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Original Article

Study on the Susceptible Factor for Each Type of Uveitis

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ABSTRACT

Background and Aim: Uveitis is a group of inflammatory eye disorders with various etiologies, including genetic susceptibility. Certain Human Leukocyte Antigen (HLA) types are known to be associated with different forms of uveitis. This study aims to identify disease-susceptible HLA types (DSHTs) for each type of uveitis. **Methods:** 120 patients with uveitis (47 patients with anterior uveitis, 33 patients with posterior uveitis and 32 patients with panuveitis) were enrolled in the study. After determining the relative risk values according to the types of uveitis, we have revealed HLA types with relative risk values bigger than 1(DSHTs) for each type of uveitis. **Results:** 1) For patients with anterior uveitis, DSHTs were HLA-B27, HLA-A26, HLA-DR10. 2) For patients with posterior uveitis, DSHTs were HLA-A29, HLA-B44 and HLA-DR4. 3) For patients with panuveitis, DSHTs were HLA-DR4, HLA-B51, HLA-A26 and HLA-DR11. **Conclusion:** These findings highlight genetic predispositions that may aid in early diagnosis and targeted management.

Keywords: Anterior Uveitis, Genetic Susceptibility, Human Leukocyte Antigen, Panuveitis, Posterior Uveitis, Uveitis,

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INTRODUCTION

Uveitis is a group of inflammatory eye diseases affecting the uveal tract, which includes the iris, ciliary body and choroid. It can be triggered by various factors such as infections, trauma, or systemic inflammatory disorders. However, in most cases, the primary underlying mechanism is believed to be intrinsic autoimmunity. Recent studies emphasize the significance of immune dysregulation in the pathogenesis of uveitis, with genetic and environmental factors playing a crucial role in disease onset and progression.[1-4] One important mechanism contributing to autoimmune uveitis is molecular mimicry, wherein an immune response directed against an external antigen cross-reacts with self-antigens due to structural similarities. This phenomenon may lead to chronic inflammation and tissue damage, further exacerbating disease severity.[2] While the precise pathophysiology of uveitis remains incompletely understood, strong evidence suggests that genetic susceptibility, particularly variations in the Human Leukocyte Antigen (HLA) system, influences disease risk and progression.

The HLA complex, located on chromosome 6, plays a central role in antigen presentation and immune system regulation. Since HLA alleles remain unchanged throughout an individual's lifetime, they serve as genetic markers for disease susceptibility. Numerous studies have established associations between specific HLA types and various autoimmune diseases, including uveitis. However, Disease-Susceptible HLA Types (DSHTs) differ across populations, ethnicities and geographic regions due to variations in HLA allele distribution. For example, while HLA-B27 is strongly linked to anterior uveitis worldwide, other HLA types such as HLA-A29 have been specifically implicated in birdshot chorioretinopathy, a form of posterior uveitis that predominantly affects Caucasians.[5-9]

Given these population-specific variations, it is essential to determine the specific DSHTs associated with different types of uveitis in diverse ethnic groups. Understanding these genetic predispositions can improve diagnostic accuracy, risk assessment and the development of targeted immunotherapies. Therefore, this study aims to identify DSHTs for each type of uveitis in the Democratic People's Republic of Korea (DPRK). By elucidating the genetic factors contributing to uveitis susceptibility in this population, we hope to enhance disease prediction, early diagnosis and personalized treatment strategies.

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MATERIALS AND METHODS

Subject

Male Wistar rats (260 g) were provided by Laboratory Animal Centre of Sinuiju University of Medical Sciences and adapted in a lab environment before experiments for a week. 21 rats are randomly chosen and during the experiment, feed and water were available to rats at any time. The temperature was maintained at 20±2ºC and the humidity was 55%. The study was approved by the Ethics Committee for Animal Experimentation, Faculty of Basic Medicine, Sinyuju University of Medical Sciences.

Methods

After confirming the diagnosis of uveitis, HLA profile was determined for each patient with PCR-SSP (Sequence Specific Primer-Polymerase Chain Reaction). PCR-SSP is based upon the principle that when PCR is performed with primers with 3' terminal sequence specific to each allele, amplification product is obtained only for the given allele, but not for other alleles due to low PCR efficiency. HLA types were determined and relative risk values were calculated for each type of uveitis. Relative risk is a parameter that shows how many times the risk of the disease increases in cases with a certain HLA type compared with those cases without the given antigen. If the value was bigger than 1, Etiologic Fraction (EF) was determined and if it was more than 0.1, then the antigen type was defined as DSHT of the disease.

Statistical Analysis of Data

Statistical analysis was performed using SPSS, with the chi-square test and Fisher's exact test applied to compare HLA allele frequencies. Relative Risk (RR) and Etiologic Fraction (EF) were calculated to identify Disease-Susceptible HLA Types (DSHTs). A p-value < 0.05 was considered statistically significant, with Bonferroni correction applied for multiple comparisons. Results were expressed as mean±SD for continuous variables and percentages for categorical data.

RESULTS

In this study, we identified Disease-Susceptible HLA Types (DSHTs) associated with different types of uveitis. For anterior uveitis (Table 1), the most significant DSHTs were HLA-B27, HLA-A26 and HLA-DR10. Among these, HLA-B27 showed the highest relative risk (RR=8.1667) and etiologic fraction (EF=0.3921), suggesting a strong genetic predisposition.

For posterior uveitis (Table 2), significant DSHTs included HLA-A29, HLA-B44 and HLA-DR4. HLA-A29 demonstrated the highest risk association (RR=26.9444, EF=0.4377), reinforcing its

Table 1: Disease-Susceptible HLA Types (DSHTs) for Anterior Uveitis.

Sl. No.	HLA (antigen type)	Frequency of phenotype		*P*	RR*	EF**
		Study group (*n*=47)	Control group (*n*=100)			
1	B27	0.4468 (21)	0.0900 (9)	< 0.01	8.1667	0.3921
2	A26	0.2340 (11)	0.0500 (5)	< 0.05	5.8056	0.1937
3	DR10	0.1702 (8)	0.0500 (5)	<0.05	3.8974	0.1265

*RR (Relative Risk): a parameter that shows how many times the risk of the disease increases in cases with a certain HLA type compared with those cases without the given antigen **EF (Etiologic Fraction): Determined when RR value is bigger than 1. Its value ranges from 0 to 1. If the value is close to 1, it means that the specific antigen locus is close to the etiological gene.

Table 2: Disease-Susceptible HLA Types (DSHTs) for Posterior Uveitis.

Sl. No.	HLA (antigen type)	Frequency of phenotype		*P*	RR	EF
		Study group (n=33)	Control group (n=100)			
1	A29	0.4545 (15)	0.0300 (3)	< 0.01	26.9444	0.4377
2	B44	0.5455 (18)	0.2300 (23)	< 0.01	4.0174	0.4097
3	DR4	0.5758 (19)	0.3200 (32)	< 0.05	2.8839	0.3761

Table 3: Disease-Susceptible HLA Types (DSHTs) for Panuveitis.

Sl. No.	HLA (antigen type)	Frequency of phenotype		*P*	RR	EF
		Study group (n=32)	Control group (n=100)			
1	DR4	0.5313 (17)	0.3200 (32)	< 0.05	2.4083	0.3107
2	B51	0.3125 (10)	0.0900 (9)	< 0.05	4.5960	0.2445
3	A26	0.2500 (8)	0.0500 (5)	< 0.05	6.3333	0.2105
4	DR11	0.1875 (6)	0.0300 (3)	< 0.05	7.4615	0.1624

well-established link with posterior uveitis, particularly birdshot chorioretinopathy. HLA-B44 and HLA-DR4 also exhibited elevated relative risk values, indicating their role in disease susceptibility.

For panuveitis (Table 3), four HLA types-HLA-DR4, HLA-B51, HLA-A26 and HLA-DR11-were identified as DSHTs. HLA-DR4 was the most frequently observed (RR=2.4083, EF=0.3107), followed by HLA-B51, which has been previously associated with Behçet's disease. Additionally, HLA-A26 and HLA-DR11 showed significant relative risk values, suggesting their role in the genetic predisposition to panuveitis.

DISCUSSION

Uveitis is a heterogeneous group of inflammatory diseases that can affect different parts of the uveal tract, with varying clinical presentations and underlying etiologies. A strong genetic predisposition, particularly linked to specific Human Leukocyte Antigen (HLA) types, plays a critical role in disease susceptibility. In this study, we identified Disease-Susceptible HLA Types (DSHTs) for anterior uveitis, posterior uveitis and panuveitis, highlighting key genetic markers that could aid in early diagnosis and targeted management strategies.

Anterior uveitis, the most common form of uveitis, is characterized by sudden-onset eye pain, redness, photophobia and visual disturbances. Previous studies have consistently shown a strong association between HLA-B27 and anterior uveitis, with HLA-B27-positive individuals being at significantly higher risk of developing the disease. Our findings align with this, as HLA-B27 exhibited the highest Relative Risk (RR=8.1667) and Etiologic Fraction (EF=0.3921) among anterior uveitis patients. Additionally, HLA-A26 and HLA-DR10 were also identified as DSHTs, suggesting that genetic susceptibility may extend beyond HLA-B27, particularly in the population studied. These findings emphasize the importance of HLA typing in risk assessment and early intervention for anterior uveitis.

Posterior uveitis, which affects the choroid and retina, is associated with a higher risk of vision loss due to its insidious onset and potential for retinal damage. A well-established genetic marker for posterior uveitis, particularly birdshot chorioretinopathy, is HLA-A29. Our study confirmed this strong association, as HLA-A29 exhibited the highest Relative Risk (RR=26.9444) and Etiologic Fraction (EF=0.4377). This finding is consistent with previous reports in Caucasian populations, where HLA-A29 is found in over 95% of birdshot chorioretinopathy patients. Interestingly, our study also identified HLA-B44 and HLA-DR4 as DSHTs for posterior uveitis, suggesting potential regional or ethnic variations in genetic susceptibility. In contrast, studies in Japanese populations have reported lower frequencies of HLA-A29 in posterior uveitis patients, reinforcing the need for population-specific research. These variations highlight the complexity of genetic predisposition and the necessity for tailored diagnostic and therapeutic approaches.

Panuveitis, an inflammatory condition affecting all segments of the uveal tract, is associated with a diverse range of autoimmune and infectious triggers. The genetic predisposition to panuveitis has been linked to multiple HLA types, particularly HLA-B51, which is strongly associated with Behçet's disease-a systemic vasculitis with a high prevalence in the Middle East and Asia. In our study, HLA-B51 was identified as a significant DSHT for panuveitis (RR=4.5960, EF=0.2445), supporting its role in disease susceptibility. Additionally, we found that HLA-DR4, HLA-A26 and HLA-DR11 were also associated with increased risk, indicating that panuveitis has a broader genetic predisposition compared to anterior or posterior uveitis. The presence of multiple DSHTs suggests a complex interplay of immune mechanisms in panuveitis pathogenesis, warranting further investigation into their roles in disease progression and severity.

CONCLUSION

We have clarified the DSHTs for each type of uveitis. HLA types with RR bigger than 1.0 and EF bigger than 0.1 were HLA-B27, HLA-A26, HLA-DR10 for anterior uveitis, HLA-A29, HLA-B44 and HLA-DR4 for posterior uveitis and HLA-DR4, HLA-B51, HLA-A26 and HLA-DR11 for panuveitis, respectively.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

HLA: Human Leukocyte Antigen; **DSHT:** Disease-Susceptible HLA Type; **RR:** Relative Risk; **EF:** Etiologic Fraction.

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