Original Article

Clinical Analysis of 240 Patients with HLA-B27 Associated Acute Anterior Uveitis

Yuqin Wang[1], Xiaoya Lu[1], Yulin Wang[2], Liping Mao[1], Yunfeng Gu[1], Pengfei Chen[1], Meiqin Zheng[1,*]
1 Zhejiang Ophthalmologic Hospital, Eye Hospital of Wenzhou Medical College, Wenzhou 325027, China
2 Department of Ophthalmology, First Affiliated Hospital of Nanchang University, Nanchang 330006, China

Abstract

Purpose: To analyze the prevalence of HLA-B27 associated acute anterior uveitis and to identify its clinical features.

Methods: A total of 240 patients with HLA-B27 associated acute anterior uveitis, who were admitted to Zhejiang Ophthalmologic Hospital between December 2006 and October 2012, were retrospectively analyzed. The age of onset, sex, affected eyes, HLA-B27 antigen detection, recurrence, joint involvement, and surgical complications were investigated.

Results: The average age of onset was 37.0±12.0 years and the ratio of male to female patients was 2.4:1. Most cases had alternate unilateral or bilateral involvement. Among all participants, 234 cases (97.5%) were HLA-B27 positive, and 124 cases (51.7%) had spondyloarthropathies (SpA), dominated by 108 cases with ankylosing spondylitis (AS, 45.0%), and mostly seen in male subjects (P<0.05). Six patients were HLA-B27 negative (2.5%) and on statistical significance was noted between male and female patients (P>0.05). A total of 193 cases (80.4%) presented with complications, mainly fibrinous exudation, posterior synechia, and vitreous opacity.

Conclusion: HLA-B27 that is associated acute anterior uveitis with a relatively high incidence and recurrence presents with more severe clinical features than does idiopathic acute anterior uveitis, and it often accompanies systemic arthritic diseases. HLA-B27 antibody detection is associated with the diagnosis and treatment of acute anterior uveitis. (***Eye Science 2012; 27: 169-172***)

Keywords: HLA-B27; acute anterior uveitis; epidemiology; clinical feature

The human leukocyte antigen (HLA) system describes the major histocompatibility complex (MHC) in humans. This super locus contains a large number of genes related to immune system function in humans. In 1973, Brewerton et al found an association between HLA-B27 antigen and acute anterior uveitis (AAU), and subsequently noted certain relationships between HLA-B27 antigen and many other diseases. HLA-B27 associated AAU has distinctive clinical features and it is regarded as an independent disease. This study is designed to analyze the general information and clinical features of 240 patients with HLA-B27 associated AAU, and to further investigate the potential pathogenic factors and the clinical significance of HLA-B27 antigen detection.

Materials and methods

General information

Methods: A total of 240 patients with HLA-B27 associated AAU who were admitted to Zhejiang Ophthalmologic Hospital between December 2006 to October 2012 were retrospectively analyzed. The age of onset, sex, affected eyes, recurrence, HLA-B27 antigen detection, joint involvement, and surgical complications were investigated.

Diagnosis criteria of acute anterior uveitis

The subjects included in the study presented with sudden incidence of iritis or iridocyclitis, accompanied by red eye, ocular pain, photophobia, lachrymation, anterior chamber cell (+), flare (+), and a duration of inflammation of < 3 months[2]. Those with infectious and traumatic AAU were excluded from this study.

Detection of HLA-B27 antigen

The gene sequencing of HLA-B27 in AAU patients was performed using the polymerase chain reaction (PCR). Patients with HLA-B27 positive and other types of uveitis, such as Behcet and Vogt-

DOI: 10.3969/j.issn.1000-4432.2012.04.003
Funding: The building and feasibility study of UBM monitoring system in the diagnosis and treatment of anterior uveitis (NO. Y20090284), granted by Science and Technology Bureau of Wenzhou, China

* **Corresponding author**: Meiqin Zheng, E-mail: yqwang57@163.com

Koyanagi-Harada syndrome, were excluded from this study.

History of disease and clinical presentations

The conditions of illness, including ocular signs, systemic presentations, age of first onset, recurrence, ocular involvement at onset, complications, and sequelae, were explicitly inquired and recorded.

Laboratory and auxiliary examinations

All patients received examinations for rheumatoid factor to eliminate the possibility of rheumatoid arthritis (RA). CT scanning was conducted to identify whether the patients had accompanying spondy loarthropathies. The diagnosis of spondyloarthropathies was made based on the classification criteria proposed by European Spondyloarthropathy Study Group (ESSG)[3].

Statistical analysis

SPSS 15.0 statistical software was used for data analysis. The data were expressed as means ±SD. Measurement data were analyzed by a *t*-test, and enumeration data were statistically analyzed by a *chi*-square test. $P<0.05$ was considered as statistically significant.

Results

Sex and age of onset

A total of 240 cases with HLA-B27 associated AAU, including169 males and 71 females (2.4:1), were enrolled, suggesting a significantly higher incidence in the male population. Age of onset ranged from 6 to 80 years (37.0±12.0 years on average). The mean age of onset for male patients was 36.0±11.4 years, which was significantly younger than the 39.5±12.9 for female patients ($P<0.05$).

Eye involvement and recurrence

Among the 240 cases, 149 were unilateral involvement and 91 were alternate bilateral involvement, with a ratio of 1.6:1. Statistical significance was noted ($P<0.05$). For the unilaterally involved cases, 74 involved right eyes and 75 were left eyes, with no significant difference ($P>0.05$). A total of 113 patients (47.1%) suffered for the first time, and 127 were recurrent cases (52.9%), ranging from 1 to over 20 times.

Detection of HLA-B27 antigen

A total of 234 patients were HLA-B27 positive, including 166 males (70.9%) and 68 females (29.1%) with a ratio of 2.4:1. The positive rate of HLA-B27 was 98.2% (166/169) for males and 95.8% (68/71) for females. Among the 6 HLA-B27 negative cases, 2 had AS and 4 had undifferentiated spondyloarthropathies.

Concomitant spondyloarthropathies

All of the 240 patients (100%) were negative for RF. A total of 124 patients (51.7%) were negative for SpA, mainly AS (n=108, 45%) and dominated by male patients (male: female=82.4%: 17.6%; $P<0.05$); 16 cases (6.7%) were undifferentiated SpA, and 43.8% were male. There were 116 cases who were not accompanied by systemic SpA, accounting for 48.3%.

Complications

Among the 240 AAU patients, 193 (80.4%) had anterior segment complications, such as anterior chamber fibrinous exudation, posterior synechia, hypopyon, complicated cataract, and secondary glaucoma; 66 (27.5%) had posterior segment complications, mainly vitreous opacity, cystoid macular edema, and retinal vasculitis. A total of 59 patients presented with both anterior and posterior segment complications.

Table 1 Complications of HLA-B27 associated AAU

Complications	No. of case(n)	Percentage(%)
Anterior chamber fibrinous exudation	180	75.0
Posterior synechia	60	25.0
Complicated cataract	22	9.2
Secondary glaucoma	12	5.0
Hypopyon	13	5.4
Vitreous opacity	49	20.4
Cystoid macular edema	17	7.1
Retinal vasculitis	11	4.6

Discussion

HLA-B27 associated AAU is a common anterior uveitis, with a percentage of 37% to 60% among all cases with anterior uveitis, second only to idiopathic anterior uveitis[4-6]. HLA-B27 associated AAU mainly affects the young population and is more frequently seen in male than in female subjects. The recurrence rate is higher for HLA-B27 associated AAU than for HLA-B27 negative AAU. In the present study, the

mean age of onset was 39.5±12.9 years, the ratio of males to females was 2.4, and more than half of the cases (52.9%) were recurrent, consistent with previous investigations[7,8]. The outcomes also suggested that the age of onset was significantly younger for male subjects than for their female counterparts.

HLA-B27 associated AAU has distinctive clinical features and it is regarded as an independent disease. Rothova et al[9]. summarized the clinical features as follows: 1. unilateral acute AAU; 2. anterior chamber fibrinous exudation or cellular exudation 3+; 3. no keratic precipitates; 4. a history of AAU; 5. age of onset<40 years; and 6. accompanied by SpA. The diagnosis can be confirmed if 5 of these criteria are met. HLA-B27 associated AAU is likely to occur in a variety of SpA diseases including AS, Reither syndrome, inflammatory intestinal disease, and psoriatic arthritis, etc. The prevalence of HLA-B27 varies markedly in the general population, occurring, for example, in about 8–10% of Caucasians, 1–6% of Asians, and 2–5% of Chinese[10,11].

The probability of uveitis in a normal population with HLA-B27 positivity was approximately 2%, while that in the SpA patients with HLA-B27 negativity was considerably increased. In this study, 124 patients (51.7%) had SpA, mainly AS (45.0%), and undifferentiated SpA accounted for 6.7%; the other 48.3% were not accompanied by SpA. Three patients had recurrent AAU complicated by psoriasis, but chest X-rays and sacroiliac joint CT scans showed no signs of SpA. One case had a history of acute unilateral anterior uveitis, conjunctivitis, and urethritis, but radiological examination indicated no signs of SpA. Some scholars reported that up to 41% of SpA patients presented with uveitis as the primary presentation[12]. Thus, the possibility of SpA cannot be eliminated for those who were qualified for clinical features while lacking radiological evidence. These patients should not only receive treatment for uveitis but should also undergo examination of the spinal joints for early diagnosis and treatment of SpA.

Common clinical symptoms of HLA-B27 associated AAU include acute unilateral nongranulomatous uveitis, recurrent anterior uveitis, sudden onset, unilateral or alternate bilateral involvement, and a self-limiting course of disease. HLA-B27 associated AAU has severe complications, such as posterior synechia, fibrinous exudation, hypopyon, cystoid mac ular edema, and retinal vasculitis, etc., which threaten visual acuity. Compared to AAU with HLA-B27 negativity, the recurrence rate of HLA-B27 associated AAU is higher and the symptoms are more serious. The recurrence of uveitis is likely to cause vitreous opacity, while complicated cataract and secondary glaucoma can severely damage visual function and even cause blindness. About 83.3% of patients with HLA-B27 associated AAU had complications: 80.4% had anterior segment complications, 27.5% had posterior segment complications and 24.5% were affected by both anterior and posterior segment complications. The major complications included anterior chamber fibrinous exudation, posterior synechia, and vitreous opacity.

For patients with severe anterior segment complications, glucocorticoid eyedrops, madriatics, and subconjunctival injections have been utilized to ease and control the inflammation. For patients with posterior segment involvement, the recommended treatment is provision of retrobulbar injections and systemic glucocorticoid to alleviate complications. The AAU cases with complicated cataract and secondary glaucoma should be treated surgically following anti-inflammation therapy.

References

1 Brewerton.Acute anterior uveitis and HLA-B27.Lancet, 1973, 2:994.

2 Jabs DA, Nussenblatt RB, Rosenbaum JT: Standardization of Uveitis nomenclature (SUN) Working Group.Standardization of Uveitis nomenclature for reporting clinical data.Results of the First International Workshop.Am J Ophthalmol, 2005, 140(3):509–516.

3 Dougados M, van der Linden S, Juhlin R, et al.The European Spondyloarthropathy Study Group preliminary criteria for the classification of pondyloarthropathy.Arthritis Rheum, 1991, 34(10):1218–1227.

4 Luger D, Silver PB, Tang J.Either a Th17 or Th1 effector response can drive autoimmunity : conditions of disease induction affect dominant effector category.J Exp Med, 2008, 205(4): 799–810.

5 Chang JH, McCluskey PJ, Wakefield D.Acute anterior uveitis and HLA-B27.Survey of Ophthalmology, 2005, 50(4):364–388.

6 Sun SM, Xue NP, Liu HY, et al. Detection of HLA-B27

and F cell subsets for former pigment meningitis patients. Chinese Journal of Ophthalmology,1990,26 (5):258-260.
7 Goto H,Mochizuki M,Yamaki K,et al.Epidemiological survey of intraocular inflammation in Japan.Jpn J Ophthalmol,2007,51(1):41-44.
8 Chung YM,Liao HT,Lin KC,et al.Prevalence of spondyloarthritis in 504 Chinese patients with HLA-B27 associated acute anterior uveitis.Scand J Rheumatol, 2009,38(2):84-90.
9 Rothova A,van Veenedaal WG,Linssen A,et al.Clinical features of acute anterior uveitis.Am J Ophthalmol, 1987,103:137-145.
10 Zhou HY,Yang PZ,Huang XK,et al.The association of various forms of anterior uveitis with HLA-B27 antigen and its clinical implication.Chinese Ophthalmic Research,2006, 24(3):197-199.
11 Yabuki K,Inoko H,Ohno S.HLA testing in patients with uveitis.Int Ophthamol Clin,2000, 40(2):19-35.
12 Femandez-Melon J,Munoz-Femandez S,H idalgo V,et al.Uveitis as the initial clinical manifestation in patients with spondyloarthropathies.J Rheumatol,2004,31 (3): 524-527.
13 Zheng RZ,Shi YC.Clinical features of acute anterior uveitis with HLA-B27 positive.Ophthalmology in China, 2004,13(2):100-102.

(from page 168)

the human eye.Invest Ophthalmol Vis Sci,2001,42: 1390-1395.
7 Takashi Fujikado,Teruhito Kuroda,Sayuri Ninomiya,et al.Age-related Changes in Ocular and Corneal Aberrations.Am J Ophthalmol,2004,138(1):143-146.
8 Guirao A,Redondo M,Artal P.Optical aberrations of the human cornea as a function of age.J Opt Soc Am A, 2000,17:1697-1702.
9 Li HW,Guo HK,Zhang HY,et al.Analysis of corneal asphericity in patients after phacoemulsification.Chinese journal of ophthalmology,2010,46:337- 341
10 Marcos S,Rosales P,Llorente L,et al.Change in corneal aberrations after cataract surgery with 2 types of aspherical intraocular lenses. J Cataract Refract Surg, 2007,33 (2):217-226.
11 Iseli HP,Jankov M,Bueeler M,et al.Corneal and total wavefront aberrations in phakic and pseudophakic eyes after implantation of monofocal foldable intraocular lenses.J Cataract Refract Surg,2006,32(5):762-771.
12 Yao K,Tang X,Ye P.Corneal astigmatism, high order aberrations,and optical quality after cataract surgery:microincision versus small incision.J Refract Surg,2006,22 (9 Suppl):S1079-1082.
13 Denoyer A,Denoyer L,Marotte D,et al.Intraindividual comparative study of corneal and ocular wavefront aberrations after biaxial microincision versus coaxial small-incision cataract surgery.Br J Ophthalmol,2008,92: 1679-1684.