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CLINICAL INVESTIGATION

Epidemiology and characteristics of common forms of anterior uveitis at initial presentation in a tertiary facility in Japan

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Abstract

Purpose To elucidate detailed epidemiological profile of common types of anterior uveitis (AU) in real-world clinical setting of a tertiary facility in Japan, and to evaluate the characteristic clinical findings at initial presentation.

Study design Retrospective cohort study.

Methods Clinical charts of 275 patients (335 eyes) aged 52.5 ± 19.1 years were reviewed retrospectively. Herpetic AU was diagnosed by multiplex polymerase chain reaction tests using aqueous humor. Time of uveitis onset, gender, laterality, disease course since the initial onset of AU, visual acuity (VA) and intraocular pressure (IOP) at first visit, and definitive diagnosis were collected from clinical charts.

Results Acute AU (AAU) was the most common (21.8%) form of AU; followed by herpetic AU (20.7%) comprising Herpes Simplex Virus (HSV) (8.0%), Varicella Zoster Virus (VZV) (9.1%) and cytomegalo virus (CMV) (3.6%); scleritis (13.5%); diabetic iritis (7.6%), and Posner-Schlossman syndrome (5.5%). Unilateral AU constituted 78.2%, and VA less than 20/30 accounted for 31.2%. Of all the eyes, 16.1% had an IOP higher than 20 mmHg, out of which 37.0% had herpetic AU, followed by scleritis in 25.9%, and Posner-Schlossman syndrome (PSS) in 11.1%. AU patients over 60 years of age were 40.4%, in which 34.2% had herpetic AU, followed by scleritis in 14.4% and AAU in 13.5%. Herpetic AU patients were significantly older and had higher IOP compared with AAU patients.

Conclusion The most frequent AU was AAU, followed by herpetic AU. Herpetic AU patients were older and had higher intraocular pressure than AAU patients, although VA was equally impaired in both groups.

Keywords Uveitis · Anterior uveitis · Acute anterior uveitis · Herpetic anterior uveitis

Introduction

Uveitis is a sight-threatening inflammatory ocular disease with an annual incidence of 17–52 per 100,000 and a prevalence of 38–370 per 100,000 population [1, 2]. Up to 10% of patients with uveitis experience severe permanent visual impairment mainly as a result of direct ischemic and inflammatory damage of ocular tissues or serious ocular complications [3]. Depending on the primary anatomical location of ocular inflammation, uveitis can be classified into anterior uveitis (AU), intermediate uveitis, posterior uveitis, and panuveitis [4]. The term AU is used for the subset of uveitis with the major inflammation site in the iris (iritis), the anterior part of the ciliary body (anterior cyclitis) or both structures (iridocyclitis). AU is the most common form of uveitis and the incidence in the general population varies among countries [5–11]. Some AU entities are caused by infectious agents and others appear to be associated with abnormal immune reactions with only ocular involvement or with systemic diseases, but may also present as masquerade syndrome. AU is also classified by clinical course into acute AU (AAU) with sudden onset and limited duration, recurrent AU with repeated episodes separated by periods of inactivity without treatment for ≥ 3 months, and chronic AU that persists and relapses in less than 3 months

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after discontinuing treatment [4]. AU is a benign disease, and serious complications can be avoided if the causative disease is diagnosed accurately and treated early. To this end, it is critical to know the background characteristics of the patient's causative disease whenever known, or to estimate the clinical course based on ocular findings even if the causative disease cannot be identified.

Noninfectious AU is represented by AAU (including HLA-B27–negative AAU) with or without ankylosing spondylitis [12–14], while the most common infectious AU is herpetic AU mainly caused by reactivation of herpes simplex virus (HSV), varicella-zoster virus (VZV) or cytomegalovirus (CMV) [15–17]. In children, juvenile idiopathic arthritis (JIA) and tubulointerstitial nephritis uveitis syndrome (TINU) are frequent causative diseases of AU [18–20]. In real-world clinical setting, however, typical ocular findings of different AU entities may not always be observable because of variations in patient background including age, duration from onset to consultation, severity, other concomitant ocular diseases, and disease modification by initial treatment. Therefore, understanding the general demographic and clinical characteristics such as age distribution, gender ratio, laterality, visual acuity (VA), and intraocular pressure (IOP) at initial onset of different entities of AU may provide diagnostic clues. To the best of our knowledge, no study has comprehensively investigated the frequencies of clinical findings at presentation and patient background related to the causative diseases of common forms of AU encountered in clinical practice. The purpose of this study was to elucidate detailed epidemiological profiles of common types of AU in real-world clinical setting of a tertiary facility in Japan, and to evaluate the characteristic clinical findings at initial presentation.

Methods

Clinical charts of consecutive patients diagnosed with AU for the first time at National Defense Medical College Hospital between April 2010 and March 2020 were reviewed retrospectively. The present study was approved by the ethics committee of National Defense Medical College Hospital IRB (2201-34). Anatomical types of uveitis were classified according to the Standardization of the Uveitis Nomenclature (SUN) Working Group criteria [4]. Behçet disease (BD) was diagnosed by the criteria established in Japan [21–23]. AAU (including HLA-B27– negative cases) was diagnosed on the basis of typical symptoms including blurred vision, ocular redness, pain and photophobia, ocular findings of non-granulomatous anterior inflammation characterized by fine keratic pretipitates, numerous anterior chamber cells occasionally with hypopyon and lack of iris nodules, and no systemic complications except for ankylosing spondylitis or psoriasis [13, 24–26]. AU with mild anterior ocular inflammation indistinguishable between granulomatous and non-granulomatous uveitis was classified as idiopathic AU, even when accompanied by typical AAU symptoms. The multiplex PCR qualitatively measured the genomic DNA of 8 HHVs: herpes simplex virus (HSV) type 1 (HHV-1), HSV-2 (HHV-2), varicella-zoster virus (VZV; HHV-3), Epstein-Barr virus (EBV; HHV-4), CMV (HHV-5), HHV-6, HHV-7, and HHV-8 using the aqueous humor [27, 28]; whenever herpetic AU was suspected judging from clinical features including unilateral involvement, presence of granulomatous keratic precipitates, and/or elevated IOP [29], a definitive diagnosis was made according to the SUN Working Group criteria [30–32]. Patients with suspected herpetic AU who had negative PCR results were not classified as herpetic AU; the cases with clinical features similar to CMV-associated AU were diagnosed as Posner-Schlossman syndrome (PSS) whereas any others were classified as idiopathic AU. Since, to date there are no diagnostic criteria for diabetic iritis, non-granulomatous AU occurring in patients who had uncontrolled diabetes with highly elevated HbA1c (> 10.0%) was diagnosed as diabetic iritis [33]. Diagnosis of TINU and Fuchs uveitis syndrome (FUS) was made according to the SUN Working Group criteria [34, 35]. Other uveitis diseases such as JIA-associated uveitis and lens-induced uveitis were diagnosed according to a previous report [38].

Time of uveitis onset, gender, laterality, disease course since the initial onset of AU, VA, IOP at first visit, and definitive diagnosis were collected from clinical charts. Statistical analysis was performed using JMP Pro ver. 15 (Business Unit of SAS). Continuous variables were compared by Mann–Whitney U test, and categorical variables were analyzed using Pearson χ^2 test or Fisher's exact test. P values lower than 0.05 were considered statistically significant.

Results

Background and ophthalmological data of all AU patients

A total of 335 eyes of 275 consecutive patients were enrolled in this retrospective cohort study. Background and ophthalmological data of AU patients at presentation are shown in Table 1. Mean patient age was 52.5 ± 19.1 years (median 53 years), and 45.1% were men. Unilateral uveitis was predominant (215 patients, 78.2%). Mean logMAR of AU eyes was 0.27 ± 0.78 (median 0), and 107 eyes (32.0%) had a BCVA of less than 20/30. Mean IOP of AU eyes was 16.1 ± 7.6 mmHg (median 14 mmHg). Fifty-four eyes (16.1) had IOP higher than 20 mmHg, and mean IOP of this subset was 29.5 ± 9.3 mmHg (median 25.8 mmHg, range 21–59 mmHg). Figure 1 shows the age distribution

Table 1 Background and ophthalmological data of anterior uveitis patients enrolled in this study

	AU* patients (n = 275)
Age; years	
Mean (SD)	52.5 (19.1)
Median (range)	53 (2–99)
Sex ratio	
Male; no. of patients (%)	124 (45.1)
Female; no. of patients (%)	151 (54.9)
Affected eye	
Unilateral; no. of patients (%)	215 (78.2)
Bilateral; no. of patients (%)	60 (21.8)
	AU eyes (n = 335)
LogMAR	
Mean (SD)	0.27 (0.78)
Median (range)	0 (-1.18–5)
Best corrected visual acuity; no. of eyes (%)	
< 20/200	27 (8.1)
20/200 – <20/30	80 (23.9)
20/30 -	228 (68.1)
Intraocular pressure; mmHg	
Mean (SD)	16.1 (7.6)
Median (range)	14 (4–59)
Intraocular pressure > 20 mmHg; no. of eyes (%)	54 (16.1)
Mean (SD); mmHg	29.5 (9.3)
Median (range); mmHg	25.8 (21–59)

* AU: anterior uveitis

of male and female AU patients, and mean logMAR and IOP in AU eyes. AU was predominant in age groups of 40–70 s, and female predominance was observed in juvenile patients (aged up to 20) and older patients (aged 70 and above). LogMAR tended to increase with age.

AU types diagnosed and the frequencies

Table 2 shows AU types diagnosed and their frequencies. The most frequent form of AU was AAU, found in 60 patients (21.8%), followed by herpetic AU in 57 patients (20.7%) [comprising herpes simplex virus (HSV) in 22 patients (8.0%), varicella zoster virus (VZV) in 25 patients (9.1%), and cytomegalovirus (CMV) in 10 patients (3.6%)], scleritis in 37 patients (13.5%), diabetic iritis in 21 patients (7.6%), and PSS in 15 patients (5.5%). Idiopathic AU was diagnosed in 47 patients, constituting 17.1% of the total. Lens-induced uveitis had the highest mean age of 85.0 ± 12.1 years, followed by CMV-related AU of 65.4 ± 9.9 years.

Unilateral AU types and the frequencies

Unilateral uveitis was found in 215 patients, accounting for 78.2% of total AU cases. Table 3 shows the frequencies of AU types in unilateral AU cases, and the percentage of unilateral disease in AU cases for each AU type. The most frequent unilateral AU was herpetic AU found in 55 patients (25.6%) [comprising HSV in 22 patients (10.2%), VZV in 25 patients (11.6%), and CMV in 8 patients (3.7%)], followed by AAU in 52 patients (24.2%), scleritis in 28 patients (13.0%), PSS in 15 patients (7.0%), and diabetic iritis in 12 patients (5.6%). The percentage of unilateral disease in AU patients was 100% for VZV- and HSV-associated AU, PSS, and lens-induced uveitis; 88.9% for FUS; 86.7% for AAU; 80% for CMV-associated AU; and 77.8% for AU with inflammatory bowel disease.

AU types with disturbed visual acuity

The number of AU eyes with VA less than 20/30 was 107, accounting for 31.9% of all AU eyes. Table 4 shows the frequencies of AU types in AU eyes with disturbed VA, and the percentage of disturbed VA in AU eyes for each AU type. The most frequent AU with disturbed VA was herpetic AU found in 29 eyes (29.3%), in which HSV in 12 eyes (12.1%), VZV in 12 eyes (12.1%), and CMV in 5 eyes (5.1%), followed by AAU in 29 eyes (28.3%), diabetic iritis in 13 eyes (10.1%), scleritis in 8 eyes (6.1%), and FUS in 5 eyes (5.1%). The percentage of disturbed VA in AU eyes was 100% for lens-induced uveitis, 61.9% for diabetic iritis, 55.6% for FUS, 54.5% for HSV-associated AU, 50.0% for CMV-associated AU, 48.3% for AAU, and 48.0% for VZV-associated AU.

AU types with high intraocular pressure

The number of AU eyes with IOP higher than 20 mmHg was 54, accounting for 16.1% of all AU eyes. Table 5 shows the frequencies of AU types in AU eyes with high IOP, and the percentage of high IOP in AU eyes for each AU type. The most frequent AU with high IOP was herpetic AU found in 20 eyes (37.0%) [comprising HSV in 7 eyes (13.0%), VZV in 6 eyes (11.1%), and CMV in 6 eyes (11.1%)] followed by scleritis in 14 eyes (25.9%), PSS in 6 eyes (11.1%), AAU in 4 eyes (7.4%), and diabetic iritis in 3 patients (5.6%). The percentage of high IOP in AU eyes was 60% for CMV-associated AU, 40% for PSS, 37.8% for scleritis, 33.3% for lens-induced uveitis, 31.8% for HSV-associated AU, and 24.0% for VZV-associated AU.

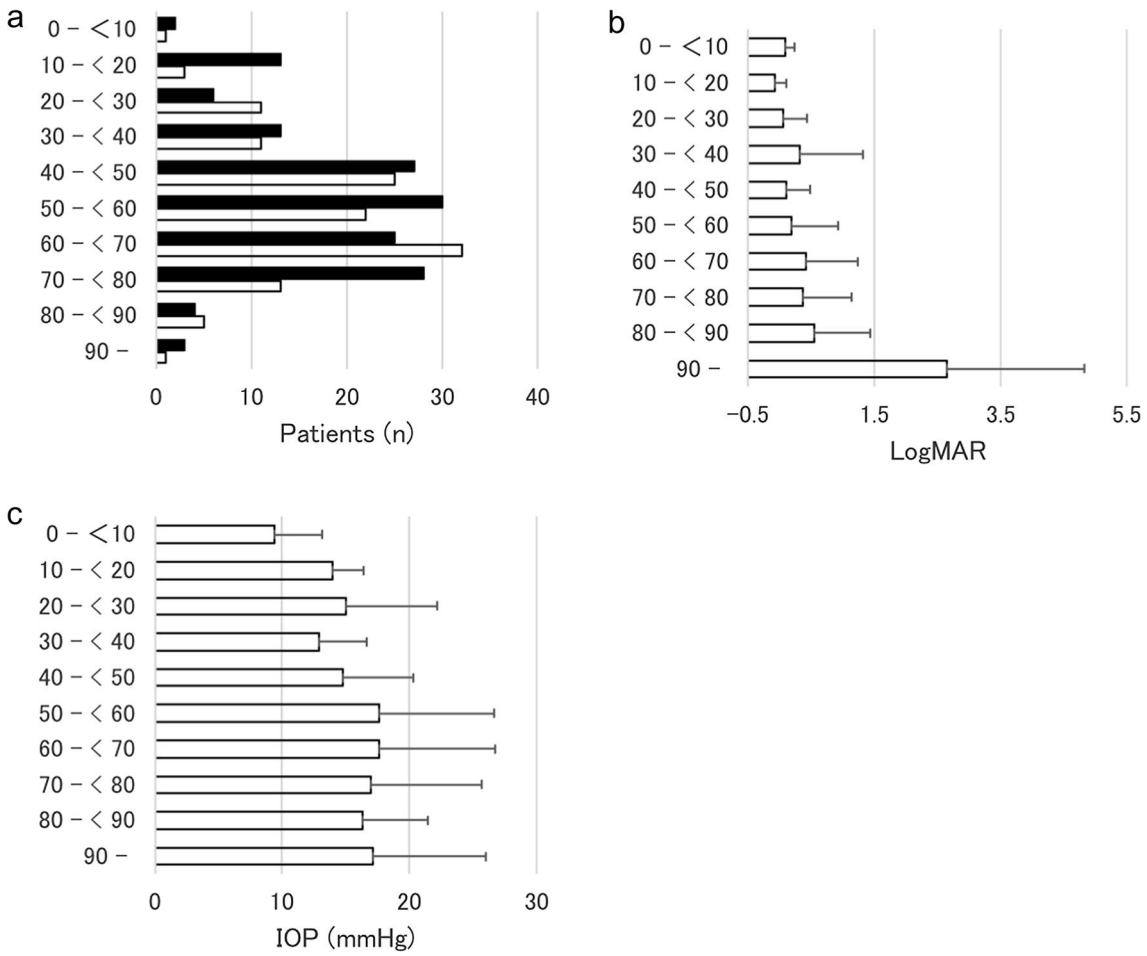

Fig. 1 Age distribution of male and female patients with anterior uveitis (AU), visual acuity, and intraocular pressure (IOP). Bar graphs show the number of male (*open bars*) and female (*closed bars*) patients with AU (A), mean logMAR in eyes with AU (B), and mean IOP in eyes with AU (C) according to age groups

AU types in patients over 60 years of age

The number of AU patients over 60 years of age was 111, accounting for 40.4% of total AU patients. Table 6 shows the frequencies of AU types in AU patients aged over 60 years, and the percentage of over age 60 in AU patients for each AU type. The AU with the highest frequency of patients aged over 60 was herpetic AU found in 38 patients (34.2%) [comprising HSV in 14 patients (12.6%), VZV in 16 patients (14.4%), and CMV in 8 patients (7.2%)], followed by scleritis in 16 patients (14.4%), AAU in 15 patients (13.5%), PSS in 7 patients (6.3%), and diabetic iritis in 5 patients (4.5%). The percentage of age over 60 in AU patients was 100% for lens-induced uveitis, 80% for CMV-associated AU, 64.0% for VZV-associated AU, and 63.6% for HSV-associated AU. The percentage of patients aged over 60 in other AU types was less than 50%.

Comparison of acute anterior uveitis with herpetic anterior uveitis

Figure 2 compares the male/female ratio, age, logMAR, and IOP between AAU and herpetic AU. Herpetic AU patients were significantly older than AAU patients and IOP was higher in herpetic AU eyes than in AAU eyes, although there was no significant difference in male/female ratio or logMAR between AAU and herpetic AU.

Comparison of cytomegalovirus-associated anterior uveitis with Posner-Schlossman syndrome

Figure 3 shows the comparisons of male/female ratio, age, logMAR, and IOP between CMV-associated AU and PSS. LogMAR was significantly higher in CMV-associated AU than in PSS. Although the CMV-associated AU group had

Table 2 Background and frequencies of anterior uveitis types

	Diagnosis	Number (%)	Mean age (SD)	Male/Female
1	AAU	60 (21.8)	48.4 (15.0)	26/34
2	Herpetic AU	57 (20.7)	60.6 (17.1)	31/26
	HSV	22 (8.0)	57.0 (21.6)	12/10
	VZV	25 (9.1)	61.7 (14.6)	11/14
	CMV	10 (3.6)	65.4 (9.9)	8/2
3	Scleritis	37 (13.5)	56.1 (19.1)	14/23
4	Diabetic iritis	21 (7.6)	52.1 (12.7)	13/8
5	PSS	15 (5.5)	52.3 (18.8)	9/6
6	FUS	9 (3.3)	51.9 (14.3)	3/6
7	AU with IBD	9 (3.3)	50.9 (15.3)	4/5
8	Behçet's disease	7 (2.5)	40.0 (20.3)	4/3
9	TINU	5 (1.8)	12.6 (1.7)	2/3
10	Lens-induced uveitis	3 (1.1)	85.0 (12.1)	1/2
	Others	5 (1.8)	49.4 (22.6)	1/4
	Idiopathic	47 (17.1)	50.3 (22.5)	16/31
	Total	275 (100)	52.5 (19.1)	124/151

AU: anterior uveitis; HSV: herpes simplex virus; VZV: varicella zoster virus; CMV: cytomegalovirus; PSS: Posner-Schlossman syndrome; FUS: Fuchs uveitis syndrome; IBD: inflammatory bowel disease; TINU: tubulointerstitial nephritis and uveitis syndrome

Table 3 Frequencies of anterior uveitis types in unilateral anterior uveitis patients

	Diagnosis	Number of unilateral AU patients (%)	Number of unilateral AU patients/AU patients (%)
1	Herpetic AU	55 (25.6)	55/57 (96.5)
	HSV	22 (10.2)	22/22 (100)
	VZV	25 (11.6)	25/25 (100)
	CMV	8 (3.7)	8/10 (80)
2	Acute AU	52 (24.2)	52/60 (86.7)
3	Scleritis	28 (13.0)	28/37 (75.7)
4	PSS	15 (7.0)	15/15 (100)
5	Diabetic iritis	12 (5.6)	12/21 (57.1)
6	FUS	8 (3.7)	8/9 (88.9)
7	AU with IBD	7 (3.3)	7/9 (77.8)
8	Behçet's disease	3 (1.4)	3/7 (42.9)
9	Lens-induced uveitis	3 (1.4)	3/3 (100)
10	TINU	1 (0.5)	1/5 (20)
	Others	2 (1)	2/5 (40)
	Idiopathic	29 (13.5)	29/47 (61.7)
	Total	215 (100)	215/275 (78.2)

AU: anterior uveitis; HSV: herpes simplex virus; VZV: varicella zoster virus; CMV: cytomegalovirus; PSS: Posner-Schlossman syndrome; FUS: Fuchs uveitis syndrome; IBD: inflammatory bowel disease; TINU: Tubulointerstitial nephritis and uveitis

apparently higher male/female ratio, higher age, and lower IOP than the PSS group, the differences were not statistically significant.

Discussion

In the present study population, AU occurred in all age groups, but was more common in middle-aged and older groups. Unilateral AU occupied 78% of all AU cases and there was no gender predominance. On the other hand, juvenile AU was bilateral and more common in girls. Although there were only 19 (14.5%) AU patients younger than 20 years of age, our results are comparable with a previous report [39].

AU is the most common uveitis in Western and some Asian countries [1, 5–11], but occupies the second place in Japan [38, 40, 41]. The epidemiology of uveitis varies considerably depending on the geographic location, race, and social and economic environment [42]. Panuveitis, represented by sarcoidosis, Vogt-Koyanagi-Harada disease and BD, is the most common form of uveitis in Japan, although BD has been decreasing in recent years [38, 43, 44]. In addition, although AAU has the highest frequency among all uveitis diseases in Western countries, the proportion of AAU in uveitis in Japan is less than 10% [38, 44]. One of the contributing factors to AAU is considered to be the HLA-B27 allele. Approximately 55% of Caucasian patients with AAU are HLA-B27–positive, and the HLA-B27 allele is found in 8–10% of the general population [45, 46]. However, the frequency of the HLA-B27 allele is only 0.4% in Japanese [47]. This does, at least in part, explain the relatively low frequency of AAU in Japan [38, 44].

In the 2009 epidemiological survey of uveitis in Japan, the frequency of herpetic AU was 4.2% of all uveitis cases, lower than the 6.5% frequency of AAU [44]. In the 2016 survey, however, the proportion of herpetic AU increased to 6.5%, higher than the 5.5% rate of AAU [38]. The frequency of herpetic AU was 6.5% in all uveitis cases and 21.4% in AU cases; the latter is comparable to the frequency of 20.7% in this study. AAU is more common in young and middle-aged adults [48, 49], while herpetic AU occurs more frequently in older patients [37, 50, 51]. In the present study also, the mean age of herpetic AU patients was 60.6 ± 17.1 years, significantly higher than that of AAU (48.4 ± 15.0 years). A notable finding is that more than 40% of all AU patients were over 60 years of age, and one-third of these patients had herpetic AU. A study investigating characteristics of de novo uveitis in patients older than 60 years reports that herpetic AU had the highest frequency among the AU types with specific diagnosis, although idiopathic uveitis accounted for the majority of cases [52]. A review article also shows that herpetic AU was a common cause of AU

Table 4 Anterior uveitis types with disturbed visual acuity

	Diagnosis	Number of AU eyes with disturbed VA* (%)	Number of AU eyes with disturbed VA/AU eyes (%)
1	Herpetic AU	29 (29.3)	29/57 (50.9)
	HSV	12 (12.1)	12/22 (54.5)
	VZV	12 (12.1)	12/25 (48.0)
	CMV	5 (5.1)	5/10 (50.0)
2	Acute AU	29 (28.3)	29/60 (48.3)
3	Diabetic iritis	13 (10.1)	13/21 (61.9)
4	Scleritis	8 (6.1)	8/37 (21.7)
5	FUS	5 (5.1)	5/9 (55.6)
6	Lens-induced uveitis	3 (3.0)	3/3 (100)
7	AU with IBD	2 (2.0)	2/9 (22.2)
8	PSS	1 (1.0)	1/15 (6.7)
	Behçet's disease	1 (1.0)	1/7 (14.3)
	TINU	1 (1.0)	1/7 (14.3)
	Others	2 (2.0)	2/5 (40)
	Idiopathic	13 (11.1)	13/47 (27.7)
	Total	107 (100)	107/335 (31.9)

VA; visual acuity; AU: anterior uveitis; HSV: herpes simplex virus; VZV: varicella zoster virus; CMV: cytomegalovirus; FUS: Fuchs uveitis syndrome; IBD: inflammatory bowel disease; PSS: Posner-Schlossman syndrome; TINU: Tubulointerstitial nephritis and uveitis

*VA less than 20/30

Table 5 Anterior uveitis types with high intraocular pressure

	Diagnosis	Number of AU eyes with high IOP* (%)	Number of AU eyes with high IOP/AU eyes (%)
1	Herpetic AU	20 (37.0)	20/57 (35.1)
	HSV	7 (13.0)	7/22 (31.8)
	VZV	6 (11.1)	6/25 (24.0)
	CMV	6 (11.1)	6/10 (60)
2	Scleritis	14 (25.9)	14/37 (37.8)
3	PSS	6 (11.1)	6/15 (40)
4	Acute AU	4 (7.4)	4/60 (6.67)
5	Diabetic iritis	3 (5.6)	3/21 (14.3)
6	AU with IBD	1 (1.9)	1/9 (11.1)
	Lens-induced uveitis	1 (1.9)	1/3 (33.3)
	Others	2 (3.7)	2/5 (40)
	Idiopothic	4 (7.4)	3/47 (6.38)
	Total	54 (100)	54/335 (16.1)

IOP: intraocular pressure; AU: anterior uveitis; HSV: herpes simplex virus; VZV: varicella zoster virus; CMV: cytomegalovirus; PSS: Posner-Schlossman syndrome; IBD: inflammatory bowel disease

*IOP higher than 20 mmHg

among elderly patients [53]. Aging of the population is progressing all over the world including Japan, and the increase in herpetic AU may be related to the demographic change underlying the aging society.

Since severe anterior inflammation reduces the function of the ciliary body, IOP is usually lower in AAU patients [54]. Mean IOP of AAU eyes was 13.3 ± 4.2 mmHg, lower than the 16.1 ± 7.6 mmHg in total AU eyes. However, IOP higher than 20 mmHg was observed in 4 AAU eyes (6.67%), 3 of whom had high IOP caused by pupillary block whereas 1 eye had primary open angle glaucoma. On the other hand, high IOP is a characteristic complication of herpetic AU; especially, CMV-associated AU may lead to glaucomatous optic neuropathy [55]. However, the proportions of herpetic AU with high IOP were relatively low in this study; 60% of CMV-associated AU, 31.8% of HSV-associated AU, and 24.0% of VZV-associated AU. Some herpetic AU patients were referred to our facility after the elevated IOP at initial AU onset had been controlled by eyedrops prescribed by other facilities, but some were not. Therefore, even when medical history of high IOP is unknown, PCR using aqueous humor samples is highly recommended for AU patients with unilateral disease, keratic precipitates characteristic of herpetic AU, and elderly onset.

Chee and Jap [56] detected CMV viral DNA in the aqueous humor of eyes with presumed PSS by PCR analysis, leading to the recognition of CMV-associated AU as a new entity separate from PSS. Unilateral hypertensive AU with a few white granulomatous keratic precipitates is the characteristic clinical finding of CMV-associated AU, but is also commonly found in PSS [55, 57]. Loss of corneal endothelial cells during the clinical course is observed in

Table 6 Anterior uveitis types in patients aged over 60 years

	Diagnosis	Number of AU patients aged over 60 (%)	Number of AU patients aged over 60/AU patients (%)
1	Herpetic AU	38 (34.2)	38/57 (66.7)
	HSV	14 (12.6)	14/22 (63.6)
	VZV	16 (14.4)	16/25 (64.0)
	CMV	8 (7.2)	8/10 (80)
2	Scleritis	16 (14.4)	16/37 (43.2)
3	Acute AU	15 (13.5)	15/60 (25)
4	PSS	7 (6.3)	7/15 (46.7)
5	Diabetic iritis	5 (4.5)	5/21 (23.8)
6	FUS	3 (2.7)	3/9 (33.3)
	Lens-induced uveitis	3 (2.7)	3/3 (100)
7	Behçet's disease	1 (0.9)	1/7 (14.3)
	Others	4 (3.6)	4/5 (80)
	Idiopathic	19 (17.1)	19/47 (40.4)
	Total	111 (100)	111/275 (40.4)

AU: anterior uveitis; HSV: herpes simplex virus; VZV: varicella zoster virus; CMV: cytomegalovirus; PSS: Posner-Schlossman syndrome; FUS : Fuchs uveitis syndrome

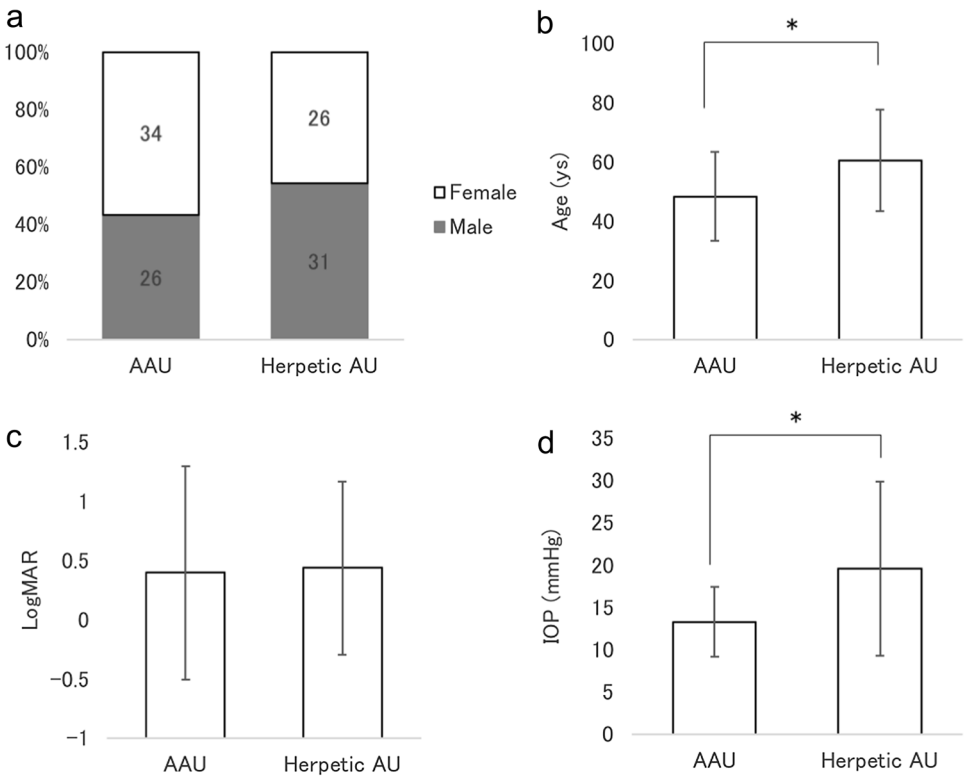

Fig. 2 Comparison between acute anterior uveitis (AAU) and herpetic anterior uveitis AU). Bar graphs show percentage of male and female patients (A) and age (B) in patients with AAU and herpetic AU; and logMAR (C) and intraocular pressure (IOP) (D) in AAU and herpetic AU eyes. *$P < 0.05$

CMV-associated AU [55, 58], but this feature is not present at the initial onset. Chee and Jap [56] report no differences in clinical features between CMV-negative and CMV-positive PSS (CMV-associated AU) eyes. On the other hand, Murata et al. [59] report that CMV-positive PSS patients (CMV-associated AU) were of older age, had higher IOP, and a more disturbed VA than CMV-negative PSS patients. Hence, the diagnosis of CMV-associated AU requires the detection of CMV-DNA by PCR or anti-CMV antibodies in the aqueous humor. In the present study, patients suspected of CMV-associated AU from their clinical findings but who were tested negative for CMV were classified as PSS. However, PSS patients, in whom a CMV-association was reconsidered following the clinical course, were treated as

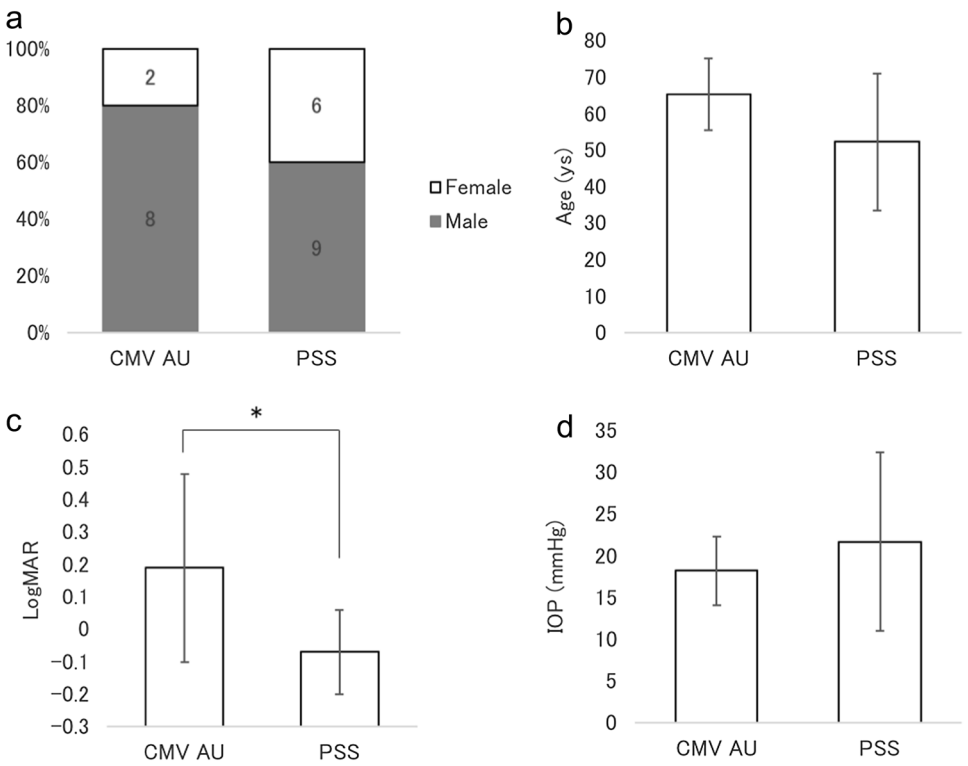

Fig. 3 Comparison between CMV-associated anterior uveitis (AU) and Posner-Schlossman syndrome (PSS).
Bar graphs show percentage of male and female patients (A) and age (B) in patients with CMV-associated AU and PSS; and logMAR (C) and intraocular pressure (IOP) (D) in CMV-associated AU and PSS eyes.
*$P < 0.05$
CMV: cytomegalovirus

CMV-associated AU. In some of them, PCR using the aqueous humor was repeated. Therefore, in this study there were some CMV-associated AU patients among the PSS patients. That may be the reason that CMV-associated AU differed significantly from PSS only in logMAR VA, although CMV-associated AU patients apparently had higher male/female ratio and were older.

The proportion of CMV-associated AU among herpetic AU was 17.5%, lower compared to previous reports in Japan [37, 50, 51]. Judging from clinical findings at presentation alone CMV-associated AU is undistinguishable from PSS as described above, although the characteristic clinical course of chronic anterior ocular inflammation, repeated IOP elevation, and decrease in corneal endothelial cells strongly suggests CMV infection. In this study, PCR tests were basically performed only once for each patient. CMV DNA is not always detected by PCR using aqueous humor [60, 61], and test results may be affected by severity of AU and the clinical course. As mentioned above, in this study CMV-associated AU patients tested negative for CMV at the initial presentation was primarily diagnosed as PSS. If PSS patients diagnosed as CMV-associated AU later on in the clinical course were included in CMV-associated AU, the proportion of CMV-associated AU would increase.

The frequency of FUS in this study was higher than in a recent national survey of uveitis in Japan [38]. FUS is non-granulomatous uveitis with latent onset and low-grade activity [62]. It is unlikely that FUS patients visit an ophthalmologist with complaints associated with AU, and the diagnosis is frequently made during routine ophthalmologic examination for blurred vision or floaters related to cataracts or vitreous opacity. Disturbed VA was found in 55.6% of FUS patients, but the cause was cataract and the patients were referred to our facility with unilateral cataracts. In addition, heterochromia is often subtle or even absent in FUS patients with dark irises such as Japanese [63, 64]. Therefore, FUS is potentially an overlooked cause of AU.

There are several limitations to our study. The small number of patients, the retrospective design, single-centre study, the diagnosis of uveitis by ophthalmologists only throughout the study period, and medical information recorded by different observers during follow-up visits may have biased the data. Additionally, because most of patients were referred from other clinics or hospitals, there was a selection bias as some of them had already been treated.

In conclusion, AU occurs in all age groups, but is more common in middle and older age groups. Unilateral AU accounted for approximately 80% of total AU and showed no sex difference in prevalence. AAU was the most common form of AU, followed by herpetic AU and scleritis, and the three together constituted more than 50% of total AU. Visual impairment was observed in one-half of AAU and herpetic AU patients, and high IOP occurred mainly in herpetic AU, PSS and scleritis. Patients with AAU were significantly younger and had lower IOP than those with herpetic AU. On the other hand, more than 40% of all AU

patients were over 60 years of age, and herpetic AU was the causative disease in one-third of the AU patients.

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