense sneezing and rhinorrhea for about 6 months. The symptoms manifested occasionally after encounters with her former pet – a cat. She gave the cat up after being diagnosed with thyroid cancer one year before. She underwent surgery, radiation therapy and chemotherapy with good outcome. However, the visits to the cat’s new home were followed by the occurrence of the symptoms. The patient admitted that in the previous two summers she had intermittent rhinorrhea that she interpreted as common colds and treated it accordingly, without significant results. The symptoms subsided spontaneously in mid-September. The patient is a certified accountant and has lived in the Oltenia region all her life. She is married without children. Her father is suffering of adult-onset asthma.

Upon examination we recorded a smaller size woman (1,65 m, 57 kg) without significant clinical features, except for mild redness of her upper lip and a large wig. The chest and abdomen examination provided no suggestive information for the diagnosis.

Previous to the examination, after searching the Internet, the patient referred herself to a lab, where usual hematological and biochemical tests were performed. We recorded the elevated eosinophil count as well as the high level (532 IU/mL) of the IgE titer. The symptoms were suggestive in their manifestation for allergic rhinitis (nasal pruritus, sneezing, rhinorrhea that occurred after contact with animal/cat dander). However, the almost continuous symptoms over the summer that subsided in the beginning of autumn were pointing in the direction of pollen allergy.

We performed the standard skin prick-test using the allergen test kit from Stallergenes. We applied dust mite (Dermatophagoides pteronyssinus, Dermatophagoides farinae), molds (Alternaria alternata, Cladosporium cladosporioides, Aspergillus fumigatus), pet animals epithelia - cat (Felis domesticus), dog (Canis familiaris), spring tree pollens (Betula verrucosa, Alnus glutinosa, Corylus avellana), humid-zone tree pollens (Salix caprea, Populus alba, Olea europaea), grass pollens (Dactylis glomerata, Festuca rubra, Holcus lanatus, Lolium perenne, Phleum pratense, Poa pratensis, Secale cereale) and weed pollens (Ambrosia artemisiifolia var. eliator, Artemisia vulgaris, Rumex acetosela, Plantago lanceolata, Urtica dioica) standardized cutaneous extracts for prick tests. Histamine hydrochloride (10 mg/mL) was used as a positive control. The negative control consisted of a phenolated glycerol-saline solution.

The allergy prick testing was performed by pricking the volar forearm skin with adequate lancets through individual drops of allergen extracts. The mean wheel size was recorded after 15 minutes and a skin prick test was considered positive when the induced wheal size was at least 3 mm larger than the negative control (35). Because antihistamine treatment may significantly reduce responses to skin prick tests, we made sure the patient didn’t receive rapid acting antihistamines within the last 48 hours, as well as ketotifen,
hydroxyzine, and tricyclic antidepressants for at least two weeks before testing. She did not take any glucocorticosteroids or leukotriene modifiers either, although the last ones wouldn’t change the intensity of the skin test reaction.

**Discussions**

**Definition**

Allergic rhinitis is a major IgE-mediated chronic respiratory disorder. It has traditionally been subdivided, based on the time of exposure, into seasonal and perennial disease.

Seasonal allergic rhinitis (SAR) is usually caused by a wide variety of outdoor allergens such as pollen and molds while perennial allergic rhinitis (PAR) is most frequently caused by indoor allergens, such as dust mites, animal dander, insects and molds. This subdivision is not ideal as there are many examples which fall outside of the “norm”. (10)

In 2001, the Allergic Rhinitis and its Impact on Asthma (ARIA) workshop group, in collaboration with the World Health Organization (WHO), introduced a new classification system for allergic rhinitis based on the duration of symptoms and their severity (8,9,10).

1 Intermittent allergic rhinitis: symptoms are present for <4 days a week or for <4 weeks.
2 Persistent allergic rhinitis (PER): symptoms are present for >4 days a week and for >4 consecutive weeks.
3 Mild: all of the following items should be present: normal sleep; no impairment of daily activities, sport or leisure; no impairment of work or school; and no troublesome symptoms.
4 Moderate to severe: one or more of the following events should occur: abnormal sleep; impairment of daily activities, sport or leisure; impaired work or school; or troublesome symptoms.

This new classification recognizes allergic rhinitis as a significant chronic respiratory disease with important co-morbidities, including asthma, for which allergic rhinitis is a risk factor (10).

**Mechanisms**

Allergic rhinitis is a complex and multifactorial IgE-mediated immunological disorder, which is associated with the epithelial accumulation of effector cells such as mast cells, eosinophils and basophils as well as the formation and release of a variety of different inflammatory mediators. The accumulated inflammatory cells are in an activated state and the mediators released by these cells are responsible for the early symptoms of rhinitis such as nasal itch, sneezing and rhinorrhea (27).

Pathophysiologically, the disease is characterized as a two-phase process involving an initial sensitization phase (allergen exposure resulting in IgE over-expression and binding to receptors on mast cells and basophils) with subsequent allergen exposure provoking an allergic response. Clinically the allergic response can be divided into two phases:

1 The early-phase (immediate) inflammatory response, which is initiated within minutes of re-exposure to the allergen and is primarily caused by mast cell degranulation and the release of preformed mediators such as histamine and proteases, and newly generated mediators such as cysteinyl leukotrienes (LT), cytokines [various interleukins (IL-4, 5 and 6), bradykinin, tumour necrosis factor (TNF-α)], chemotactic factors, PAF, and granulocyte macrophage-colony stimulating factor (GM-CSF). For the patient, the most obvious effect of these mediators is to produce the early symptoms of allergic rhinitis such as sneezing, itching, and rhinorrhea. In addition, they stimulate the production, adhesion and infiltration into local tissue of circulating inflammatory cells such as eosinophils, basophils, monocytes, and lymphocytes (27, 37).
2 The late-phase inflammatory response begins 2–4 h after allergen exposure and, generally speaking, involves the activated inflammatory cells which release further mediators, promoting local edema and tissue damage, and continuation of the overall inflammatory process. Symptomatically, the late-phase allergic reaction is characterized by nasal congestion and obstruction (37).

In rhinitis, the recruitment of eosinophils, neutrophils, and other effector cells, as part of the late-phase response of the allergic reaction, appears to underline the clinical expression of the disease.

**Diagnosis**

The allergic rhinitis diagnosis starts with a thorough history of the patient. It needs to define the onset and duration of the symptoms and to emphasize any relationship to seasons or life events. Thus, secretions, degree of congestion, sneezing and nasal itching, or sinus pressure and pain as well as ocular symptoms, such as itching, lacrimation, puffiness, and chemosis and pharyngeal symptoms of mild sore throat, throat clearing, and itching of the palate and throat may be present and need to be defined. One has to identify the exacerbating factors, such as seasonal or perennial allergens and nonspecific irritants and other associated allergic diseases, such as asthma or atopic dermatitis, or a family history of allergic diathesis.

The physical findings, which are usually confined to the nose, ears, and eyes, aid in the diagnosis. The most common physical findings in the seasonal exacerbation are: nasal obstruction, associated mouth breathing, clear nasal secretions (whistish secretions may be seen in patients experiencing severe allergic rhinitis), conjunctival erythema, lacrimation, puffiness of the eyes.

In the perennial rhinitis, certain facial characteristics have been associated with chronic allergic disease (32). These include a gaping appearance due to the constant mouth breathing and a broadening of the midsection of...
the nose. The mucous membranes are pale, moist, and boggy and polyps may occur. Based on the clinical features, our patient was diagnosed as having moderate/severe intermittent allergic rhinitis. The diagnostic investigations should start with the skin tests that should be performed to determine the reactivity of the patient against the suspected allergens. It is important to remember that patients with allergic rhinitis may exhibit positive skin tests to allergens other than those that are clinically important. Allergy skin prick testing is the standard method to assess IgE-mediated sensitization to inhalant allergens, commonly used because it is rapid, accurate and reproducible (24).

The radioallergosorbent test (RAST) is an in vitro procedure for assessing the presence of specific IgE antibodies to various allergens and has been employed as a diagnostic aid in allergic diseases. RAST determination of circulating IgE antibody can be used instead of skin testing when high-quality extracts are not available, when a control skin test with the diluents is consistently positive, when antihistamine therapy cannot be discontinued, or in the presence of a widespread skin disease such as atopic dermatitis (38). In the recent years the ImmunoCap systems that use fluorescent-labeled antibodies have been introduced due to their reduced cost and increased effectiveness. As previously stated, our patient already presented a high IgE titer. The skin prick testing revealed moderate reaction (3 mm wheal, about 10 mm flare) to cat dander allergens and an extensive reaction to *Ambrosia artemisiifolia*, *Artemisia vulgaris* and 5 grasses mix (> 10 mm wheal with pseudopodes and a 30 mm flare). The result came to a surprise only because of the intensity of the reaction, while the patient had lately symptoms only in the presence of her former cat. The explanation could have been explained by the “priming” effect that may account for the presence of symptoms in some patients beyond the termination of the pollinating season because an allergen not important clinically by itself may induce symptoms in the “primed” nose (38). In our case, the patient had positive skin tests to cat dander antigens and ragweed, and no symptoms until summer, but having symptoms even after mid-September, after the ragweed-pollinating season was over.

**Causes**

Pollen and mold spores are the allergens responsible for intermittent allergic rhinitis. The pollens important in causing allergic rhinitis are from plants that depend on the wind for cross-pollination. Many grasses, trees, and weeds produce lightweight pollen in sufficient quantities to sensitize individuals with genetic susceptibility. The major perennial allergens responsible for the persistent allergic rhinitis are house dust mites, mold antigens, feather pillows, animal dander, and cockroaches. Pollen allergy may contribute to seasonal exacerbations of rhinitis in patients with perennial symptoms. PAT

Allergic rhinitis accounts for the largest number of patients with respiratory allergy. Because of a variety of factors, including geographic location, allergen load, weather conditions, and emotions, the course and prognosis for any single patient cannot be predicted. Allergic rhinitis is a global health problem and it is one of the top 10 reasons for patients visiting their general practitioner (20). Furthermore, many patients self-treat and do not visit their physician. This leads often to misdiagnosis, delaying the time of the real diagnosis and the beginning of adequate treatment. In Europe, the prevalence of clinically confirmable allergic rhinitis was estimated to range from 17% (Italy) to 29% (Belgium) with a mean value of 23% across the six countries involved in the study (3), while other authors from Belgium reported a prevalence of 45.5% in the age group 20-40 years old.

In the United States, allergic rhinitis is the most common atopic disease and it has been estimated that it affects up to 25% of adults and >40% of children at some stage (33). Staggeringly, 80 million individuals experience symptoms of allergic rhinitis for >7 days/year and the socio-economic costs are significant as the disorder impacts quality of life (QoL), school performance, socialization and work performance/productivity (33, 14). In terms of the type of allergic rhinitis, it has been estimated that SAR occurs in about 10% of the general population whilst PAR occurs in about 10–20% (40).

The American Academy of Allergy, Asthma & Immunology (AAAAI) estimates that as many as 3.8 million days per year are lost from school or work in the US as a result of allergic rhinitis. Furthermore, it is now recognized that a number of co-morbid conditions are associated with allergic rhinitis including asthma, sinusitis, otitis media, nasal polyposis, lower respiratory tract infection (RTI), and dental occlusion. The cost of treating these conditions needs to be considered too when assessing the overall socio-economic impact of the disease (41). Asthma and rhinitis are linked by physiological, pathological and epidemiological characteristics and their co-morbid link has led to the concept of “one airway, one disease” (21) or “united airway disease”. If asthma develops, the patient’s concern for the symptoms of asthma usually overshadows the symptoms of allergic rhinitis (38). Over the years the researchers have elaborated several hypotheses about the cause of the increased prevalence of allergic diseases. The most considered are the hygiene hypothesis, which speculates that reduced exposure to antigens during childhood increases the risk of allergy and the pollution hypothesis, which suggests that changes in allergen-distribution patterns and/or individual responses to specific allergens may be responsible, these being exacerbated by atmospheric pollution.
Climatic and agricultural changes are also influencing sensitization to pollen aeroallergens from weeds that have expanded in recent years (23). Nowadays the allergenic pollen of Ambrosia artemisiifolia is of great concern because it can interact with environmental aspects, such as pollution and climate changes, in a synergic way, increasing the risks to public health. Ambrosia artemisiifolia is the most invasive of all the species, being included on The Official List of Quarantine Weeds. Besides the fact that this weed causes significant agricultural damages, the aeroallergens spread during the quite long pollen season may cause severe respiratory allergies (35).

In Europe, some areas are heavily infested, such as the Rhone Valley and the Burgundy, expanding towards the northwestern regions of France (13), and in the Po Valley, mainly the Lombardy region, in Italy (7). In Belgium, Switzerland, Bavaria in southeastern Germany, Czech Republic and Austria, many foci, mainly in urban areas, were reported. It seems that ragweed is not yet fully established in many of these countries (4,5,6). In Hungary, Ambrosia became instead the most important agricultural weed during the last twenty years. Almost 80% of the agricultural surface is infested (30). This country has shown great spreading of ragweed since the early nineties, when the abandonment of large collective agriculture resulted in uncultivated fields with Ambrosia invasion (12). In Romania, Ambrosia artemisiifolia was first identified in Banat (at Orsova railway station) in 1908 (36). Its expansion manifested after 1990 as well as in the neighboring countries. According to Ianovici (29) nowadays ragweed can be seen over the whole area of our country.

Ambrosia species are annual or short-lived perennial plants in the family Asteraceae, placed in the tribe Heliantheae and subtribe Ambrosinae. Ambrosia is said to contain between 21 (39) and 41 species (34) worldwide. The two species of main concern to Europe, A. artemisiifolia and Ambrosia trifida L., both apparently speciated after the genus had radiated. The regions most severely invaded in Europe are central (Hungary, Austria, Slovakia), eastern (Ukraine, European part of Russia), south-eastern (Romania, Croatia, Serbia) and southern Europe (southern France, Italy) (19).

Ambrosia artemisiifolia is an annual pioneer species and flourishes in disturbed habitats, such as roadsides, waste places, construction sites, agricultural fields, disturbed or abandoned fields, waterways and urban areas (17). The plant overwinters as seed that germinates in spring. Plants are in the vegetative phase from May to August and bloom from August to October (11). Pollen production recorded for individual A. artemisiifolia plants collected in France ranged from 4 million to 10 billion grains and seed production from 346 to 6114 seeds per plant (15). Ambrosia artemisiifolia has a long-term persisting seedbank, with seeds remaining viable for more than 39 years (2).

Dispersal by seed occurs mostly by human activities through soil and seed transport (2). In addition, seeds can float and hydrochory appears to be an important dispersal mechanism along rivers, explaining the rapid colonization of newly formed sand and gravel bars (16).

Common ragweed has a high allergenic potential and Ambrosia pollen sensitization in Europe suggests an increasing prevalence (12). The flowers are pollinated by wind. One gram of Ambrosia artemisiifolia pollen contains about 30-35 million pollen grains, and one well-grown plant can produce more than 45 grams of pollen in one year, depending on the quality of the habitat (18). About 10 ragweed pollen grains per cubic meter of air provoke allergic rhinitis symptoms in sensitive subjects, compared to 50 grass pollen grains (43). In Hungary, Ambrosia generates about half of the total pollen production (31).

Analysis of the ragweed pollen counts using a volumetric method in Timișoara, in the season of 2004, revealed that the highest concentration was 220 pollen grains per cubic meter of air per day. In September, 65.71% of the total aeropollen concentration is due to Ambrosia (28).

Ambrosia pollen has reached at this moment the threshold for high prevalence allergen in the European Union. The prevalence for ragweed pollen sensitization is above 2.5% in many European countries, except Finland (2.4%). While Hungary is expected to show high prevalence of ragweed sensitization, several central and western European countries, such as Germany and the Netherlands show unexpectedly high sensitization rates (14.2% and 15.2% respectively). Denmark is also heavily affected, with a prevalence of 19.8% (12).

Because ragweed and mugwort have nearly identical flowering periods, and clinical and serological studies show that ragweed and mugwort sensitization are often associated, there are questions regarding co-sensitization or corecognition and possible decision problems in patients for whom allergen specific immunotherapy is indicated (1). In addition, concomitant sensitization to mugwort pollen could lead to overestimation of the sensitization rate to ragweed pollen due to cross-reactivity (44). Also, high sensitization rates to Ambrosia pollen found in patients from one region may be due hypothetically either to the weed dissemination in that area or to a long distance travel of the ragweed pollen.

Treatment
There are three types of management of allergic rhinitis. These methods are avoidance therapy, symptomatic therapy, and immunotherapy.

Complete avoidance of an allergen results in a cure when there is only a single allergen. For this reason, attempts should be made to minimize contact with any important allergen, regardless of what other mode of treatment is instituted. In most cases of allergic rhinitis,
complete avoidance therapy is difficult, if not impossible, because aeroallergens are so widely distributed (38). Avoidance of pollen exposure during the pollen season, especially in the hours of the day with high pollen count, frequent change of the pollen filter of the cars may be of help in preventing the symptoms. Attempts to eradicate sources of pollen or molds have not proved to be significantly effective. Reduction of the abundance and the spread of ragweed in Europe can only be achieved by reducing flowering, seed set and dispersal (both naturally and by human activities) at the local and regional scale (19). This is best achieved using mechanical means of plucking or cutting the plants. The cutting techniques avail in reducing the pollen production but do little in preventing the spread of the plants by increased biomass. However, to mitigate crop losses because of competition with ragweed, ragweed biomass needs to be reduced quickly. Plucking, on the other hand, is beneficial in reducing both pollen production and biomass. Although Artemisia is recognized as dangerous for the human health, in Romania it is not yet officially recognized as a quarantine plant. However, as early as 2007 the Local Council in Timisoara stated that weeds control (Ambrosia, Artemisia sp.) is mandatory and non-compliance is punishable.

Other proposed methods including insects as biological control agents, invertebrates as well as fungal pathogens or associations of these methods may prove themselves in the future (19).

The symptomatic treatment uses several classes of drugs. Firstly, the oral non-sedating antihistamines are the foundation of symptomatic therapy for allergic rhinitis and are most useful in controlling the symptoms of sneezing, rhinorrhea, and pruritus that occur in allergic rhinitis. Loratadin, cetirizine, desloratadine, levocetirizine, rupatadine do not appreciably penetrate the CNS and are also free of anticholinergic side effects, such as dry mouth, constipation, difficulty voiding, and blurry vision (10,38).

Sympathomimetic drugs are used as vasoconstrictors for the nasal mucous membranes. Nose drops or nasal sprays containing sympathomimetic agents may be overused. Because of the duration of symptomatic allergic rhinitis, it is best not to use topical vasoconstrictors in the allergic patient except when nasal blockage is severe and for short courses.

Corticosteroids are generally considered the most effective medications for the management of the inflammatory component of allergic rhinitis. At the present time, several nasal corticosteroids are available for treating patients with allergic rhinitis, including beclomethasone dipropionate, flunisolide, triamcinolone acetonide, budesonide, fluticasone propionate, and mometasone furoate. Intranasal steroids have been helpful in relieving the common allergic symptoms of the upper airway, such as sneezing, congestion, and rhinorrhea. In addition, they may be of value in relieving throat pruritus and cough associated with allergic rhinitis and may also improve concomitant seasonal allergic asthma (10,38).

Other drugs as anticholinergic agents, intranasal cromolyn as well as nedocromil have been used. The latter ones have only prophylactic value in the treatment of the allergic rhinitis.

Our patient received desloratadine 5 mg a day administered in the morning and levocetirizine 5 mg a day administered in the evening, beside budesonide 32 mcg b.i.d. each nostril.

Another possible option would be allergen immunotherapy, that attempts to increase the threshold level for symptom appearance after exposure to the aeroallergen. The clinical response to conventional therapy will dictate the decision concerning the initiation and duration of specific treatment, where a minimum of 3 years of immunotherapy should be given to avoid the rapid recurrence of symptoms.

In conclusion, allergic rhinitis among the allergic diseases and the sensitization to weeds / Ambrosia sp. pollen should represent a major concern for both the specialists in the medical and agricultural field as these have become major public health and economic problems. Both specialists’ categories need to be aware of the social impact they present for the contemporary European society.

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