·Clinical Research·

Clinical patterns and characteristics of uveitis in a secondary hospital in southern China

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Abstract

• AIM: To investigate the characteristics of uveitis in a secondary hospital in southern China.

• METHODS: We reviewed all records of patients with uveitis at Hengli Hospital from January 2008 to December 2011. Demographic data, past history, ophthalmic examinations and other laboratory tests were analyzed.

• RESULTS: One hundred and ninety-nine uveitis patients were enrolled in this study, including 134 (67.3%) males and 65 females (32.7%) with an average age of 41.0±15.1y. The anatomical distribution included 103 (51.8%) cases of anterior uveitis, followed by panuveitis (65, 32.7%), posterior uveitis (29, 14.6%) and intermediate uveitis (2, 1.0%). Of the 98 (49.2%) non-idiopathic cases, there were 10.1% Behcet's disease, 9.5% Vogt-Koyanagi-Harada (VKH) syndrome, 7.5% infectious uveitis, 7.5% traumatic uveitis and 3.5% postoperative uveitis.

• CONCLUSION: Idiopathic anterior and posterior uveitis, Behcet's disease, VKH syndrome, infectious uveitis and traumatic uveitis are the most common uveitis entities in a secondary hospital in southern China. Additional measures should be taken to prevent infectious and traumatic uveitis.

• **KEYWORDS:** uveitis; southern China; epidemiological studies
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INTRODUCTION

Uveitis is a relatively common eye disease and one of the most important causes for visual impairment throughout the world. The causes of uveitis are numerous, including infection, trauma, noninfectious systemic or ocular disease, and masquerade syndromes. Differences in social economic, environment, genetic factors and standards of living all make clinical patterns and characteristics varied in different populations[1-4].

Numerous studies addressing the clinical features of uveitis have been based on patients from the United States [2,3,5,6], European countries [2,4,7] and Australia [8]; whereas data from Asian countries is relatively scarce [1-3,9,10]. Most studies on the epidemiology of uveitis are performed in tertiary uveitis referral centers and include many severe and complicated cases of uveitis. An earlier study carried out by University of California Los Angeles (UCLA) [5,6] showed a significant difference in the prevalence of uveitis entities between referral and non-referral centers.

Few studies addressing the prevalence of uveitis etiologies in Chinese patients are available[11,12]. We, therefore, investigated the profile and characteristics of uveitis by retrospectively analyzing 199 uveitis cases seen at the Department of Ophthalmology in Dongguan Hengli Hospital from January 2008 to December 2011. Dongguan Hengli Hospital is a regional hospital (secondary hospital) that provides comprehensive medical and health services to all 17 communities in Hengli town, which is located in the southern portion of the Guangdong province in China. In this study, we discuss a number of possible explanations for differences in the prevalence of various uveitis entities between China and other regions in the world.

SUBJECTS AND METHODS

Subjects One hundred and ninety-nine uveitis patients at Hengli Hospital were enrolled in this retrospective study from January 2008 to December 2011. The medical history included a detailed record, especially with respect to systemic diseases, such as cutaneous diseases, arthropathy, neurologic/auditory disorders, vitiligo, alopecia, poliosis, gastrointestinal diseases, genital ulceration, tuberculosis (TB), leprosy, diabetes, and severe diarrhea. The study was conducted according to the recommendations of the

Declaration of Helsinki [13]. Ethics approvals were obtained from the ethics committees of Chongqing Medical University, Dongguan Hengli Hospital, Dongguan People's Hospital, and Guangdong Province Eye Disease Prevention and Control Research Institute. Before both routine screening and detailed examinations, the consent statement was read to each individual, and written or verbal informed voluntary consent was obtained from all participants, since a small proportion of this population is illiterate.

Methods

Examinations All patients underwent a routine eye examination by qualified medical personnel. The examination included best corrected visual acuity (BCVA), intraocular pressure, anterior segment evaluation including applanation tonometry and gonioscopy by slit-lamp biomicroscopy and fundus examination. In addition, visual field analysis, ultrasound biomicroscopy, optical coherence tomography (OCT), fundus fluorescein angiography (FFA), indocyanine green angiography (ICGA), B-scan ultrasonography, and skin allergy testing were performed in certain cases. Routine laboratory examinations included routine blood tests, erythrocyte sedimentation rate, serum angiotensin converting enzyme (ACE) levels, treponema pallidum hemoagglutition (TPHA) test, enzyme linked immunosorbent assay (ELISA) for toxoplasma, toxocara, human immunodeficiency virus (HIV) and human leukocyte antigen (HLA) typing. Aqueous and vitreous tap was done in selected cases for cytological examination and polymerase chain reaction (PCR). Other tests included antinuclear antibodies, C-reactive protein, venereal disease research laboratory (VDRL), fluorescent treponemal antibody absorption (FTA-ABS) and imaging techniques (CT scan, MRI, and X-ray of the chest, sacroiliac joints and knee joints) when indicated.

No PCR testing was done to confirm the herpetic uveitits cases. The diagnosis of herpetic uveitis was made based on the clinical findings of unilateral anterior uveitis with epithelial and/or stromal keratitis, decreased corneal sensation, and sectoral iris atrophy as previously reported[14]. Anterior chamber or vitreous taps for PCR were applied to test for suspicious acute retinal necrosis (ARN).

The Mantoux test was selectively performed in cases that presented with clinical signs of uveitis suggesting intraocular TB, such as granulomatous anterior uveitis, active periphelebitis, neuroretinitis, retinochorioditis, and subretinal granuloma/ abscess. A skin induration of 15 mm or larger was considered as a positive result.

Medical consultation and evaluation were requested to reach the final etiological diagnosis whenever systemic involvement was suspected.

Medical records of all patients were initially evaluated by two trained uveitis specialists (Zheng Y and Meng QL) and intractable cases were chosen to be further discussed with a uveitis specialist from a tertiary referral center (Pei-Zeng Yang). The diagnosis was made according to the International Classification of Diseases, ninth revision (ICD10) [15] and the criteria for uveitis that were recently revised by the International Uveitis Study Group (IUSG) in 2008 [16] and The Standardization of Uveitis Nomenclature (SUN) working group[17].

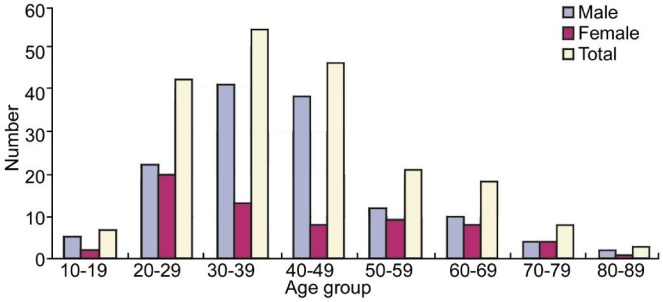

Figure 1 Age distribution of 199 patients with uveitis in southern China.

Statistical Analysis Statistical analysis was performed using SPSS 12.0 (SPSS 12.0 for Windows). Descriptive statistics were expressed as mean ±standard deviation. The mean of normally distributed variables were compared with a t-test. All tests were two-tailed and $P<0.05$ was considered to be statistically significant.

RESULTS

A total of 199 patients were identified as having evidence warranting a diagnosis of present or past uveitis involving 311 eyes at the Ophthalmology Department during the past 4y. There were 134 (67.3%) males and 65 (32.7%) females. The mean age of the patients at uveitis presentation was 41.0±15.1y (range 11-86y). The number of patients aged 20 to 60y was 163 in total, accounting for 81.9% of patients (Figure 1).

According to the anatomical criteria established by the International Uveitis Study Group in 2008 [17], the distribution of the major types of uveitis included 103 anterior uveitis (51.8%), 65 panuveitis (32.7%), 29 posterior uveitis (14.6%), and 2 intermediate uveitis (1.0%) (Table 1).

Among the 199 patients with intraocular inflammation, 15 (7.5%) had traumatic uveitis in 15 eyes (8 cases of traumatic iridocyclitis and 7 cases of traumatic panuveitis) and 7 had postoperative uveitis in 7 eyes. Of the 15 cases of traumatic uveitis, 12 were male and 3 were female and all cases were unilateral. The mean age was 26.7±7.6y (range 14-42y). The remaining 177 (88.9%) cases had uveitis unrelated to prior surgery or trauma (endogenous uveitis) involving 289 eyes (Table 2).

As shown in Table 2, we did not identify any specific etiology in 101 (50.8%) cases, while in the other 98 (49.2%) cases, a pathogenic factor (such as herpes zoster/herpes simplex keratouveitis), systemic disease (such as ankylosing spondylitis), or a definite entity (such as Fuchs heterochromic iridocyclitis)contributed to the specific etiology.

In our study, infectious uveitis contributed to a significant proportion (7.5%) of uveitis. Of the 15 cases of infectious uveitis, 9 were male, 6 were female, and 8 cases were

Table 1 Anatomical diagnosis of uveitis

Classification	No. of patients	Percentage of total cases (%)	M/F	Bilateral	$\bar{x} \pm s$ (a)
Anterior uveitis	103	51.8	62/41	49	39.8±14.5
Intermediate uveitis	2	1.0	2/0	0	53.0±5.6
Posterior uveitis	29	14.6	19/10	16	41.3±15.5
Panuveitis	65	32.7	51/14	47	42.2±16.1
Total	199	100	134/65	112	41.0±15.1

Table 2 The diagnoses of 199 patients with uveitis in southern China

Diagnosis	No. of patients	Percentage of total cases (%)	M/F	Bilateral
Anterior	103	51.8	62/41	49
Idiopathic iridocyclitis	67	33.7	39/28	36
Fuchs heterochromic iridocyclitis	6	3.0	2/4	2
Ankylosing spondylitis	4	2.0	4/0	4
Traumatic iridocyclitis	8	4.0	6/2	0
Glaucomatocyclitic crisis	3	1.5	3/0	0
Psoriatic arthritis	1	0.5	1/0	1
Juvenile idiopathic arthritis	1	0.5	1/0	1
Zoster/simplex keratouveitis	8	4.0	4/4	5
Intraocular lens related uveitis	5	2.5	2/3	0
Intermediate	2	1.0	2/0	0
Posterior	29	14.6	19/10	16
Idiopathic posterior uveitis	23	11.6	15/8	13
Toxoplasmosis	2	1.0	1/1	0
Acute retinal necrosis syndrome	1	0.5	0/1	0
Serpiginous choroiditis	1	0.5	1/0	1
Eales disease	2	1.0	2/0	2
Panuveitis	65	32.7	51/14	47
Behcet's disease	20	10.1	16/4	18
Vogt-Koyanagi-Harada Syndrome	19	9.5	13/6	19
Idiopathic panuveitis	9	4.5	9/0	6
Traumatic panuveitis	7	3.5	6/1	0
Endophthalmitis	3	1.5	2/1	2
TB associated panuveitis	2	1.0	2/0	1
Lens-induced	2	1.0	1/1	0
Intraocular lens–related panuveitis	2	1.0	1/1	0
Sympathetic ophthalmia	1	0.5	1/0	1
Total	199	100	134/65	112

bilateral. The mean age was 39.1 ±15.2y (range 19-71y). Zoster/simplex keratouveitis (n=8) was the most common cause of infectious uveitis, followed by infectious endophthalmitis (n=3), TB associated panuveitis (n=2) and toxoplasmosis(n=2) (Table 2).

Of the 103 cases of anterior uveitis, recurrences occurred in 30 (29.1%) cases. Acute anterior uveitis was noted in 57 (55.3%) patients and chronic anterior uveitis was noted in 46 (44.7%) patients. Of the panuveitis cases, Behcet's disease (20, 10.1%) and Vogt-Koyanagi-Harada (VKH) syndrome (19, 9.5%) were the two most common entities, followed by idiopathic panuveitis (9, 4.5%), traumatic panuveitis (7, 3.5%), endogenous endophthalmitis (3, 1.5%), lens-induced uveitis (2, 1.0%), intraocular lens-related panuveitis (2, 1.0%), TB associated panuveitis (2, 1.0%) and sympathetic ophthalmia (1, 0.5%) (Table 2). Of the 29 cases of posterior uveitis, recurrences occurred in 17 (58.6%) cases and the mean interval between the onset and first recurrence was 19.8mo. Of the 67 cases of idiopathic iridocyclitis, 39 were male, 28 were female, and 36 cases were bilateral. The mean age was 41.4±15.2y (range 15-86y). Recurrences occurred in 28 (41.8%) cases and the mean interval between the onset and first recurrence was 11.1mo. The relapse was associated with the withdrawal or switching of glucocorticoids or immunosuppressive agents in 57.1% of recurrent patients. Of the 19 VKH cases, recurrence occurred in 12 (63.2%) cases and the mean interval between the onset and first recurrence was 9.1mo. Of the 20 cases of Behcet's disease, recurrence occurred in 14 (70%) cases and the mean interval between the onset and first recurrence was 14.2mo.

DISCUSSION

In both the developed and developing world, uveitis is most

often seen in adults [1,3]. The mean age of first presentation with uveitis in previous clinic-based surveys was reported to range between 35 and 45y [1-3,5] and roughly 60%-80% of all patients were in the third through sixth decade of life [2,3]. Children constitute 5%-10% of the patients with uveitis seen at tertiary referral centers and the most common cause of anterior uveitis is juvenile idiopathic arthritis[18]. In our study, the mean age of the uveitis patients was 41y and 82% of the patients were between 20 and 60 years old. This finding is consistent with the age distribution reported in the literature. In most published reports, uveitis patients showed a relatively equal gender distribution. However, more male cases were included in our study. This may be related to the fact that the family status is a "patriarchal" society in rural China, which means that males may have more access to care and adequate medical treatment if they are ill.

In our study, anterior uveitis was the predominant anatomical entity (51.8%). The prevalence in our study was higher than that reported in Japan (45.1%)[19], Iran (38.4%)[2,3], France (28.5%)[2,3], Argentina (34.4%)[2,3], Iran (42.9%)[10], Thailand (35%)[9], England (46%)[7],and our previous retrospective study from a tertiary center for uveitis in southern China (45.6%)[12]. However, the prevalence of anterior uveitis in our study was lower than that reported from Saudi Arabia (59.5%)[2, 3] and the USA (60.6%)[6]. The exact reason for the observed differences is not clear and may depend on various factors such as occupation, ethnic background and unknown factors influencing the need to seek medical attention. In our study, idiopathic anterior uveitis was the most frequently diagnosed entity (65% of anterior uveitis), in which acute anterior nongranulomatous uveitis contributed to 57% of cases of anterior uveitis.

The proportion of intermediate uveitis in our study is low. A variety of pathogenic factors or diseases, including sarcoidosis, TB, and multiple sclerosis, are associated with intermediate uveitis [1-3]. However, we have not found evidence to support any specific diagnosis according to the typical clinical features. Interestingly, we observed no cases of sarcoid uveitis. Sarcoidosis can remain subclinical for a long time and may also be misdiagnosed as TB [20]. The current major diagnostic tests for the diagnosis of sarcoidosis are undoubtedly chest X-ray (CXR) or chest CT. However, a confirmation by tissue biopsy is required for the definitive diagnosis of sarcoidosis [20]. If patients are otherwise asymptomatic and the disease is only in the eye, treatment would be unchanged if the systemic diagnosis of sarcoidosis is made. However, it was impossible to perform additional diagnostic tests such as chest CT or tissue biopsy in all patients with uveitis to diagnose sarcoidosis in a secondary hospital, because of limited medical resources. Therefore, sarcoidosis in our study may be somewhat undervalued. As a result, it is necessary to improve the capacity and effectiveness of diagnosis and treatment of uveitis in secondary hospitals. The proportion of posterior uveitis in our series is lower than most reports from Europe and America. Nutritional status, environment and lifestyle may contribute to the differences in posterior uveitis prevalence between China and western counties. An example is the low frequency of ocular toxoplasmosis in China as compared to other regions in the world. Recent epidemiologic studies [1,2] suggest that socio-economic factors and the circulating parasite genotypes may play an important role in the epidemiology of ocular toxoplasmosis. Drinking untreated water is considered the major source of toxoplasma infection in developing countries, whereas the consumption of raw or undercooked meat is the most important cause in the western world. The low frequency of ocular toxoplasmosis in China may be associated with socio-economic factors leading to low meat consumption overall, and when meat is consumed it is typically well-cooked. However, compared with our previous study from a tertiary center of uveitis in China, the proportion of posterior uveitis in our current study from a secondary hospital center is higher, especially the idiopathic posterior uveitis [12]. The cause may be explained by the serious imbalance in the distribution of medical resources in China. Patients with severe uveitis entities, such as VKH syndrome and Behcet's disease, tended to have treatment in the uveitis referral center over a non-tertiary center or secondary hospital. This could lead to a relatively higher prevalence of idiopathic posterior uveitis and a relatively lower proportion of VKH syndrome and Behcet's disease cases in secondary hospitals[12,21].

Panuveitis, a relatively uncommon type of uveitis in western counties [2,3,5,7,19], has been found in the current study to be the second most common anatomical entity of uveitis. As mentioned above, sarcoidosis, a relatively common cause of panuveitis in reports from Western counties[1,2,6], is not seen in China, whereas Behcet's disease and VKH syndrome are significant causes of panuveitis.

Both traumatic uveitis [1-3] and intraocular lens-related panuveitis [1-3,6,22] are more common in developing nations as compared with developed countries. We observed a large number of cases of ocular inflammation related to trauma and intraocular surgery. The occupation, socioeconomic status, and quality of medical care most likely contribute to the high prevalence of traumatic and lens-induced uveitis. The use of protective eyewear for workers, which has been introduced in many western countries, also needs to be introduced in China to reduce the incidence of these preventable causes of uveitis.

Although infectious causes form a minority cause of uveitis in developed countries[1-3,5,6], infectious uveitis caused by TB[1,23], syphilis [1-3], toxoplasmosis [1,2,23], and other specific infectious causes [1,3] account for 30% to 50% of cases in developing countries[1,3,5,23,24]. China seems to form an exception, as shown from our recent study from a referral center in southern China, in which an infectious etiology was observed in less than 2.6% of cases [12]. In our current study, an infectious etiology accounts for 7.5% of cases, which is nearly three times that of our previous study from a referral center [12]. In our study, zoster/simplex keratouveitis was the most common entity of infectious uveitis, followed by endophthalmitis, TB associated panuveitis and toxoplasmosis. Although TB

infection as a cause of uveitis was also reported in southern and northern India as the possible cause of uveitis in 10.1% and 20.8% of patients [2,23], respectively, TB is a rare cause of uveitis in our study and in mainland China [12] and Taiwan[11]. The reason for this phenomenon may be related to a limited sensitivity of the Mantoux test in patients with an active TB infection as well as patients with suppressed cellular immunity. Unfortunately, the newer TB tests that have a higher specificity, such as PCR for mycobacterium tuberculosis or interferon gamma release assay, are still unavailable in secondary hospitals in China. Hence, it's worth mentioning that, in our study, inaccuracies involving ocular TB diagnosis as well as its underdiagnosis are possible. However, AIDS as an underlying cause of uveitis was not seen in our study, despite the fact that the AIDS epidemic has also reached China. It should be noted that history of multiple sexual partners could only be assessed in a few patients in our study since discussion about these issues is still a delicate matter in China.

One limitation of the study is that this is a retrospective study. We could not obtain more data in a portion of patients because some patients had obtained improved visual acuity after treatment and were lost to follow-up. Therefore, we had to focus on age and gender features, etiology and classification of uveitis in the uveitis patients in the current study.

In summary, there are differences concerning the distribution of uveitis entities not only between China and western countries, but also between tertiary and secondary hospital centers in China itself. Idiopathic anterior and posterior uveitis, Behcet's disease, VKH syndrome, infectious uveitis, and traumatic uveitis are the most common entities of uveitis in secondary hospitals in southern China. As trauma and infection contribute to a significant proportion of uveitis in the present study, we suggest that additional measurements be taken to prevent or decrease the proportion of infectious and traumatic causes in secondary hospital in China.

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