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A preliminary report on the prevalence and clinical features of allergic rhinitis in ankylosing spondylitis patients

Arif Turgan[1], Ahmet Ural[1], Abdülcemal Ümit Işık[1], Selçuk Arslan[1], Erhan Çapkın[2], Refik Ali Sarı[3]

[1]*Department of Otorhinolaryngology, Medical School, Karadeniz Technical University, Trabzon, Turkey*
[2]*Department of Physical Medicine and Rehabilitation, Medical School, Karadeniz Technical University, Trabzon, Turkey*
[3]*Department of Clinical Immunology, Medical School, Karadeniz Technical University, Trabzon, Turkey*

Abstract

Objective: Our aim was to investigate the prevalence and clinical features of allergic rhinitis in patients with ankylosing spondylitis.

Methods: This cross-sectional, clinical study was performed on 64 patients (24 females, 40 males) between October 2011 and November 2012. The Score for Allergic Rhinitis (SFAR) questionnaire was carried out to the patients with a recent diagnosis of ankylosing spondylitis. Skin prick test was performed to the cases who responded positively to SFAR. Descriptive parameters, clinical features and skin prick test results were documented.

Results: The mean age of the study group was 41.7±11.2. Eight patients (12.5%) were presumably diagnosed for allergic rhinitis according to SFAR questionnaire. Skin prick test yielded positivity for *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* in one of the 8 cases who responded positively for SFAR. The most common symptoms were sneezing (n=15; 23.4%), nasal obstruction (n=12; 18.8%), and nasal itching (n=12; 18.8%).

Conclusion: Our results demonstrate that prevalence of allergic rhinitis is lower in ankylosing spondylitis patients. However, clinical and pathophysiological features of allergic rhinitis accompanying autoimmune diseases must be investigated in further trials.

Keywords: Allergic rhinitis, ankylosing spondylitis, prevalence, symptom, cytokines.

Özet: Ankilozan spondilit hastalarında alerjik rinit sıklığı ve klinik özelliklerine ilişkin bir ön çalışma

Amaç: Bu çalışmanın amacı ankilozan spondilit hastalarında alerjik rinit sıklığı ve klinik özelliklerini araştırmaktır.

Yöntem: Bu kesitsel, klinik çalışma bir üniversite hastanesinin kulak burun boğaz hastalıkları kliniğinde Ekim 2011 – Kasım 2012 arasında gerçekleştirildi. Toplam 64 ankilozan spondilit hastasına (24 kadın, 40 erkek) "*The Score for Allergic Rhinitis*" (SFAR) anketi uygulandı. Anket sonucuna göre alerjik rinit olduğu düşünülen olgulara deri testi yapıldı. Tanımlayıcı parametreler, klinik özellikler ve deri testi bulguları analiz edilerek sunuldu.

Bulgular: Çalışma grubunda ortalama yaş 41.7±11.2 olarak bulundu. Anket sonucuna göre alerjik riniti olduğu düşünülen 8 hastaya (%12.5) deri testleri yapıldı. Deri testi sonucunda bu olgulardan yalnızca birinde *Dermatophagoides farinae* ve *Dermatophagoides pteronyssinus* için pozitiflik saptandı. Ankilozan spondilit hastalarında rinitle ilgili olabilecek klinik bulgulardan hapşırma (n=15; %23.4), burun tıkanıklığı (n=12; 18.8%) ve burun kaşıntısı (n=12; %18.8) gözlendi.

Sonuç: Çalışmamızın sonuçlarına göre ankilozan spondilit olgularında alerjik rinit sıklığının daha düşük olduğu gözlenmiştir. Otoimmün hastalıklarda alerjik rinit sıklığı ve klinik bulgularına ilişkin daha ileri çalışmalara gereksinim bulunmaktadır.

Anahtar sözcükler: Alerjik rinit, ankilozan spondilit, prevalans, sitokinler.

Allergic rhinitis (AR) is a common disorder that constitutes a considerable burden both for the individual patient and the society. It is important due to its high prevalence, adverse effects on the quality of life and sleep, impairment of work/school performance and the links with other comorbidities. Its prevalence is estimated as 5–40% with a tendency to increase.[1,2] Beyond the data collected from studies performed on large populations, an important contribution to

Correspondence: Ahmet Ural, MD. Department of Otorhinolaryngology, Medical School, Karadeniz Technical University, Trabzon, Turkey.
e-mail: ahmetural2001@yahoo.com

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the accumulation of knowledge on AR may be obtained by the epidemiological studies conducted in specific subgroups.

Symptoms of allergic rhinitis occur due to an IgE mediated inflammatory immune response. Pathophysiology is based on the secretion of cytokines due to an imbalance between allergen specific T helper 1 (Th1) and Th2 cells.[3] The allergic reaction cascade is triggered with the contact of allergen with IgE on mast cells and basophils. Predominance of Th2 cells and cytokines secreted from these cells sustain the subsequent allergic process. Key pathogenetic features of allergic rhinits are raised levels of IgE and a characteristic Th cell cytokine pattern.[3,4]

Ankylosing spondylitis (AS) is a systemic in?ammatory disease that involves the axial skeleton, the peripheral joints, the eye, and occasionally the aortic root may also be affected. Ankylosing spondylitis affects primarily the joints of the hand and feet in a symmetrical fashion and the primary site of in?ammation seems to be the enthesis and sites where ligaments insert into bone. The onset of AS is usually observed in the second or third decades and men are affected more than women. Similar to allergic rhinitis, ankylosing spondylitis results in substantial morbidity.[5,6]

While atopic disorders are associated with a predominant Th2 cytokine pattern, the cytokine pattern of AS can be described as an "impaired Th1 cytokine pattern".[7] Impairment of physiological immune response and Th1 function may be accompanied with a relatively amplified Th2 activity. Based on the reciprocal inhibition of the development of Th1 and Th2 responses, it has been suggested that Th1 and Th2 polarized immune responses and diseases mutually exclude each other.[7,8]

In summary, the aim of the current study was to investigate the prevalence and clinical features of allergic rhinitis in AS patients in Trabzon, Turkey.

Patients and Methods

Study Design

This cross-sectional, clinical study was performed between January 2011 and October 2012 in the otorhinolaryngology department of our tertiary care center. Adherence to the guidelines of the Declaration of Helsinki of 1975, as revised in 2008, was accomplished. The approval of local Institutional Review Board and written informed consent from all participants were obtained.

Patients with a recent diagnosis of AS in either clinical immunology or physical medicine and rehabilitation departments of our tertiary care center were recruited. Exclusion criteria were previous diagnoses of allergic, non-allergic or other forms of rhinitis, nasal polyposis, paranasal sinus tumors, septal deviation, turbinate hypertrophy, history of sino-nasal surgery, and use of systemic or nasal medications (steroids, decongestants or antihistamines) within last 4 weeks. Routine otorhinolaryngological examination involving nasal endoscopy was made for ruling out conditions consistent with exclusion criteria.

In this study, the Score for Allergic Rhinitis (SFAR) questionnaire, which has recently been used for estimation of AR prevalence in our country, was applied (Appendices A, B).[1,2] In the study, a SFAR score ≥7 was accepted to suggest the presence of AR.

Patients recently diagnosed as AS completed the SFAR questionnaire (Appendix A). The AR symptoms of blocked nose, nasal discharge, sneezing and itchy eyes were questioned and the total SFAR score was calculated by summing the scores of different items according to the questionnaire (Appendix B). Each item in the questionnaire has a number of point and the total score range from 0 to 16.[1]

Skin prick test *(ALK Abello A/S, Horsholm, Denmark)* was performed on 8 patients who responded positively to SFAR questionnaire. A 20-item test was applied to the skin overlying the ventral surfaces of the arms of patients and the diameter of enduration was measured 15 minutes after the application (Box 1). Diameters ≥3 mm was accepted as positive according to the instructions of the manufacturer.

Box 1. Allergens used in skin prick test.

Trees mix *(Alnus, Betula, Corylus)*
Olea europaea
Populus nigra
Quecus robur
Pollens IV *(Dactylis, Festuca, Lolium, Phelum, Poa)*
Pollens III *(Avena, Hordeum, Triticum, Seceale)*
Seceale cereale
Pollens V *(Artemisia, Chenopodium, Pariteria, Plantago)*
Artemisia vulgaris
Pariteria Judaica
Alternaria alternata
Aspergillus fumigatus
Dermatophagoides farinae
Dermatophagoides pteronyssinus
Dog epithelia
Feather mix
Cat epithelia
Blatella germanica
Saline solution
Histamine

Descriptive parameters and frequency of clinical symptoms of AR were noted and compared in AS patients with and without AR.

Statistical Analysis

Statistical Package for Social Sciences (SPSS version 13.0; SPSS Inc., Chicago, IL, USA) was used for analysis of data. Continuous variables were expressed as mean±standard deviation while categorical variables were termed as %. Comparison of continuous variables between groups was performed via Mann-Whitney U test, whereas chi square test was used for categorical variables. Level of significance was set at $p<0.05$.

Results

This study was performed on 64 recently diagnosed ankylosing spondylitis patients (24 females, 37.5%; 40 males, 62.5%) who do not report intake of any anti-inflammatory medications in the last 3 weeks. The average age of the series was 41.3±11.2, ranging from 17 to 65.

Analysis of responses to SFAR questionnaire have demonstrated that 8 AS patients (12.5%) were likely to suffer from AR. Application of skin prick test to these cases revealed that 1 patient was sensitive to antigens derived from mites *(Dermatophagoides farinae and Dermatophagoides pteronyssinus)*.

Age distribution of AS patients responding positively to SFAR was as follows: Four patients (50%) were at fifth decade, 3 cases (37.5%) were at fourth decade and 1 patient (12.5%) was at third decade. The most common symptoms found in AS patients were recurrent sneezing (n=15, 23.4%), nasal congestion (n=12, 18.8%), nasal itching (n=12, 18.8%) and postnasal drip (n=12, 18.8%) (Table 1).

Table 1. Comparison of the descriptive data and frequencies of nasal symptoms detected in AS patients responding positively (Group 1) or negatively (Group 2) to SFAR.

Descriptive data	Group 1	Group 2	p
Age (mean ± SD, years)	45.3 ±12	40.4 ±11.1	0.161
Gender (male) n (%)	4 (50%)	36 (64.3%)	0.460
Nasal congestion n (%)	4 (50%)	8 (14.3%)	0.035*
Nasal discharge n (%)	4 (50%)	6 (10.7%)	0.016*
Nasal itching n (%)	7 (87.5%)	5 (8.9%)	<0.001*
Recurrent sneezing n (%)	7 (87.5%)	8 (14.3%)	<0.001*
Postnasal drip n (%)	6 (75%)	6 (10.7%)	<0.001*

*: Statistically significant

Comparison of AS patients who responded negatively or positively to SFAR with respect to descriptive and clinical variables is plotted in Table 1. No difference was noted regarding distribution of age (p=0.161) and gender (p=0.460). Symptomatologic analysis has shown the frequencies of nasal congestion (p=0.035), nasal discharge (p=0.016), nasal itching (p<0.001), sneezing (p<0.001) and postnasal drip (p<0.001). Two groups were similar with respect to the duration of ankylosing spondylitis (p=0.722).

Discussion

We designed the current study to investigate the prevalence and clinical features of AR in AS patients. Our results demonstrated that AR rhinitis occurs less frequently in ankylosing spondylitis patients and SFAR seems to be an effective measure for monitoring allergic symptoms in special patient subgroups.

T lymphocytes are classified into two subgroups according to their surface antigens. Lymphocytes having CD4 molecules are termed as T helper cells which are further divided into Th1 and Th2 categories with respect to the cytokine secreted. Th cells exhibit two opposite poles of immune responses based on the secretion of cytokines. Th1 cytokine pattern is linked with a cellular immune response, whereas Th2 cytokine pattern is related with a humoral immune response, which is evident in atopic disorders including allergic rhinitis.[3,9] Rudwaleit et al. suggested that Th1/Th2 balance has been disturbed in favor of Th2 in ankylosing spondylitis.[8] In this circumstance, an impaired Th1 response is more prominent rather than an exaggerated Th2 activity. Prevalence of allergic rhinitis in AS was found to be slightly higher (16.1%) than the control group (15.3%); however, this difference was not statistically significant. Zochling et al. has found a significantly higher prevalence of AR in AS patients as 20.6%, while it was 7.8% in the control group.[10]

Our study possesses some variations from these forementioned studies. First, we did not send questionnaires to the patients by mail. Each patient was interviewed and examined separately in the outpatient clinic of our tertiary care center. Second, we performed skin prick test to patients responding positively to SFAR questionnaire. At first glance, lack of a control group may seem to be an important limitation of our study. However, we have recently participated in a multi-centric trial conducted for estimation of allergic rhinitis prevalence in our country.

We have monitored 500 cases with SFAR questionnaire in our region and found an AR prevalence of 29.8%.[1] We have referred these recent results to compare to the data obtained from AS patients in this study. This comparison may be still debateful due to the noteworthy difference between sample sizes; however, it must be kept in mind that recently diagnosed AS patients who do not use any medications do not constitute a large population.

Bergameschi et al. suggested that prevalence of AR was decreased (9.5%) in (Th1 dominant) multiple sclerosis patients compared to control group (23.5%). A similar correlation was demonstrated between another Th1 dominant disease, type 1 diabetes mellitus and allergic rhinitis.[11]

In the literature, various results have been reported on the prevalence of AR in rheumatologic conditions. Rudwaleit et al. suggested that atopic disease was less frequent in rheumatoid arthritis (RA) patients (8.6% versus 15.3%, $p<0.001$), while there was a slight increase in prevalence of AR in RA (16.1% versus 15.3%), but it was not statistically significant.[8] A noteworthy point emphasized in this study was that RA exhibited a milder course in patients who were diagnosed for AR prior to the onset of RA. This finding is conjunction with the hypothesis suggesting that intensity of an immunologic process may alleviate the course of another pathology sharing a similar immunological mechanism.[3] Rudwaleit et al. have stated that cytokine response seen to drift towards Th1 predominance in RA was more prominent than that impairs Th1 response in AS.[8] Interestingly, pregnancy is a Th2 dominant condition and severity of AS, which is characterized with an impaired Th1 response, was found to be unchanged during the course of pregnancy.[12] Therefore, it can be pronounced that impact of reciprocal effect is more obvious in RA than AS. All in all, we think that understanding the immunological basis of inflammatory disorders cannot be accomplished with simplified theories such as “reciprocal inhibition of Th1 and Th2 cells”.

The prevalence of AR in our geographical region of Turkey was found to be 29.8% according to SFAR questionnaire.[1,2] The reason for the lower prevalence of AR in our AS series may be attributed to several factors. First, prevalence studies based on questionnaires are more likely to yield an exaggerated rate of disease. Second, most of our patients were around 4th or 5th decades, which is a relatively old age for manifestation of allergic symptoms.[1,2] Third, even though it has acceptable rates of sensitivity and specificity, allergen sensitivity cannot be precisely documented in every patient with skin prick test.[13]

The reason for the lower incidence of AR in our series of AS patients may be attributed to the suppressive effect of Th2 dominant AS over Th2 dominant AR. It must be remembered that reciprocal activity of Th1 and Th2 cells is more complex than it sounds. Possible roles of other inflammatory cells, including regulatory T cells, genetic predisposition and environmental factors must not be overlooked. In addition, autoimmune diseases including AS may present with a distinct form of non-allergic rhinitis rather than a typical AR characterized with skin prick test positivity.

Another important aspect is that nonallergic rhinitis represents a diverse entity including gustatory, hormonal, occupational and other types of rhinitis.[14,15] Manifestation of rhinitis in the setting of autoimmune diseases such as ankylosing spondylitis may be different and distinct from its usual clinical presentation.[14,15] The relatively advanced age of patients responding positively to SFAR questionnaire reminds an atypical presentation of chronic rhinitis accompanying AS. Systemic vasculitides such as Wegener’s granulomatosis or Churg-Strauss disease may involve the upper respiratory tract and present as chronic rhinosinusitis. These clinical presentations may constitute both diagnostic and therapeutic challenges.[16] Our results have shown that at least some of the sinonasal disorders classified as nonallergic or vasomotor rhinitis may actually represent atypical rhinitis forms either linked with autoimmunity or atypical presentations of rhinitis modified by co-existent disease.

Main limitations of our study include the small sample size and cross-sectional design. Moreover, lack of definite criteria for selection of patients and any possible misdiagnosis of problems prone to influence the results constitute other restrictions. Therefore, extrapolations must be made with caution.

In conclusion, results of the current study indicate that prevalence of AR is lower in AS patients. Inflammatory and autoimmune disorders may alter the immune system reactions resulting in atypical prevalence and presentation of atopic disorders. The pathophysiological mechanism underlying atopic and inflammatory disorders remain to be elucidated in prospective, randomized, controlled trials on larger series.

Conflict of Interest: No conflicts declared.

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Appendix A.

SCORE FOR ALLERGIC RHINITIS QUESTIONNAIRE[2]

In the past 12 months, have you had a problem apart from cold or flu?	a. Sneezing b. Runny nose c. Blocked nose	Yes ☐ Yes ☐ Yes ☐	No ☐ No ☐ No ☐
In the past 12 months, has this nose problem been accompanied by itchy watery eyes?	Yes ☐		
In which of the past 12 months (or in which season) did this nose problem occur?	Jan ☐ Apr ☐ July ☐	Feb ☐ May ☐ Aug ☐	Mar ☐ June ☐ Sept ☐
Alternatively	Winter ☐	Summer ☐	Autumn ☐
What triggering factors provoke or increase your nose problem?	a. House dust ☐	b. Pollens ☐	c. Animals (cat, dogs) ☐
Do you think you are allergic?	Yes ☐	No ☐	
Have you already been tested for allergy (skin prick tests for allergens, IgE)?	Yes ☐	No ☐	
If Yes: Were they positive?	Yes ☐	No ☐	
Has a doctor already diagnosed that you suffer/suffered from an allergy (asthma, eczema, allergic rhinitis)?	Yes ☐	No ☐	
Is there anyone in your family who suffers from:	Father ☐	Mother ☐	Siblings ☐
Asthma	Yes ☐	No ☐	
Eczema	Yes ☐	No ☐	
Allergic rhinitis	Yes ☐	No ☐	

Appendix B.		
ATTRIBUTED SCORE AND REPARTITION OF THE ITEMS FOR THE SCORE FOR ALLERGIC RHINITIS[2]		
Items Discriminators	**Score**	**Cumulative score**
Nasal symptoms (blocked, runny nose, and or sneezing) in the past year	1 for each symptom	3
Months of the year	1 for perennial 1 for pollen season	4
Itchy eyes	2	6
Triggers		
Pollens, house-dust mites, and / or dust	2	8
Epithelia (cats and /or dogs)	1	9
Perceived allergic status	2	11
Previous positive allergic tests	2	13
Previous medical diagnosis of allergy	1	14
Familial history of allergy	1	16
Total		16

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