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The Distribution of HLA B27 in Patients with Ankylosing Spondylitis in Eastern Anatolia

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Ankilozan spondilit (AS) etyolojisi bilinmeyen kronik enflamatuvar bir hastalıktır. Patogenezde genetik ve çevresel faktörlerin önemli rol oynadığı bilinmektedir. AS gelişimi ile HLA B27 arasında güçlü bir birliktelik saptanmıştır. Bu çalışma ile daha önceki literatür bilgileri ışığında bölgemizdeki HLA B27-AS ilişkisi karşılaştırıldı.
Bu çalışmada, modifiye New York kritelerine göre sınıflandırılmış AS'li hasta ve sağlıklı kontroller üzerinde HLA B27 frekansı araştırılmıştır. Çalışmaya birbirleri ile akraba olmayan 84 AS'li hasta ile 73 gönüllü kemik iliği donörü dahil edildi. HLA B27 tiplendirilmesi PCR-SSP yöntemi ile belirlendi.
Elde edilen bulgulara göre çalışmaya alınan AS'li hastaların yaş ortalaması 31±11yıl olarak bulundu. Aynı grupta erkeklerde (%39.3) HLA B27 frekansı kadınlardan (%19.0) çok daha yüksekti. Ankilozan spondilitli hastalar (%58,3) ile kontrol grubu (%4.3) karşılaştırıldığında hasta grubunda HLA B27 pozitifliğinin yüksek olduğu görüldü ($p<0.05$).
Sonuç olarak AS hastalarında HLA B27 frekansının sağlıklı bireylerden daha yüksek olduğu görülmektedir. Doğu Anadolu Bölgesinin hasta populasyonunda HLA B27 pozitifliği, literatürde verilen diğer oranlardan daha düşük olabilir. Bu durumu inceleyecek yeni klinik çalışmaların yapılması faydalı olacaktır.
Anahtar Sözcükler: HLA B27; Ankilozan Spondilit; erkek.

Doğu Anadolu Bölgesinde Ankilozan Spondilitli Hastalarda HLA B27 Frekansının Dağılımı

Ankylosing spondylitis (AS) is a chronic inflammatory disease with unknown etiology. Genetic and environmental factors are known to play important roles in the pathogenesis of the disease. A strong association has been detected between AS development and HLA B27. In this study, relationship between HLA B27 and AS in our region has been investigated in the light of literature.
In this study, distribution of HLA B27 frequency has been investigated in AS patients classified according to modified New York criteria and in healthy controls. Sequence specific primer polymerase chain reaction (SSP-PCR) technique was used for HLA B27 typing unrelated 84 AS patients and 73 bone marrow volunteer donors.
Mean age of AS patients were 31±11 years**.** In the same group, HLA B27 frequency was found higher in males (39.3%) compared to females (19.0%). HLA B27 positivity was found significantly higher in AS patients (58.3%) when compared the control group (4.3%) ($p<0.05$).
In conclusion, the frequency of HLA-B27 in AS patients observed as higher than healthy subjects. The positivity of HLA-B27 in patient population of Eastern Anatolia is lower than the literature. Further controlled studies are needed to investigate this outcome.
Key Words: HLA B27; Ankylosing Spondylitis; male.

Introduction

In genetic studies, individuals with certain HLA alleles have been detected to be more prone to specific autoimmune diseases compared to individuals who do not have these alleles.[1] Since recent 30 years, definition of HLA B27 and AS association has become the milestone in investigating the relationship of HLA and other genetic markers with SpA diseases.[2]

The overall prevalence of AS is 0.2–1.1%, and the incidence of AS is 0.5–14 per 100 000 people per year according to studies from different countries.[3] AS prevalence was found as 0.25% in a study screening 4031 patients in Turkey.[4] Mainly, although role of HLA

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B27 in AS etiology has not been fully understood, HLA B27 is encountered in the ratio of 8-14% in healthy European individuals and more than 90% of AS cases.[5] In our country, this ratio was found as 6.8-8% in healthy individuals and 73.7-80% in AS patients.[4,6,7] AS prevalence is 2% in HLA B27 positive individuals and 20% in HLA B27 positive relatives of AS patients. HLA B27 was seen to be negative in 5-10% of AS patients.[8] AS was reported to be more prevalent in males compared to females, thereby females were detected to have been affected less than males. [3]

In our country, this ratio was found as 1.8-4.2. [6,9-11] Social and cultural properties of the women in the study region are considered to contribute this. In our region, AS and HLA B27 association was not searched before. So, in this study, it was aimed to type HLA B27 in AS patients who were diagnosed according to New York diagnostic criteria and to investigate its prevalence in our region.

Material and Method

In 2009-2011 years, 84 unrelated (54 males and 30 females) who were admitted to Physical Therapy and Rehabilitation outpatient clinics at Ataturk University from various provinces, diagnosed as AS according to modified New York criteria was included in the study. 73 unrelated controls who had been applied to our laboratory for volunteer bone marrow donation, whose tissue typing had been performed. These patients were questioned in terms of AS, reactive arthritis, psoriatic arthritis and other autoinflammatory or inflammatory immune diseases.

2 ml of peripheral blood samples were taken into the tubes from each patient and control. Genomic DNA isolation was performed in automatized DNA isolation device (MagNA Pure LC DNA Isolation Kit I, Roche). HLA typing of the samples were done in Tissue Typing and Molecular Diagnosis Laboratory of Medical Biology Department, Ataturk University. HLA B27 positivity of patients and controls was detected with the aid of low resolution sequence specific primers (PCR-SSP) (Onelambda). PCR products were loaded to agarose gel and documented under UV light.

Statistical analysis were done using SPSS statistical package program (version 17.0). HLA B27 distribution of AS and healthy groups was analyzed with chi square method. Difference between obtained results was accepted significant at level of $p<0.05$.

Results

A total of 73 (35 male/38 female) controls were included in this study. Mean age of the controls was found as 32±10 years. Characteristics of patients with AS in our study were shown on Table 1.

Ratio of HLA B27 positive patients among AS patients is 58.3%. In this study, male/female ratio of AS patients is 1.8. In the same group, HLA B27 frequency was found much higher in males (39.3%) compared to females (19.0%). HLA B27 positivity was higher in AS patients (58.3%) when compared with donors in control group (4.3%), ($p<0.05$).

Table 1. Clinical, demographic features and distribution of HLA B27 in patients with ankylosing spondylitis.

Characteristics	AS patients (n=84)
Age, mean ± SD (years)	31 ± 11
Sex (male/female)	54/30 = 1.8
Disease duration ± SD (years)	4.6 ± 4
CRP (mg/L)	1.4 (0.3-48.1)
ESR (mm/h)	25(6-71)
HLA B27 frequency	58.3%
Male HLA B27 frequency	39.3%
Female HLA B27 frequency	19.0%

Discussion

AS is a chronic inflammatory disease with unknown etiology. Although HLA B27 has a strong relationship with AS and SpA, etiopathogenesis of the disease has not been fully understood yet.[12] In a study conducted with the patients who were not carrying HLA B27 alleles or not, disease was reported to emerge in older ages in the ones who were not carrying HLA B27 alleles.[13] Prevalence of AS and SpA was estimated using different study methods like screening HLA B27 positive individuals of whom most were blood donors or patients' relatives, medical records or population studies in a certain area in various European populations.

HLA B27 was found most frequent among healthy individuals in Pawaia tribe who live in high areas of Papua New Guinea (53%).[14] In literature, HLA B27 frequency in AS patients has been frequently reported as 90%. This high positivity most commonly seen in Northern European countries has not been found in our country despite limited number of studies. In the study of Kasapoglu et al. carried out with 112 AS patients, HLA B27 positivity was found as 70%.[9] In Turkey carried out by the TRASD AS study group on 262 patients, HLA B27 positivity was found as 73.7%. This ratio was 7-8% in healthy individuals.[15] In our study, HLA B27 positivity was found significantly higher in AS patients (58.3%) compared to healthy controls (4.3%).

HLA B27 positivity was reported to be seen in most of the AS patients with positive family history [16]. In this study, unrelated AS patients were evaluated and family history was questioned. HLA B27 positivity was found higher in patients of whom family members had AS complaints.

AS was reported to be seen more frequently in males compared to females thereby females are affected less from the disease. In our region, this ratio was found 4.2 in adult onset AS.[11] In our study, number of HLA B27 positive male AS patients was found much higher than that of females, male/female ratio for AS is 1.8. This ratio may be related to mild course of the disease and low disease index. An alternative explanation may be that women's who live in this area using health services less or less hospital admissions.[17]

In conclusion, although role of HLA B27 in AS etiology has not been fully understood, literature data about HLA B27 positive patients in our country is limited. This study revealed that HLA B27 prevalence in our study is different from the ratio of other study. Further investigation of the causal factors is needed.

References

1. Thorsby E. Invited Anniversary Review: HLA Associated Diseases. Hum Immunol 1997; 53: 1-11. DOI: 10.1016/S0198-8859(97)00024-4
2. Khan MA. HLA-B27 and Its Pathogenic Role. J Clin Rheumatol 2008; 14: 50-2. DOI: 10.1097/RHU.0b013e3181637a38
3. Weisman M, Van der Heijde D, Reveille J. Ankylosing Spondylitis and Spondyloathropathies. London: 2008; 10: 121-8.
4. Onen F, Akar S, Birlik M, et al. Prevalence of Ankylosing Spondylitis and Related Spondyloarthritides in an Urban Area of Izmir, Turkey. J Rheumatol 2008; 35: 305-9.
5. Bakland G, Nossent HC, Gran JT. Incidence and Prevalence of Ankylosing Spondylitis in Northern Norway. Arthritis Rheum 2005; 53: 850-5. DOI: 10.1002/art.21577
6. Bodur H, Ataman S, Bugdaycı DS, et al. Description of the Registry of Patients with Ankylosing Spondylitis in Turkey: TRASD-IP. Rheumatol Int 2012; 32:169-76. DOI: 10.1007/s00296-010-1599-7
7. Birinci A, Bilgici A, Kuru O et al. HLA-B27 Polymorphism in Turkish Patients with Ankylosing Spondylitis. Rheumatol Int 2006; 2: 285-7. DOI: 10.1007/s00296-005-0614-x
8. Arnett FC. Ankylosing spondylitis. In: Koopman WJ, (ed).Arthritis and Allied Conditions.A Texbook of Rheumotology. William and Wilkins 1997; 1197-208.
9. Low frequency of HLA-B27 in Ankylosing Spondylitis Patients from Turkey. Joint Bone Spine 2008; 75: 299-302. DOI: 10.1016/j.jbspin.2007.06.021
10. Bodur H, Ataman S, Bulut L, et al. Characteristics and Medical Management of Patients with Rheumatoid Arthritis and Ankylosing Spondylitis. Clin Rheumatol 2008; 27: 1119-25. DOI: 10.1007/s10067-008-0877-1
11. Ozgocmen S, Ardicoglu O, Kamanlı A, et al. Pattern of Disease Onset, Diagnostic Delay, and Clinical Features in Juvenile Onset and Adult Onset Ankylosing Spondylitis. J Rheumatol 2009; 36: 2830-3. DOI: 10.3899/jrheum.090435
12. Khan MA, Ball EJ. Genetic Aspects of Ankylosing Spondylitis. Best Pract Res Clin Rheumatol 2002; 16: 675-90.
13. Feldtkeller E, Khan MA, Van der Heijde D, et al. Age at Disease Onset and Diagnosis Delay in HLA-B27 Negative vs. Positive Patients with Ankylosing Spondylitis. Rheumatol Int 2003; 23: 61-6.
14. Bhatia K, Prasad ML, Barnish G, et al. Antigen and Haplotype Frequencies at 3 Human-Leukocyte Antigen Loci (HLA-A, HLA-B, HLA-C) in the Pawaia of Papua-New-Guinea. Am J Physical Anthropol 1988; 75: 329-40. DOI: 10.1002/ajpa.1330750304
15. Gul A, Uyar FA, Inanc M, et al. A Weak Association of HLA-B*2702 with Behcet's Disease. Genes Immun 2002; 3: 368-72.
16. Sieper J, Rudwaleit M, Khan MA, et al. Concepts and Epidemiology of Spondyloarthritis. Best Pract Res Clin Rheumatol 2006; 20: 401-17. DOI: 10.1016/j.berh.2006.02.001
17. Chen HH, Chen TJ, Chen YM, et al. Gender Differences in Ankylosing Spondylitis-Associated Cumulative Healthcare Utilization: A Population-Based Cohort Study. Clinics (Sao Paulo) 2001; 66: 251-4. DOI: 10.1590/S1807-59322011000200012

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