

Clinical statistics of endogenous uveitis: comparison between general eye clinic and university hospital

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Abstract We compared uveitis patients who attended a general eye clinic ($n = 183$) with those who attended the ophthalmology department of a university hospital ($n = 550$) to examine factors that affect the clinical statistics of uveitis outpatients. We observed that diabetic iritis and herpetic iritis were significantly more frequent in the clinic whereas Vogt–Koyanagi–Harada disease and Behcet’s disease were significantly more common in the university hospital. Among the so-called three leading uveitis, Behcet’s disease and Vogt–Koyanagi–Harada disease were relatively rare in the general clinic; they might be concentrated in the university hospital setting because these diseases require treatment at specialist hospitals. In addition, uveitis secondary to underlying diseases such as diabetic iritis and transient non-granulomatous iridocyclitis was generally not referred to specialist hospitals. These factors may account for the differences in disease frequencies observed between the two facilities.

Keywords Endogenous uveitis · General practice · University hospital · Referral

The clinical statistics of endogenous uveitis differ between Japan and European and American countries in terms of the frequency of uveitic diseases. In Japan, sarcoidosis, Behcet’s disease, and Vogt–Koyanagi–Harada disease constantly occupy the highest ranks [1] and thus are known as the three leading uveitis in that country. The same trend has been reported from surveys conducted in various regions of Japan [1–3]. However, almost all statistical studies on uveitis in Japan were conducted in specialist outpatient departments of university hospitals and patients were mainly referred from other facilities. These data can hardly represent the actual status of uveitis in the Japanese population.

The objectives of this study were to examine factors affecting the clinical statistics of special uveitis clinics by comparing uveitis patients who visited a general eye clinic with those who attended the ophthalmology department of a university hospital, and accurately to delineate the status of uveitis in the Japanese population.

Subjects and methods

Between January 2000 and December 2002, patients with endogenous uveitis who attended either a general

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eye clinic in Metropolitan Tokyo (Sakai Eye Clinic) or the Department of Ophthalmology of Tokyo Medical University were included in this study.

Patients with endogenous uveitis in the two facilities were compared according to age, sex, and distribution of disease classified by anatomical location and etiology. To ensure that the diagnostic criteria in both facilities were identical, the same specialist (J.-I. S.) verified the diagnosis in all cases.

A definitive diagnosis of uveitis was made as follows. Complete ocular examinations, health history, and further tests as considered necessary were conducted according to International Ocular Inflammation Society (IOIS) guidelines [4, 5]. Sarcoidosis and Behcet's disease were diagnosed according to the diagnostic criteria of the Ministry of Health, Labour, and Welfare Designated Disease Study Group [6, 7] and Vogt–Koyanagi–Harada disease according to the new international diagnostic criteria [8]. Diabetic iritis was defined as that which was observed in poorly controlled diabetic patients, abated along with improvement of diabetes, and was not associated with other causes. Other forms of noninfectious uveitis were diagnosed by characteristic ocular findings. Infectious uveitis was diagnosed by identification of the pathogen on the basis of evidence provided by the following tests. Acute retinal necrosis and herpetic iridocyclitis were diagnosed on the basis of results of PCR or antibody titers in intraocular fluid, HTLV-1-related uveitis and ocular toxocariasis from serum specific antibodies, syphilitic uveitis from serological tests for syphilis, tuberculous uveitis from tuberculin reaction and anti-cord factor antibody, fungal uveitis from culture or antigen detection, and toxoplasmosis from serum antibody (in some patients, PCR and antibody titer in intraocular fluid).

PCR analysis for herpetic patients attending both university hospital and private clinic was conducted at the same reliable independent laboratory (SRL).

Among cases of unidentifiable (cause unknown) uveitis, those manifesting acute unilateral fibrinous iridocyclitis were classified as acute anterior uveitis. Cases showing inflammatory cells predominantly in the anterior chamber rather than the anterior vitreous and small white keratic precipitates in the Arlt's triangle were classified as one type of intermediate uveitis when peripheral retinal vasculitis was present as an essential condition with or without snowbank in the pars plana of the ciliary body.

The chi-squared test was used for statistical analysis. A P -value <0.05 was considered significant.

Results

Prevalence

Among 7210 patients who attended the general eye clinic during the 2-year study period, 183 patients were found to have endogenous uveitis, with a prevalence of 2.54%. On the other hand, a total of 25,608 patients attended the Department of Ophthalmology of Tokyo Medical University during the same period, 550 of whom were diagnosed as having endogenous uveitis, with a prevalence of 2.15%. No difference in prevalence of uveitis was observed between the general eye clinic and university hospital (Table 1).

Age and sex differences

The mean age (\pm standard deviation) of patients with endogenous uveitis attending the general clinic was 55.1 ± 17.4 years, and was significantly ($P < 0.001$) higher than that of those attending university hospital (47.0 ± 18.2 years). The male-to-female ratio of patients with endogenous uveitis in the two clinical settings was 64:119 and 233:317, respectively, with no significant difference detected (Table 1).

Frequencies of uveitis classified by position or anatomical location

Among the four anatomic types of uveitis, the proportion of anterior uveitis was significantly ($P < 0.0001$) higher in cases of endogenous uveitis in the

Table 1 Prevalence of uveitis in patients attending a general clinic and a university hospital and demography of patients with endogenous uveitis

	Clinic ($n = 183$)	University hospital ($n = 550$)	P -value
Prevalence, n (%)	183/7210 (2.54)	550/25,608 (2.15)	NS
Age, years	55.1 ± 17.4	47.0 ± 18.2	<0.001
Sex (M:F)	64:119	233:317	NS

Table 2 Frequency of uveitis classified by anatomical location

	Clinic (<i>n</i> = 183)	University hospital (<i>n</i> = 550)	<i>P</i> -value
Anterior, <i>n</i> (%)	119 (65.0)	254 (46.2)	<0.0001
Intermediate, <i>n</i> (%)	5 (2.7)	35 (6.4)	NS
Posterior, <i>n</i> (%)	14 (7.7)	104 (18.9)	0.0005
Diffuse uveitis, <i>n</i> (%)	45 (24.6)	157 (28.5)	NS

general eye clinic, whereas the proportion of posterior uveitis was significantly ($P = 0.0005$) higher in the university hospital (Table 2).

Frequencies of uveitis classified by etiology

A definitive diagnosis was obtained in 118 of 183 (64.5%) patients with endogenous uveitis who visited the general eye clinic. The disease with the highest frequency was diabetic iritis (30 patients, 16.4%), followed in descending order by anterior uveitis associated with herpes virus infection (herpes simplex virus and varicella-zoster virus; 13 patients, 7.1%), sarcoidosis (11 patients, 6.0%), acute anterior uveitis with unknown etiology (10 patients, 5.5%), uveitis secondary to scleritis (7 patients, 3.8%), and Fuchs heterochromatic iridocyclitis (6 patients, 3.3%).

At the university hospital, on the other hand, a definitive diagnosis was achieved in 310 of 550 (64.5%) patients with endogenous uveitis. The diseases in descending order of frequency were sarcoidosis (55 patients, 10.0%), Vogt–Koyanagi–Harada disease (40 patients, 7.3%), Behcet's disease (38 patients, 6.9%), acute anterior uveitis with unknown etiology (29 patients, 5.3%), HLA-B27-associated anterior uveitis (17 patients, 3.1%), herpetic iritis (17 patients, 3.1%), and acute retinal necrosis (13 patients, 2.4%).

Comparing disease types in the general eye clinic and university hospital settings, diabetic iritis and herpetic iritis were significantly ($P < 0.0001$ and 0.0309, respectively) more frequent in the former whereas Vogt–Koyanagi–Harada disease and Behcet's disease were significantly ($P < 0.0086$ and 0.0049, respectively) more common in the latter. The proportions of other diseases were not different between the two facilities.

Table 3 Referral rate from general eye clinic to university hospital

Anatomical location of uveitis	Referral rate, <i>n</i> (%)
Anterior	48/119 (40.3)
Intermediate	4/5 (80.0)
Posterior	10/14 (71.4)
Diffuse uveitis	44/45 (97.8)
Total	106/183 (57.9)

Referral to university hospital

A total of 106 patients (57.9%) were referred from the general eye clinic to the university hospital for the purpose of diagnosis or treatment. Table 3 shows the proportions of referral cases based on anatomical classification. Whereas most cases of intermediate uveitis, posterior uveitis, and panuveitis were referred, over half the anterior uveitis cases were treated at the clinic.

Discussion

The etiologies and disease types of endogenous uveitis differ depending on many factors including ethnicity, geographical region, and age. Statistics of Japan and European or American countries show distinct characteristic distribution patterns of uveitic diseases [1, 9–11]. In Japan, sarcoidosis, Behcet's disease, and Vogt–Koyanagi–Harada disease rank top in disease frequency regardless of whether the survey was conducted in Hokkaido, Kanto, or Kyushu district [1–3, 12, 13], and these entities have thus been called the three leading uveitis in Japan [9]. Syphilis and tuberculosis ceased to be the leading causes of uveitis in recent years, and this trend has continued to date according to statistical reports.

Although the data on uveitis in Japan are believed to be reliable, the statistics amassed so far are almost exclusively based on records of uveitis outpatient departments at university hospitals and the patients are mostly referral cases, posing a possibility of sampling bias. The same issue has been debated in European and American countries, and reports from facilities caring mostly for referral cases are considered not to reflect accurately the actual status of uveitis in the community [11]. In this study we examined factors that could affect the clinical

statistics of uveitis outpatient departments by comparing social background-matched uveitis patients at a general eye clinic with those attending a university hospital.

When uveitis is detected in a general eye clinic, the motive for referring the case to a specialist uveitis outpatient department is either to obtain a definitive diagnosis or to receive treatment. For cases of iritis concurrent with diabetes or of herpetic iritis manifesting typical skin or corneal symptoms, mild cases are often not referred because a diagnosis is already established. Furthermore, cases with transient anterior uveitis responding to steroid eye drops are usually not referred even though the etiology is undetermined. On the other hand, uveitis accompanied by chorioretinal lesion is recognized as high-risk, and in principle all cases with concurrent fundus lesion are referred from general eye clinics to specialists. From these viewpoints, over half of anterior uveitis cases are not referred and are treated at the clinic, whereas most intermediate uveitis, posterior uveitis, and panuveitis cases are referred. On the other hand, cases with recurrence, those that follow a chronic or prolonged course, and cases showing rapid deterioration of visual acuity are usually managed in uveitis outpatient departments. As a result, we observed that the proportion of anterior uveitis was higher in the general eye clinic whereas that of posterior uveitis was higher in the university hospital setting. This trend may also account for our finding that when classified by etiology, diabetic iritis and herpetic iritis were significantly more common in the general eye clinic whereas Vogt–Koyanagi–Harada disease and Behcet's disease were significantly more frequent in the university hospital. Among the so-called three leading uveitis, Behcet's disease and Vogt–Koyanagi–Harada disease are relatively rare in general eye clinics; they may be concentrated in uveitis outpatient departments because these diseases require treatment at specialist hospitals. Furthermore, the significantly higher mean age of patients with endogenous uveitis attending the general eye clinic in our study might be related to the high prevalence of diabetic iritis and herpetic iritis in the elderly.

Diabetic iritis observed in general clinics consists of two types: severe iridocyclitis with fibrin precipitation and hypopyon in the anterior chamber, and mild serous iritis. In the latter, the disease state may be more appropriately considered as iridopathy rather than

inflammation showing only leakage of cells into the anterior chamber, accompanying increased permeability of the iris vessels due to diabetes. Most of these cases have poor control of blood sugar, and the symptoms are improved by blood sugar regulation [14]. For this reason, mild cases are usually not referred to specialist outpatient departments but treated at clinics. On the other hand, fulminant cases are referred to uveitis outpatient departments for differentiation from acute anterior uveitis with other etiologies.

This pilot study was conducted in only one general eye clinic. In the future, a national epidemiological survey at clinic level will provide a clearer picture of the current status of uveitis in Japan. To ensure the quality of such a study, diagnostic standards should be established, and education of non-uveitis specialists on the correct examination and recording of findings is desirable.

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