Original Article

Symptoms of the olive pollen allergy: Do they really occur only in the pollination season?

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Summary. *Background*: Olive (Olea europaea; O.e.) pollen is a major cause of seasonal respiratory allergy. The O.e. pollination season lasts two months from the beginning of May till the end of June. It was expected that patients with allergic disease from O.e. sensitization were symptomatic only during this period. However, during the last few years, we have observed that the clinical symptoms appear not only during the O.e. pollination season but also during the rest of the year.
Objective: The aim of this study was to observe and document symptoms of respiratory allergic diseases in the O.e. sensitized patients during the O.e. pollination season and after it.
Methods: One hundred and twenty-seven patients with respiratory allergic disease were enrolled in the study. Allergenic sensitizations were shown by SPT. Finally, patients were split into two groups as monosensitized with O.e. (n=19) and polysensitized (n=108). Patients were assessed by using scores of respiratory allergic disease symptoms and percentage of peak expiratory flow rate values (PEFR %) (only for asthmatic patients) during the O.e. pollination season and after it.
Results: Of the patients with O.e. monosensitization, 13 had allergic rhinitis (AR) only while six had allergic asthma (AA) additionally. AR alone and accompanied by AA was present in 84 and 24 polysensitized patients respectively. Eleven patients with O.e. sensitization (57.9 %) and 86 patients with polysensitization (79.6 %) had AR symptoms throughout the year irrespective of the O.e. pollination season. Similarly, three of the O.e. monosensitized and ten of the polysensitized patients with AA had asthmatic symptoms during the O.e. pollination season and also after it.
Conclusions: In the patient group sensitive to O.e. along with other pollen extracts, it was possible to observe symptoms outside the pollination season. However, patients with O.e. monosensitization also had symptoms to a great extent outside the season.

Key words: Allergic rhinoconjunctivitis, asthma, Olea europeae, season, symptom.

Introduction

Olea europeae (O.e.) pollinosis is a major cause of seasonal respiratory allergies such as allergic rhinitis (AR) and allergic asthma (AA) in the Mediterranean region and some other countries [1-3]. In our country, particularly the Aegean region, O.e. trees are common; therefore their pollen is one of the most prevalent causes of respiratory allergy [4,5]. Among the various protein allergens detected in this pollen, eight - Ole e 1 to Ole e 8 - have been isolated and characterized. Ole e 1 is the most frequent sensitizing agent, responsible for more than 70% of patients suffering from O.e. pollinosis [6].

The O.e. pollination season lasts two months from the beginning of May till the end of June [7]. However, in our region, the O.e. pollination season starts at mid -

March, and continues till mid-June [8]. It was expected to observe signs and symptoms of O.e. sensitization during this period. Clinical spectrum of O.e. sensitization ranges from symptoms of AR and allergic rhinoconjunctivitis to symptoms of AA. Allergic rhinitis may coexist with AA in most of these patients [9,10]. Previously reported series determined that symptom scores in these patients are elevated during the O.e. pollination period [11]. Thus, allergic symptoms were not usually seen outside this season. However, a few studies reported the presence of allergic symptoms in O.e. sensitized patients outside the O.e. pollination season [7,12].

Routine follow-ups of O.e. sensitized patients of our outpatient clinic have revealed that clinical symptoms that are observed during the O.e. pollination season can also be seen during the rest of the year. Therefore, the aim of this study was to observe and document symptoms of AR with or without AA in the O.e. sensitized patients during the O.e. pollination season and outside it.

Materials and methods

One hundred and twenty-seven patients with O.e. sensitization were enrolled in to the study during the routine follow-up of seasonal respiratory allergy at our outpatient clinic between March 2002 and December 2002. All demographic features of these patients are shown in Table 1.

All patients were diagnosed as having seasonal AR with or without AA based on history, physical examination and laboratory findings. Allergic rhinitis was diagnosed when the symptoms included nasal itching, sneezing, obstruction, discharge for longer than a month during pollen season and also positive SPT reactivity according to consensus statement [9]. Allergic asthma was diagnosed according to previous consensus report and is detailed below [13].

Allergenic sensitization of all patients was shown by SPT. In addition, SPT was re-evaluated for O.e. allergen extract when allergic symptoms were observed outside the O.e. pollination season to exclude sensitization to a new allergen such as grass/cereal and/or weeds. Allergen skin prick tests were performed according to the EAACI guidelines [14]. All patients had positive skin test reactivity to O.e. pollen allergen extract with or without a reactivity to grasses/cereals allergen mixture (*Hulcus lanatus, Lolium perenne, Fectuca pratensis, Phleum pratense, Poa pratensis, Dactylis glomerata, Hordeum vulgare, Avena sativa, Seceale cerela, Triticum sativum)* or weed allergen mixture (*Artemisia vulgaris, Urtica dioica, Taraxacum vulgare, Plantago lanceolata, Parietaria officinalis);* no patients had skin sensitization to perennial allergens *(Dermatophagoides farinae* and *Dermatophagoides pteronyssinus)* (Allergopharma JGK, Reinbek, Germany).

Routine follow-up included monthly evaluation during spring, summer and autumn. However, patients were re-evaluated regardless of the time of the year, if symptoms of allergic diseases appeared. Physical examination along with scoring of nasal and/or bronchial symptoms, nose and chest examinations, sinus and/or pulmonary X-rays, PEFR% and whole blood count were recorded when the patients were admitted for re-evaluation.

The O.e. pollination season was accepted to be four months starting from the beginning of March till the end of June, according to combined information of two different sources in the medical literature [7, 8]. The rest of the year was accepted to be outside the O.e. pollination season. Patients were evaluated for nasal [itching, sneezing, congestion and secretion; each symptom was scored from 0 to 3 (0: no symptom, 1: mild, 2: moderate, and 3: severe)], and a total AR

Table 1. Demographic characteristics of subjects (O.e.: Olea europaea).

Characteristics	**Results**
Age [year ± SD (min-max)]	20.08 ± 11.35 (10-55)
Sex [F/M]	73/54
SPT [n, (%)]	
O.e. monosensitized	19, (15)
O.e., Grasses/cereals and weeds polysensitized	108, (85)
Clinical presentation [n, (%)]	
ARC without AA (O.e monosensitized/polysensitized)	13/84, (68.5/77.8)
ARC with AA (O.e. monosensitized/polysensitized)	6/24, (31.5/22.2)

symptom score was calculated as the sum of single symptom scores with a maximum of 12 points as described in the medical literature [15]. Asthma symptom scores were evaluated for wheezing, cough, chest tightness, shortness of breath [(Each symptom was scored from 0 to 3 (0: no symptom, 1: mild, 2: moderate, and 3: severe)], with a maximum of 12 points as described in the medical literature [16]. Additionally, the highest symptom scores (for AR and AA) of our patients among visits during the O.e pollination season and outside it, were used for calculating the mean symptom score of O.e. season and out of the O.e. pollination season.

The diagnosis of AA was performed according to consensus report in patients with reversible bronchospasm, intermittent chest tightness and wheezing in their histories and also positive SPT reactivity to respiratory allergen and reversibility test [13]. Reversibility was revealed by spirometric tests (Microplus, MicroMedical LTD., Rochester, England and Spida Version 3 software for pulmonary function tests). Fifteen percent or greater increase in FEV_1 following the administration of short-acting bronchodilators was accepted as positive reversibility. Additionally, best value of peak expiratory flow rate (PEFR expressed in L/min.) among three attempts of PEFR measurement by peak expiratory flowmetry (Airzone, Clement Clarke Int. LTD., Essex, ENGLAND) was recorded in patients with AA at the time of all visits. For the statistical analysis, peak expiratory flow rate values were converted to percentages of the predicted value (PEFR %) using the formula "PEFR/predicted value x 100".

Additional inclusion and exclusion criteria for all selected patients were issued. Inclusion criteria were:

1. diagnosis of seasonal AR with or without AA for at least 1 year prior to the study;
2. no history of oral and/or nasal antihistamines, corticosteroids, or other treatment that may suppress SPT reactivity like H_2 receptor blockers, decongestants, antidepressants for at least two weeks prior to SPT;
3. not taking oral and/or inhalant corticosteroids, bronchodilators, antihistamines, decongestant, antibiotics at the time of re-evaluation.

Exclusion criteria were:

1. positive allergen SPT results except for O.e. and grass/cereal pollen such as mite, mould etc.;
2. an additional sickness leading to non-specific nasal and/or bronchial hyperreactivity such as cystic fibrosis, immune deficiency etc.;
3. during nose examination, showing evidence of abnormal physical findings, viral and/or bacterial infection in upper and/or lower airway at the time of both the first evaluation, monthly evaluation and re-evaluation outside of routine follow-up, if symptoms of allergic diseases appeared;
4. refusal to be enrolled into the study.

Informed consent for the investigations described herein was obtained from all patients. Approval for the study was given by the ethics committee of our hospital.

Statistical analyses were done by paired-sample *t*-test between O.e pollination season and off-season for symptom scores of AR and AA and also PEFR values in both O.e. monosensitized patients and polysensitized patients separately. Mann-Whitney U test was used to compare the values of O.e. monosensitized patients and polysensitized patients (SPSS program/IBM).

Results

Monosensitization to O.e. allergen was detected in 19 patients (15 % of all patients) by SPT. All of the O.e. monosensitized patients had AR symptoms during the season of O.e. pollination and the mean AR symptom score was 9.27 ± 1.79 (Median: 9; 25-75 percentiles: 8-11). Additionally, during this season, six (31.5 %) O.e. monosensitized patients had accompanying asthmatic symptoms. Reversible deterioration in pulmonary function test was determined in the first evaluation of these patients. They presented with a mean asthmatic symptom score of 7.05 ± 2.34 (Median: 7.00; 25-75 percentiles: 5.00-9.25) and a PEFR% of 68.2 ± 12.2 % (Median: 74.00; 25-75 percentiles: 52.75-77.50) during the O.e. pollination season.

One hundred and eight patients had actually skin test reactivity to all of O.e., grass/cereal and/or weed allergen extracts (polysensitized patients). All of the polysensitized patients had showed AR symptoms during the O.e. pollination season and also in July, August, September, and October. Mean AR symptom score was 8.72 ± 2.11 (Median: 9.00; 25-75 percentiles: 7.00-10.00) for AR. Median AR symptom scores of O.e. monosensitized patients were not significantly different from that of polysensitized patients during the O.e. pollination season ($p>0.05$) (Fig.1-a). Similarly, 24 polysensitized patients (22.2 %) described asthmatic symptoms with a mean score of 6.76 ± 3.05 (Median: 5.50; 25-75 percentiles: 4.00-9.75) and reversible deterioration of pulmonary function test (as described for AA) during the same time period. Difference between median asthmatic symptom scores of the O.e. monosensitized and polysensitized patients was not statistically significant during the O.e. pollination season ($p>0.05$) (Fig.1-b). Mean PEFR% of polysensitized patients was 64.6 ± 14.4 % during the O.e. pollination season (Median: 58.00; 25-75 percentiles: 52.00-78.00). Median PEFR% was not different for O.e. monosensitized and polysensitized patients during the O.e. pollination season ($p>0.05$) (Fig.1-c).

Symptoms of AR were observed both during the O.e. pollination season and outside it in 11 of the O.e. monosensitized patients (57.9 %). SPT re-evaluation out of the O.e. pollination season revealed absence of a new allergen sensitization besides O.e. in these patients.

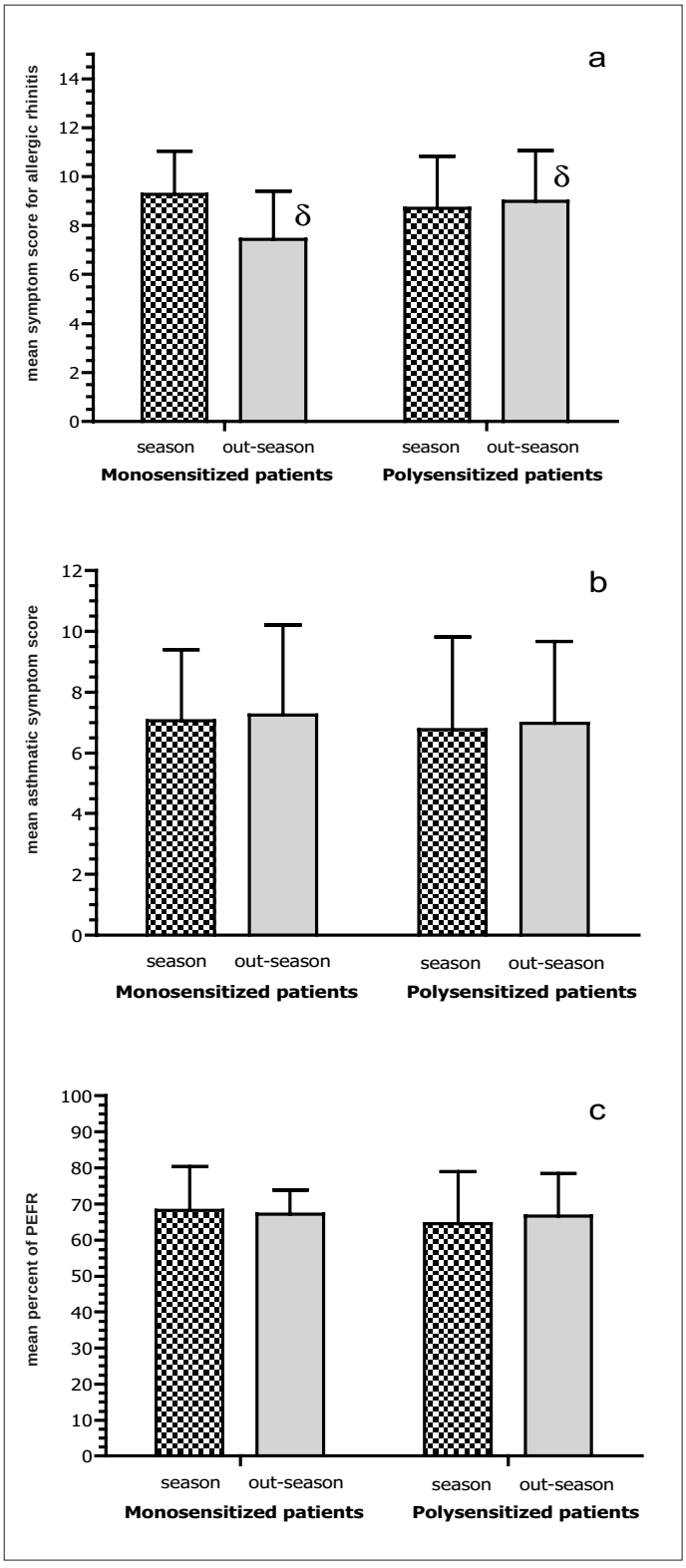

Figure 1. Mean symptom scores for allergic rhinitis (a), mean symptom scores for asthma (b) and mean percent of PEFR (c) in patients with O.e. monosensitization and patients with polysensitization during and out of the season of O.e. pollination. ℘: statistically significant. See text for mean, median and p values.

Mean symptom score for AR was calculated to be 7.45 ± 1.97 (Median: 8.00; 25-75 percentiles: 6.00-9.00) during this season. There was a significant difference of mean AR symptom scores between the O.e. pollination season and the rest of the year (p=0.036) (Fig.1-a). Three of the O.e. monosensitized patients with AA had accompanying asthmatic symptoms outside the O.e. pollination season. Mean asthmatic symptom score and mean PEFR % were 7.24 ± 2.98 nd 67.1 ± 6.8 % respectively (Median: 6.00; 25-75 percentiles: 6.00-10.00; median: 67.00; 25-75 percentiles: 60.00-74.00, respectively) outside the O.e. pollination season. These were not statistically different from the values obtained during the O.e. pollination season. (p>0.05) (Fig.1-b and Fig.1-c; respectively).

Eighty-six polysensitized patients (79.6 %) had AR symptoms with a mean AR symptom score of 9.01 ± 2.06 (Median: 9.00; 25-75 percentiles: 8.00-11.00) outside the O.e. pollination season. No difference was detected between AR symptom score during the O.e. pollination season and the rest of the year (p>0.05) (Fig.1-a). However, median symptom score for AR in O.e. monosensitized patients was significantly lower than that of polysensitized patients outside the O.e. pollination season (p=0.03) (Fig.1-a). Asthmatic symptoms were observed outside the O.e. pollination season in ten of the polysensitized patients with AA. Mean asthmatic symptom score and mean PEFR % in these patients were 6.98 ± 2.68 and 66.6 ± 11.8 % respectively (Median: 6.50; 25-75 percentiles: 4.00-8.75; median: 70.00; 25-75 percentiles: 53.75-78.00, respectively). Both mean asthmatic symptom score and mean PEFR % in polysensitized patients during the O.e. pollination season were not significantly different from those of the rest of the year (p>0.05) (Fig.1-b and Fig.1-c; respectively). Moreover, median asthmatic symptom score and median PEFR% of O.e. monosensitized patients outside the O.e. pollination season was not statistically different from those of polysensitized patients (p>0.05) (Fig.1-b and Fig.1-c; respectively).

Discussion

Olea europeae trees are widespread and their pollens are one of the major causes of AR and AA in some regions of the world including our country [1-5]. Olea europeae cultures are particularly intense around our hospital area. In this respect, we evaluate most of our patients with allergic diseases for O.e. sensitization. However, we rarely observe monosensitization to O.e. in these patients. This finding correlates with medical literature which reports that monosensitization to O.e. allergens is quite rare in allergic airway diseases [7]. In a previous study, Liccardi et al detected skin test reactivity to

O.e. along with other pollen or mite allergens in 13.49 % of allergic adults and in 8.53 % of atopic children, whereas monosensitization to O.e. allergens was detected in about 2 % of allergic adults and in about 1 % of atopic children in their area [17]. Fifteen % of our AR patients with or without AA who were selected for this study were monosensitized to O.e.

Persistence of symptoms in O.e sensitized patients outside the O.e. pollination season has attracted our attention for a long time. As a result of the study planned accordingly, we observed AR and/or AA symptoms in our selected patients outside the O.e. pollination season. There was a few number of published papers which reported out-season symptoms in patients with O.e. sensitization [12, 18, 19]. Symptoms in polysensitized patients during summer or autumn may be attributed to their sensitization to grasses/cereals and/or weeds. Sensitization to these pollens may cause allergic symptoms to persist till the end of autumn [9]. However, presence of AR and/or AA symptoms out of the pollination season in patients monosensitized to O.e. was amazing and quite difficult to explain. Spanish authors have previously documented that they observed these symptoms for several months and in a few cases all year round [18, 19]. Additionally, there is one study which reports the appearance of allergic nasal symptoms out of the pollination season in patients with monosensitization to O.e. [12]. Although to some extent late reactions after O.e. specific nasal provocation tests could explain the appearance of nasal symptoms outside the pollination season, the precise mechanism was not clear. This persistence of allergic respiratory symptoms in O.e. monosensitized patients outside the pollination season was attributed to high degree of cross-reactivity between the O.e.allergens and other pollens of the Oleaceae family (e.g. *Fraxinus excelsior* and *Ligustrum vulgare*) as reported by recent studies [20]. However, we do not agree with this explanation because the pollens which cross-react with the O.e. pollens are from trees such as ligustrum, fraxinus, privet and ash that pollinate during the O.e. pollination season and seem to have low frequency of allergic sensitization [7,21]. In the same way, these trees are extremely rare in the area around our hospital.

First SPT evaluation of O.e. monosensitized patients failed to determine a specific allergen which might be responsible for the persistence of allergic symptoms outside the O.e. pollination season. Similarly, re-evaluation of these patients with SPT outside the O.e. pollination season showed no emergence of a sensitization to an allergen other than O.e.

In patients with AR, coexistence of AA was detected in 6 (31.5 %) of O.e. monosensitized and in 24 (22.2 %) of polysensitized patients during the O.e. pollination season. Also three O.e. monosensitized patients had asthmatic symptoms outside the pollination season and ten polysensitized patients had asthmatic symptoms during the same period. Moreover, we observed that mean asthmatic symptom scores and mean PEFR % of both O.e. monosensitized and polysensitized patients during the O.e pollination season was not significantly different from those during the remaining part of the year. Similarly, mean asthmatic symptom scores and mean PEFR% of O.e. monosensitized patients did not differ significantly from those of polysensitized patients during the O.e. pollination season or outside it. Evidence of upper or lower airway infection and new air pollution was absent in all patients while asthmatic symptoms were present. Association of allergic rhinoconjunctivitis with asthma was well known both in children and adults [10,22,23]. This topic was investigated in detail by De Benedictis and Bush [24] and by ARIA [9]. O.e. allergens can induce asthmatic response besides allergic inflammation in nasal mucosa [7, 25]. Our results showed that O.e. monosensitized and also polysensitized patients plus grass/cereal allergen have had asthmatic symptoms during and outside the pollination season. Therefore, we suggest that asthmatic symptoms may be related to nature of inflammation in respiratory mucosa or pollination characteristics of O.e. allergens. Also the lower respiratory symptoms may be secondary to non-specific nasal and bronchial hyperreactivity during and outside the O.e. pollination season, particularly in O.e. monosensitized patients, due to minimal persistent inflammation constituted by these natures of inflammation and/or pollination characteristics of O.e. pollens.

In conclusion, the results of our study show that O.e. pollination season in our region may last longer than expected. Moreover, the results of our study leads to the conclusion that O.e. pollen can cause allergic inflammation of the upper and/or lower airways that may persist after the pollination season is over.

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