Original Research Article

HLA-B27 STATUS IN SPONDYLOARTHROPATHIES

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Abstract

Introduction: The human leukocyte antigens (HLA) are gene loci in the major histocompatibility complex class I of genes on chromosome 6, present on all nucleated cells. This activity reviews the varied presentations of HLA-B27 associated syndromes. Diverse disease presentations often require interprofessional approaches to care for patients with HLA-B27 syndromes.

Objectives of the study: The objective of the present study is to estimate HLA-B27 levels in patients with seronegative spondyloarthopathies.

Materials and methods: In the present study, we included the patients with seronegative spondyloarthropathies in the age group of 30-70 years. We included a total of 60 patients with SNSA. The diagnosis of SNSA include the absence of RA factor, subcutaneous nodules, sacroilitis, inflammatory peripheral arthritis, ocular inflammation, alteration of skin, buccal ulceration, enthesopathy, thrombophlebitis, pyoderma gangraenosum, familial aggregation and association with HLA-B27. Serologic-based HLA typing using Antigen-specific sera was used to determine a patient's HLA type.

Results: In the present study, we included a total of 60 patients of SNSA based on the inclusion criteria mentioned above, the patients were in the age group of 30-70 years. Majority of the patients in our study were in the age group of 30-40 years. It is evident that out of the 60 patients studied HLA-B27 was detected in 8 patients and it is not detected in 52 patients. The prevalence of HLA-B27 in patients with SNSA is found to be 13.3%.

Discussion and conclusion: In conclusion, our findings confirm the strong association of the HLA B27 allele with various types of seronagative SpAs. No association between each of major clinical manifestations with age and sex distribution. We suggest that HLA Typing would help in the diagnosis of seronagative SpAs specially AS where clinical presentation is unclear and in identifying the family members at risk.

Key-words: seronegative spondyloarthropathies, major histocompatibility complex, human leukocyte antigen, spondylitis and rheumatoid arthritis factor.

INTRODUCTION

Spondyloarthritis (SpA) is a group of seronegative arthritides, which includes ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis (ReA), undifferentiated SpA and enteropathy related arthritis (EA). The global prevalence of SpA ranges from 0.2 to 1.61% in the general population. The numbers depend on the geographic area, the study population, data sources and the case definition used to classify SpA, which has evolved considerably over the years. The above subtypes of SpA share several phenotypic characteristics, which include inflammatory lesions in the axial and peripheral joints, enthesitis (inflammation at the insertion sites of tendons and ligaments into the bone), uveitis (inflammation in the eye) and enteritis (inflammation in the small intestine), in varying combinations and frequencies. Clinically, individuals with SpA present with low back ache, alternating gluteal pain and stiffness of the spine, all of which worsen with rest and improve upon exercise. Along with these axial symptoms, individuals with SpA also have inflamed peripheral joints and entheseal sites. The skeletal manifestations are often associated with several extra-articular features in the eye, skin and gut, depending on the subtype of SpA. The features start off insidiously and progress chronically in most of the subtypes of SpA except in ReA. The human leukocyte antigens (HLA) are gene loci in the major histocompatibility complex class I of genes on chromosome 6, present on all nucleated cells. This activity reviews the varied presentations of HLA-B27 associated syndromes. Diverse disease presentations often require interprofessional approaches to care for patients with HLA-B27 syndromes. Evaluation and management strategies for these diseases are reviewed [1].

The presence of the HLA-B27 allele is not essential for the development of spondyloarthropathy, but it is highly associated with the development of the disease. Research has identified more than forty other genetic loci in genome-wide mapping studies. HLA-B27 contributes to approximately thirty percent of the heritability of ankylosing spondylitis [2]. The incidence of acute anterior uveitis in HLA-B27 positive patients has shown on meta-analysis to vary from 40 to 82.5%. It can precede the onset of ankylosing spondylitis by approximately three years.[3] In contrast to the prevalence of roughly ninety percent of patients with ankylosing spondylitis, HLA-B27 is present in less than half of patients with psoriatic arthritis and inflammatory bowel disease (IBD). Seronegative spondyloarthropathies (SNSA) include a group of diseases with arthritis that are negative for rheumatoid factor. The borders of the disease are sometimes obscure, and SNSA has its own classification criteria. The investigation on the prevalence of HLA-B27 will be important for the understanding of SNSA pathogenesis. The association of HLA-B27 with ankylosing spondylitis was first described in 1973,2 and is among the strongest described for a HLA locus.
The recent demonstration that HLA-B27 can interact with a number of different immunoreceptors on different cell types has opened up promising new avenues of research into clarifying its role in the pathogenesis of spondyloarthropathy. The finding that the natural role of HLA molecules is peptide binding and presentation to T cells led to the suggestion that the spondyloarthropathies result from the ability of HLA-B27 to bind a unique set of peptides. This ‘arthritogenic’ peptide

hypothesis proposes that disease results from an HLA-B27-restricted cytotoxic T-cell response to a peptide or peptides found only in joint and other affected tissues. Such a peptide could be bound and presented by all disease-associated HLA-B27 subtypes, but not by other class I molecules. Pathogenic T cells might be primed in the joint or at other sites such as the genital or gut mucosa. A modification of this original hypothesis could entail a breakdown of self-tolerance by initial HLA-B27-restricted presentation of a peptide or peptides derived from one of the triggering pathogens. If the disease association of HLA-B27 is indeed a consequence of its physiological role in peptide presentation, HLA-B27-restricted cytotoxic T lymphocytes (CTL), specific for self-epitopes or bacterial epitopes, should be demonstrable in the involved joints of patients with spondyloarthropathies. [4-10].

OBJECTIVES OF THE STUDY:

The objective of the present study is to estimate HLA-B27 levels in patients with seronegative spondyloarthopathies.

MATERIALS AND METHODS:

In the present study, we included the patients with seronegative spondyloarthropathies in the age group of 30-70 years. We included a total of 60 patients with SNSA. The diagnosis of SNSA include the absence of RA factor, subcutaneous nodules, sacroilitis, inflammatory peripheral arthritis, ocular inflammation, alteration of skin, buccal ulceration, enthesopathy, thrombophlebitis, pyoderma gangraenosum, familial aggregation and association with HLA-B27. Serologic-based HLA typing using Antigen-specific sera was used to determine a patient's HLA type. The complement mediated micro cytotoxicity test was performed using commercial kit including antigen-coated microplates, and the test was done according to manufacturer's instruction. This was a prospective descriptive-analytic research study. Each of HLA-B27 positive patients were evaluated for age and sex distribution and at least one of the major clinical features of NSAs. Data Analysis: Collected data were analysed with SPSS version 10.0 and Pearson's chi square test was used.

RESULTS:

In the present study, we included a total of 60 patients of SNSA based on the inclusion criteria mentioned above, the patients were in the age group of 30-70 years. The majority of the patients in our study were in the age group of 30-40 years.

Table 1: Shows age wise and gender wise distribution of study subjects		
31-40 years	26	43.33%
41-50 years	12	20%
51-60 years	12	20%
61-70 years	10	16.66%
Males: Females	38/22	63.33%/36.66%

Table 2: Shows the distribution of study subjects based on clinical presentation		
Spondylitis	22	36.66%
Peripheral arthritis	32	53.33%
Ocular inflammation	16	26.66%
Alteration of skin	10	16.66%
Buccal ulceration	8	13.33%
Enthesopathy	6	10%

Table 3: Shows the Prevalence of association of HLA-B27 positivity in patients with SNSA		
HLA-B27 detected	8	13.33%
HLA-B27 not detected	52	86.66%

DISCUSSION AND CONCLUSION:

In the present study, we included a total of 60 patients of SNSA based on the inclusion criteria mentioned above, the patients were in the age group of 30-70 years. Majority of the patients in our study were in the age group of 30-40 years. It is evident from table 2 that, 22 patients presented with spondylitis, 32 had peripheral arthritis, 16 had ocular inflammation, 10 had alteration of skin, 8 had buccal ulceration and 6 had enthesopathy. It is evident that out of the 80 patients studied HLA-B27 was detected in 8 patients and it is not detected in 52 patients. The prevalence of HLA-B27 in patients with SNSA is found to be 13.33%.

Seronegative spondyloarthropathies are a group of disorders characterized by inflammation of the spine, sacroiliac joints, and peripheral arthritis along with various characteristic extra-articular features. Their pathogenesis and immunogenetics have not yet been fully elucidated. Ankylosing Spondylitis (AS) is probably the best studied of these diseases. It has now been 35 years since the association of human leukocyte antigen (HLA) B27 and AS has been demonstrated. Since then, a plethora of association studies and linkage studies unequivocally demonstrate that genetic determinants within or near the major histocompatible complex (MHC) are critical to the etiology of AS. In population surveys, 1 to 6% of adults inheriting HLA-B27 have been found to have AS.8 In contrast in families with AS, the prevalence is 10 to 30% among adult first – degree relatives inheriting HLA-B27. The concordance rate in identical twins is approximately 65%. It is currently believed that susceptibility to AS is determined almost entirely by genetic factors, with HLA-B27 comprising about one-third of the genetic component. HLA-B27 and associate antigens incidence were studied by Rivera S. and colleagues in 620 cases of seronegative spondiloarthropathies (SNS) and 262 controls of a Venezuelan mestizo population from Zulla state between 1985 and 1995. The incidence of HLA-B27 was 20.96% of all cases of SNS. It was increased in patients with ankilosing spondylitis (AS) 33.33% and Relter's syndrome (RS) 30%, but not in uveitis (Uv) 20% and psoriatic arthropathy (PsA) 0%. Luukkain RK and colleagues investigated sacroiliitis in patients with seronegative Oligoarthritis. Thirty consecutive patients with seronegative oligoarthritis and no other signs of spondylarthropathy were included. Sacroiliac (SI) joints were investigated by both radiography and magnetic resonance imaging. HLA B27 antigen was studied and family history was reexamined in 2006. Five patients had sacroiliitis. Additionally, 15 patients had HLA B27 antigen or family history of either psoriasis or ankylosing spondylitis. Their conclusion was that during the first decade of seronegative oligoarthritis, HLA B27 antigen,

family history, and especially imaging of SI joints reveal in two thirds of the patients the spondylarthritic nature of their disease. [11-14]

In conclusion, our findings confirm the strong association of the HLA B27 allele with various types of seronagative SpAs. No association between each of major clinical manifestations with age and sex distribution. We suggest that HLA Typing would help in the diagnosis of seronagative SpAs specially AS where clinical presentation is unclear and in identifying the family members at risk.

REFERENCES:

1. Allen RL, Bowness P, McMicheal A. The role of HLA-B27 in spondyloarthritis. Immunogenetics. 1999Nov;50(3-4):220-7

2. Bowness P. HLA-B27. Annu Rev Immunol. 2015;33:29-48

3. D'Ambrosio EM, La Cava M, Tortorella P, Gharbiy M, Campanella M, lannetti l. Clinical Features and Complications of the HLA-27-associated Acute Anterior Uveitis: A Metaanalysis. Semin Ophthalmol. 2017;32(6):689-701

4. Keratiseavee S, Brent LH. Spondyloarthropathies: Using presentation to make the diagnosis. Cleveland Clin J Med 2004;71:184-206.

5. Brewerton DA, Caffrey M, Hart FD, James DCO, Nichols A, Sturrock RD. Ankylosing spondylitis and HL-A27. Lancet 1973;28:904-7.

6. Mcmichael A, Bowness P. HLA-B27: Natural function and pathogenic role in spondyloarthritis', Arthritis Res 2002;4(Suppl 3):S153-8.

7. Townsend A, Rothbard J, Gotch F, Bahadur B, Wraith D, McMichael A. The epitopes of influenza nucle oprotein recognized by cytotoxic T lymphocytes can be defined with short synthetic peptides. Cell 1986;44:959-68.

8. Gotch F, Rothbard J, Howland K, Townsend A, McMichael A. Cytotoxic T lymphocytes recognize a fragment of influenza virus matrix protein in association with HLA-A2. Nature 1987;326:881-2.

9. Benjamin R, Parham P. Guilt by association HLA B27 and ankylosing spondylitis. Immunol Today 1990;11:137-42.

10. Hermann E, Yu DT, Meyer ZBK, Fleischer B. HLA-B27-restricted CD8 T cells derived from synovial fluids of patients with reactive arthritis and ankylosing spondylitis. Lancet 1993;342:646-50.

11. Harrison TR. Principles of Internal Medidi ne, 16th Ed. Chapter 305, 1993-96. McGraw Hill, New York. 2005.

12. Rivera S, Hassanhi M. Relation of spondylarthropathies and HLA-B27 antigen in patients from the state of Zulia, Venezuela. Sanger (Barc) 1996;41:473-6.

13. Luukkainen RK, Virtanen KO, Kaarela K. Occurrence of sacroiliitis in patients with seronegative oligoarthritis. Clin Rheumatol 2006;10:7-10.

14. Shankarkumar U, Devraj JP. Seronegative spondarthritis and human leucocyte antigen association. Br J Biomed Sci 2002;59:38-41.