Endogenous Uveitis: Experiences in Kaohsiung Veterans General Hospital

**Background.** The distribution of uveitis varies in different parts of the world, which is attributed to geographic, alimentary or genetic factors. Epidemiological studies in uveitis may be extremely important in an effort to better understand the etiology of the disease and the classification of its subtypes. The purpose of this study was to determine the profile and characteristics of endogenous uveitis in southern Taiwan.

**Methods.** Retrospective chart review of the patients diagnosed and treated as endogenous uveitis in Kaohsiung Veterans General Hospital from January 1991 to December 2000 was performed. Demographic data, past history, ophthalmic examination and other laboratory tests were recorded and analyzed.

**Results.** One-hundred and sixty patients were collected, including 93 (58.1%) males and 67 (41.9%) females, with average age of 41.1 ± 17.1 years (range 16-77), and mean follow-up period of 13.7 months. The diagnoses included 46 (28.8%) cases of anterior nongranulomatous uveitis (AAU), 26 (16.3%) cases of Vogt-Koyanagi-Harada (VKH) disease, 18 (11.3%) cases of intermediate uveitis, 14 (8.8%) cases of Behcet's disease, 26 (16.3%) cases of infectious origin, 7 (4.4%) cases of other diagnoses, and 23 (14.4%) undiagnosed cases. Final visual acuity equal to or better than 0.5 was obtained in 78.2% of eyes of AAU, 65.4% of eyes of VKH disease, 48.1% of eyes of Behcet's disease, and 66.7% of eyes of intermediate uveitis.

**Conclusions.** Acute anterior nongranulomatous uveitis was the most common endogenous uveitis, while VKH was the most common panuveitis in this series. Infectious origin contributes a significant proportion of endogenous uveitis, infectious etiology should be considered in any type of uveitis that responds poorly to conventional treatment.

Epidemiological studies of uveitis within a community are important in order to enable rational investigation and management of the disease. The prevalence of uveitis varies in different races and areas. Acute anterior uveitis is prevalent in Caucasians, Behcet's disease in Japanese, and sarcoidosis in American Blacks. There are few epidemiological reports on uveitis within Taiwan. A series of studies about uveitis was reported by Chung et al.1,2 The reports revealed the high incidence of HLA-B27 (+) anterior acute uveitis (28.1%), Vogt-Koyanagi-Karada disease and sympathetic ophthalmia (10.3%) as well as Behcet's disease (9.8%) in northern Taiwan.2

The purpose of our study was to determine the profile and characteristics of endogenous uveitis in southern Taiwan by retrospective chart review of 160 cases of endogenous uveitis in Kaohsiung Veterans General Hospital from January 1991 to December 2000.
scopy and fundus examinations. Gonioscopy and fundus angiography were also performed when necessary. Routine blood and urine tests, blood chemistry, chest and sacroiliac joint roentgenography, skin anergy panel test and special immunological tests, when indicated, were performed. Furthermore, histocompatibility antigen (HLA) testing, virus isolation, bacterial culture and histopathologic study were also performed in selected cases.

Statistical analysis was performed with the SPSS (Statistical Package for the Social Science) system. Descriptive statistics were expressed as mean with standard deviation. Means of normally distributed variables were compared with the t-test. All tests were two-tailed, and \( p < 0.05 \) was considered to be significant.

RESULTS

One-hundred and sixty patients were collected, including 93 (58.1%) males and 67 (41.9%) female. Most patients had their onset between the third and fifth decades. There was no significant difference in the age distribution between male and female \( (p = 0.14) \) (Fig. 1). The average age of onset was 41.1 ± 17.1 years (range 16-77), and the mean follow-up period was 13.7 months.

The distribution of the major types of uveitis included 46 (28.8%) cases of acute anterior nongranulomatous uveitis, 26 (16.3%) cases of Vogt-Koyanagi-Harada syndrome, 18 (11.3%) cases of intermediate uveitis, 14 (8.8%) cases of Behcet’s disease, 7 (4.4%) cases of herpetic-related uveitis, 23 (14.4%) undefined cases, 4 (2.5%) cases of toxoplasmosis, 4 (2.5%) cases of syphilis, 2 (1.25%) cases of histoplasmosis, 3 (1.88%) cases of tuberculosis, 2 (1.25%) cases of CMV-related uveitis, 4 (2.5%) cases of sarcoidosis, 2 (1.25%) cases of juvenile rheumatoid arthritis, 1 (0.6%) case of SLE-related uveitis, 2 (1.25%) cases of acute retinal necrosis, and 2 (1.25%) cases of progressive outer retinal necrosis (Tables 1 and 2). Pathogen-related uveitis constituted 16.3% (26 cases) of the etiology of uveitis (Table 3).

Of the 46 cases of AAU, 28 were male and 18 were female. HLA testing was performed in 36 cases, which showed HLA-B27(+) in 26 (76.2%) cases. The mean age was 37.48 ± 15.28 years. Nine (19.6%) cases were bilateral. Forty-three (78.2%) eyes had a final visual acuity

Table 1. The diagnoses of 160 patients with endogenous uveitis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>55 (34.4%)</td>
</tr>
<tr>
<td>Acute anterior nongranulomatous uveitis</td>
<td>46</td>
</tr>
<tr>
<td>(AAU)</td>
<td></td>
</tr>
<tr>
<td>HLA-B27 (+)</td>
<td>26</td>
</tr>
<tr>
<td>HLA-B27 (-)</td>
<td>10</td>
</tr>
<tr>
<td>HLA-B27 (?)</td>
<td>10</td>
</tr>
<tr>
<td>Juvenile rheumatoid arthritis</td>
<td>2</td>
</tr>
<tr>
<td>Herpes-related</td>
<td>7</td>
</tr>
<tr>
<td>Intermediate</td>
<td>18 (11.3%)</td>
</tr>
<tr>
<td>Posterior</td>
<td>23 (14.4%)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>9</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>4</td>
</tr>
<tr>
<td>Presumed ocular histoplasmosis syndrome (POHS)</td>
<td>2</td>
</tr>
<tr>
<td>Progressive outer retinal necrosis (PORN)</td>
<td>2</td>
</tr>
<tr>
<td>Acute retinal necrosis (ARN)</td>
<td>2</td>
</tr>
<tr>
<td>Cytomegaloviruses (CMV)</td>
<td>2</td>
</tr>
<tr>
<td>Syphilis</td>
<td>1</td>
</tr>
<tr>
<td>SLE-related</td>
<td>1</td>
</tr>
<tr>
<td>Panuveitis</td>
<td>64 (40%)</td>
</tr>
<tr>
<td>Vogt-Koyanagi-Harada disease (VKH)</td>
<td>26</td>
</tr>
<tr>
<td>Behcet’s disease</td>
<td>14</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>14</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>4</td>
</tr>
<tr>
<td>Syphilis</td>
<td>3</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>160 (100%)</td>
</tr>
</tbody>
</table>

Fig. 1. Age distribution of 160 patients with endogenous uveitis.
equal to or better than 0.5. Recurrence occurred in 14 (30.4%) cases, and the mean interval between the onset and first recurrence was 19.8 months. Of the 26 cases of Vogt-Koyanagi-Harada syndrome, 12 were male and 14 were female. All cases were bilateral in involved. The mean age was 42.9 ± 17.4 years. Recurrence occurred in 8 (30.8%) cases, and the mean interval between the onset and first recurrence was 13.3 months. At the time of last follow-up (mean 11.4 months), 34 (65.4%) eyes had a final visual acuity equal to or better than 0.5.

Of the 18 cases of intermediate uveitis, nine were male and nine were female. Twelve (66.7%) cases were bilateral. The mean age was 40.17 ± 16.73 years. Recurrence occurred in 5 (27.8%) cases, and the mean interval between the onset and first recurrence was 12.0 months. At the end of the follow-up, 20 (66.7%) eyes had a final visual acuity equal to or better than 0.5.

Of the 14 cases of Behcet’s disease, twelve were male and two were female. Thirteen (92.9%) cases were bilateral. The mean age was 34.36 ± 10.43 years. HLA testing was performed in 11 of 14 cases with Behcet’s disease, which showed HLA-B5(51) in 4 (36.4%) cases. Recurrence occurred in nine (64.3%) cases, and the mean interval between the onset and first recurrence was 13.4 months. At the end of the follow-up, 13 (48.1%) eyes had a visual acuity equal to or better than 0.5 (Table 4).

Of the four cases of sarcoidosis, two cases presented panuveitis and the other two cases presented with anterior uveitis. All patients were female, with mean age of 49.8 ± 11.7 years. Of the two cases of juvenile rheumatoid arthritis, both were female (6 & 17 years old) and bilaterally involved. They presented as dominant anterior uveitis with a final visual acuity equal to or better than 0.5 in all eyes.

**DISCUSSION**

Acute anterior nongranulomatous uveitis (AAU) was the most common type of uveitis in this series. It contributed 28.8% of the total cases. AAU is also the most common type of uveitis seen in Caucasians, but it is relatively uncommon in Japans and in Africans.

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**Table 2. The frequency of endogenous uveitis**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number (%)</th>
<th>Male/Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAU</td>
<td>46 (28.8%)</td>
<td>28/18</td>
</tr>
<tr>
<td>VKH</td>
<td>26 (16.3%)</td>
<td>12/14</td>
</tr>
<tr>
<td>Pathogen-related</td>
<td>26 (16.3%)</td>
<td>16/10</td>
</tr>
<tr>
<td>Undefined</td>
<td>23 (14.4%)</td>
<td>16/7</td>
</tr>
<tr>
<td>Intermediate uveitis</td>
<td>18 (11.3%)</td>
<td>9/9</td>
</tr>
<tr>
<td>Behcet’s disease</td>
<td>14 (8.8%)</td>
<td>12/2</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>4 (2.5%)</td>
<td>0/4</td>
</tr>
<tr>
<td>URA</td>
<td>2 (1.25%)</td>
<td>0/2</td>
</tr>
<tr>
<td>SLE-related</td>
<td>1 (0.6%)</td>
<td>0/1</td>
</tr>
<tr>
<td>Total</td>
<td>160</td>
<td>93/67</td>
</tr>
</tbody>
</table>

AAU = acute anterior nongranulomatous uveitis; VKH = Vogt-Koyanagi-Harada disease.

**Table 3. Detailed types of pathogen-related uveitis**

<table>
<thead>
<tr>
<th>Pathogen-related uveitis</th>
<th>No. of patients</th>
<th>Male/Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpes</td>
<td>7</td>
<td>3/4</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>4</td>
<td>4/0</td>
</tr>
<tr>
<td>Syphilis</td>
<td>4</td>
<td>2/2</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>3</td>
<td>2/1</td>
</tr>
<tr>
<td>POHS</td>
<td>2</td>
<td>2/0</td>
</tr>
<tr>
<td>ARN</td>
<td>2</td>
<td>2/0</td>
</tr>
<tr>
<td>PORN</td>
<td>2</td>
<td>0/2</td>
</tr>
<tr>
<td>CMV</td>
<td>2</td>
<td>1/1</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>16/10</td>
</tr>
</tbody>
</table>

ARN = acute retinal necrosis; CMV = Cytomegaloviruses; POHS = presumed ocular histoplasmosis syndrome; PORN = progressive outer retinal necrosis.

**Table 4. Age of onset of uveitis**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of patients</th>
<th>Mean ± SD (yrs)</th>
<th>Minimum (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAU</td>
<td>46</td>
<td>37.5 ± 15.3</td>
<td>10</td>
</tr>
<tr>
<td>VKH</td>
<td>26</td>
<td>42.9 ± 17.4</td>
<td>16</td>
</tr>
<tr>
<td>Behcet’s disease</td>
<td>14</td>
<td>34.4 ± 10.4</td>
<td>13</td>
</tr>
<tr>
<td>Intermediate uveitis</td>
<td>18</td>
<td>40.2 ± 16.7</td>
<td>10</td>
</tr>
</tbody>
</table>

AAU = acute anterior nongranulomatous uveitis; VKH = Vogt-Koyanagi-Harada disease.
significant association between HLA-B27 antigen and AAU was found.\textsuperscript{1,3} Similar association had been reported in the literature from other countries. It is obvious that the incidence of HLA-B27 antigen in anterior uveitis depends mainly on the incidence of HLA-B27 in the general population. This antigen presented in 14% of the general population in Japan and 18% of AAU in Japan. In our series, HLA-B27 antigen presented in 76.2% cases of AAU, which was similar to the report from north Taiwan (80.9%, Chung et al., 1988).\textsuperscript{1} The frequency of HLA-B27 antigen in a normal Chinese population varies from 4 to 8%\textsuperscript{4-6} which might explain the relatively high incidence of HLA-B27 in our series. Our data was closer to those reported from Fin land and England, though we are nearer to Japan geographically and ethnically.

In our series, VKH was the most common (16.3%) panuveitis. The incidence was between those reported from north Taiwan (9.2%) and China (26%).\textsuperscript{1,7} The discrepancy might be due to the different patient sources of each hospital. Our patients presented within 2-4 years of onset, while the eyes usually look quiet. Approximately 80% of cases are bilateral.\textsuperscript{8} In our series, all patients with intermediate uveitis complained of floaters and 66.7% of cases were bilateral.

Behcet's disease is a chronic disorder that tends to recur over a 2-4 year period and may lead to blindness if ischemic optic neuropathy or retinopathy are not adequately treated. It occurs most frequently in young adults and pre dominantly in males. Association with HLA-B5 or sub set B51 has been reported.\textsuperscript{9-10} In our study, 12 of 14 patients (85.7%) with Behcet’s disease were male, which was similar to the report from Japan (75.3%, Ando et al., 1999)\textsuperscript{11} and north Taiwan\textsuperscript{6} (74.4%, Chung et al., 1988), but higher than the report from Korea\textsuperscript{12} (36.4%, Bang et al., 2001) and Spain\textsuperscript{13} (58%, Baixauli et al., 2001). In our series, HLA-B5(51) antigen presented in 36.4% cases with Behcet's disease, which was lower than the report from Japan (59.4%, Mizuki et al., 2001).\textsuperscript{14} This various incidence of HLA-B51 in Behcet's disease may depend on the different incidence of HLA-B5(51) in the general population (10.9% in Chinese and 13.6% in Japan).

In our series, ocular pathogen-related uveitis contributed a significant proportion (16.3%) of endogenous uveitis. The visual outcome depends on early diagnosis and prompt treatment. For early detection of these pathogen-related uveitis, detailed history-taking is very important, including sexual history, travel history, underlying diseases. Laboratory evaluation guided by the history could provide further information about the diagnosis, for example, venereal disease research laboratory (VDRL) for syphilis, human-immunodeficiency-virus (HIV), and chest X-ray for tuberculin test. Also, high suspicion of in fection should be made if patients with uveitis respond poorly or in limited manner to corticosteroids treatment. More aggressive procedures like vitrectomy or aqueous tap for cytology and culture should be performed in order to detect the pathogen. Polymerase chain reaction (PCR) is a rapid and sensitive tool for the detection of pathogens, such as tuberculosis in the three cases with tuberculosis.\textsuperscript{15} Spirochet was found in aqueous specimen in three of four cases with syphilis. If the diagnosis is established, prompt treatment should be started to save the eye. All the four patients with syphilis in our series had improved vision acuity after systemic penicillin treatment. Infectious etiology should be considered cautiously in the differential diagnosis of endogenous uveitis.

In our series, patients had their onset between the third and fifth decades. Acute anterior nongranulomatous uveitis is the most common endogenous uveitis, while VKH is the most common panuveitis. As in fection etiology contributes a significant proportion of endogenous uveitis (16.3%), in fection etiology should be considered in any type of uveitis that responds poorly to conventional treatment.
tional therapy.

ACKNOWLEDGEMENTS

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REFERENCES