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Clinical Patterns and Causes of Posterior Uveitis in a Tertiary Referral Eye Center in Northwest of Iran

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Abstract

Objectives: Posterior uveitis is the second most common anatomical type of uveitis after the anterior in Iran. Its incidence and etiologies are not identical in populations of different races and socioeconomic backgrounds. In this study, the researchers intended to evaluate the causes of posterior uveitis in a referral center in northwest of Iran.

Materials and Methods: In this cross-sectional retrospective study, clinical records of 120 patients with posterior uveitis referred to the Uveitis Clinic at the Nikookari hospital (during 2003 to 2017) were reviewed. Demographic findings, etiologies, clinical courses, associated systemic diseases, and ocular complications were analyzed.

Results: Infectious etiologies were found in 69.2% of the patients with posterior uveitis. The most common causes of posterior uveitis were toxoplasmosis (59.2%) followed by idiopathic (10.8%) and Behçet's (8.3%) diseases. Macular scar (5.83%) and macular edema (15%) were the most widespread complications in the patients. Posterior uveitis found in 20.8% of the patients was associated with a systemic disease. In addition, Behçet's (8.3%) and Vogt-Koyanagi-Harad (VKH) (4.2%) diseases were among the most prevalent concomitant diseases. Non-granulomatous uveitis was observed in 84.2% of cases. The course of the disease was acute in 83.33% of the patients.

Conclusions: The results of this study revealed that infectious etiologies were the most common causes of posterior uveitis. Toxoplasmosis and Behcet's disease were the most frequent cases. The most common complication of posterior uveitis was macular scar. It seems that identifying and analyzing causes of the posterior uveitis and its complications are crucial for the development of policies and treatment guidelines.

Keywords: Posterior uveitis, Etiology, Iran

Introduction

One of the main reasons the patients refer to an ophthalmologist is intraocular inflammation (1). Posterior uveitis, after the anterior uveitis and pan-uveitis, is the third most common type of uveitis with varying incidence in different populations of different countries throughout the world (2). Posterior uveitis is the second most common type of uveitis after anterior uveitis in Iran (21.4%-28%) (3,4). Ten percent to 15% of legal blindness cases in developed countries are due to uveitis (5). It can be affected by various factors including genetic, ethnic, environmental, geographical, nutritional, and socioeconomic issues in addition to diagnostic criteria and referral patterns. Patients with uveitis are usually young and face with some common complications including glaucoma, cataracts, iris adhesion, and macular edema. Therefore, early diagnosis and well-timed treatment are very important in this regard (3,6). Regional variations in terms of etiology of uveitis have been reported (7). The incidence and pattern of uveitis in each population should be determined in order to prevent excessive and costly screening with low financial resources. However, studies on uveitis in the Middle East are limited (3,8,9). Differences in socioeconomic, environmental, genetic factors, and living standards status, all make a difference in clinical patterns and different populations' characteristics (4). Several studies have evaluated the uveitis epidemiology and have identified differences in etiology based on geographical area, gender, race, age, social aspects, and immunological factors (7,10). Although posterior uveitis is usually easily treated, its complications can result in severe vision loss (9). This study evaluated the causes of posterior uveitis in the northwest region of Iran. It was intended to describe the most common leading factors of posterior uveitis and related complications in patients who referred to the uveitis clinic in order to lower the costs of unnecessary tests and to develop possible preventive policies and evidence-based guidelines for its management.

Materials and Methods

In this cross-sectional retrospective study, all clinical records of 120 patients diagnosed with posterior uveitis

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in the uveitis clinic of Nikookari eye hospital of Tabriz have been evaluated during 2003 to 2017. Patients were followed up for at least 6 months to maximum 10 years. Variables such as age, gender, types of uveitis including infectious, non-infectious and idiopathic, granulomatous or non-granulomatous, unilateral or bilateral, and acute, chronic, or relapsing were analyzed. Moreover, underlying or associated systemic diseases and ocular complications recorded in the files were analyzed. Naming of the uveitis in terms of location, onset, and course of ocular inflammation was carried out according to the uveitis nomenclature (SUN) working group criteria (11). Posterior uveitis was applied for cases with predominant posterior inflammatory signs at first visit. In cases where the clinical image did not suggest a specific etiology, several different supportive and confirmative laboratory and paraclinical tests were applied including high-chest computed tomography (CT) scan, upper body gallium scan, angiotensin-converting enzyme (ACE), purified protein derivative (PPD) skin test, QuantiFERON TB-Gold (QFT), polymerase chain reaction (PCR), and ocular fluorescein angiography (FA), indocyanine green angiography (ICGA), optical coherence tomography (OCT), and A-B scan ultrasound. In cases where no specific cause or underlying systemic disease could be found, the term "unknown" was applied.

Data Analysis

SPSS (Statistical Package for the Social Sciences) software, version 25 was run for statistical analysis. Descriptive methods (frequency, percentage, and mean ± standard deviation) were used for statistical analysis. The chi-squared tests were also applied to identify possible associations at a significance level of .05.

Results

The participants of the present study consisted of 120 patients with posterior uveitis clinical records of whom 56(46.7%; 95% CI: 38.0–55.6) were males and 64 of them (53.3%; 95% CI 44.4–62.0) were female. The mean age was 35.71 ± 14.28 years. Posterior uveitis was unilateral in 79 (65.83%; 95% CI 57.0- 73.7) and bilateral in 41 (34.2%; 95% CI 26.3-43) patients. The clinical course of uveitis was acute in 100 patients (83.33%; 95% CI 75.7-88.9), chronic in 8 of them (6.7%; 95% CI 3.4-12.6), and recurrent in 12 (10%; 95% CI 5.8-16.7) of the cases. A specific etiology was found in 107 out of 120 (89.2%; 95% CI 82.3-93.6) cases including infections in 83 (69.16%; 95% CI 60.4–76.7) and non-infection in 24 (20%; 95% CI 13.8–28) cases and the remaining were idiopathic (13/120, 10.83%; 95% CI 6.4–17.7). Posterior uveitis was mainly non-granulomatous in 101 cases (84.2%; 95% CI 76.6-89.6) whereas being granulomatous in 19 of them (15.8%; 95% CI 10.4-23.4) (Table 1). Etiologic evaluation revealed that the most common etiology of posterior uveitis was toxoplasmosis (71/120, 59.2%; 95% CI 50.2–67.5) followed by idiopathic (13/120, 10.9%; 95% CI 6.4–17.7), and Behçet's diseases (10/120, 8.3%; 95% CI 4.6–14.7) (Table 1). At all ages, infectious causes had the highest incidence of posterior uveitis (Tables 1 and 2). Most cases with posterior uveitis were in the age group of 18-36 years old (61/120, 50.8%; 95% CI 42.0-59.6). According to the results, toxoplasma retinochoroiditis was the most common type of posterior uveitis in all age groups and the most common infectious etiology was observed in patients with 50 years of age or younger (5). It was found that in 13 (18.3%; 95% CI 11.0-28.8) of the patients diagnosed with *Toxoplasma* uveitis, the active focal necrotizing retinitis, was in the macular area. Posterior uveitis was seen in 24 (20%; 95% CI 13.8-

Table 1. General Features of Patients Based on Different Schemes for Acute, Chronic, Granulomatous and Non-Granulomatous Condition of Posterior Uveitis

Etiology	Acute No. (%)	Chronic No. (%)	Recurrence No. (%)	Granulomatous No. (%)	Non-Granulomatous No. (%)
Idiopathic	9 (9)	2 (25)	2 (16.66)	1 (5.26)	12 (11.88)
Infection					
Toxoplasmosis	69 (69)	0 (0)	2 (16.66)	3 (15.78)	68 (67.32)
Toxocariasis	2 (2)	1 (12.5)	0 (0)	0 (0)	3 (2.97)
Tuberculosis	4 (4)	0 (0)	0 (0)	3 (15.78)	1 (.99)
ARN	3 (3)	0 (0)	0 (0)	3 (15.78)	0 (0)
CMV	2 (2)	0 (0)	0 (0)	0 (0)	2 (1.98)
Non-infection					
VKH	0 (0)	0 (0)	5 (41.66)	5 (26.31)	0 (0)
Behçet's disease	8 (8)	0 (0)	2(16.66)	0 (0)	10 (9.9)
SLE	2 (2)	0 (0)	0 (0)	0 (0)	2 (1.98)
Serpiginous choroiditis	0 (0)	3 (37.5)	0 (0)	0 (0)	3 (2.97)
Sarcoidosis	0 (0)	2 (25)	1 (8.33)	3 (15.78)	0 (0)
Sympathetic ophthalmia	1 (1)	0 (0)	0 (0)	1 (5.26)	0 (0)
Total	100 (100)	8 (100)	12 (100)	19 (15.83)	101 (84.16)

Abbreviations: CMV, cytomegalovirus; VKH,Vogt-Koyanagi-Harad syndrome; SLE, systemic lupus erythematosus; ARN, acute retina necrosis.

Table 2. Causes and Clinical Disease Associations of Posterior Uveitis by Age Groups

Etiology	Acute No. (%)	Chronic No. (%)	Recurrence No. (%)	Granulomatous No. (%)	Non-Granulomatous No. (%)
Idiopathic	9 (9)	2 (25)	2 (16.66)	1 (5.26)	12 (11.88)
Infection					
Toxoplasmosis	17 (62.96)	42 (68.85)	9 (40.90)	3 (30)	71 (59.1)
Toxocariasis	3 (11.11)	0 (0)	0 (0)	0 (0)	3 (2.5)
Tuberculosis	0 (0)	0 (0)	1 (4.54)	3 (30)	4 (3.33)
ARN	0 (0)	0 (0)	3 (13.63)	0 (0)	3 (2.5)
CMV	0 (0)	1 (1.63)	1 (4.54)	0 (0)	2 (1.7)
Non-infection					
VKH	2 (7.40)	3 (4.91)	0 (0)	0 (0)	5 (4.1)
Behçet's disease	1 (3.70)	3 (4.91)	4 (18.18)	2 (20)	10 (8.3)
SLE	2 (7.40)	0 (0)	0 (0)	0 (0)	2 (1.7)
Serpiginous choroiditis	0 (0)	1 (1.63)	1 (4.54)	1 (10)	3 (2.5)
Sarcoidosis	1 (3.70)	1 (1.63)	1 (4.54)	0 (0)	3 (2.5)
Sympathetic ophthalmia	0 (0)	1 (1.63)	0 (0)	0 (0)	1 (.83)
Total	27 (22.5)	61 (50.84)	22 (18.33)	10 (8.33)	120 (100)

Abbreviations: CMV, cytomegalovirus; VKH,Vogt-Koyanagi-Harad syndrome; SLE, systemic lupus erythematosus; ARN, acute retina necrosis.

28.0) patients in association with a systemic disease and most of the cases were related to Behçet's disease (10/120, 8.3%; 95% CI 4.6-14.7) and Vogt-Koyanagi-Harad (VKH) (5/120, 4.2%; 95% CI 1.8-9.4) disease. In this study, the frequency of complications in each etiologic group was evaluated. At least one ocular complication was found in 33 (27.5%; 95% CI 20.3-36.1) patients with posterior uveitis as listed in their files during their last visits. Macular scar was the most common complication among patients suffering from posterior uveitis (18/120, 15%; 95% CI 9.7-22.5). In addition, the most complicated cases were observed in the infectious group (17/120, 14.2%; 95% CI 9.0-21.5). Furthermore, it needs to be emphasized that in 18.3% of toxoplasma cases, active lesions were located in macular regions. Consequently, permanent visual loss was predictable in those patients. Among all the studied subjects 17 out of 120 (14.2%; 95% CI 9.0-21.5) of infectious cases, 9 (7.5%; 95% CI 4.0-13.6) of non-infectious, and 7 (5.8%; 95% CI 2.9-11.6) of idiopathic cases were complicated.

Discussion

The etiology and incidence of uveitis are often not the same in different regions based on the patients' demographic findings, geographical locations, and social norms (12). In addition, causes of uveitis are changing over time (13). Therefore, an accurate assessment of regional pattern of uveitis is required. In this study, the frequency of posterior uveitis in both sexes was almost equal which is similar to the reports obtained in Iran (3,4,9) and other countries (7,14,15). The mean age of patients was 35 years and the majority of them were between the age ranges of 18 to 50.These are consistent with the results of many other studies (16-18). The high prevalence of posterior uveitis in young adults and consequent social impact, show the importance of a precise evaluation of uveitis in various regions. However, according to studies conducted in Thailand, Central Virginia in the United States, and China, posterior uveitis mostly occurred in the fifth decade of patients' lives (19-21). In our recent study, posterior uveitis was unilateral in most cases (65.8%). There are similar reports from other parts of Iran which indicate that 55% to 85% of posterior uveitis has been unilateral (3,4). However, in Saudi Arabia, it has been bilateral in most of the cases (8). This discrepancy might have occurred due to higher prevalence of some etiologies. In studies conducted in Iraq (17), Tunisia (7), and Thailand (20), the unilateral and bilateral uveitis had an almost identical frequency. The present study in the northwest of Iran revealed that the majority of cases with posterior uveitis had an infectious etiology (69.2%) while non-infectious (20%) and idiopathic (10.8%) causes were less common. The most common causes of posterior uveitis were toxoplasmosis, Behçet's disease, TB, and VKH, respectively. These findings illustrate the high contamination of the toxoplasma in the northwest of Iran that would require the improvement of preventive procedures. Similar to our results, Kianersi et al, in their study conducted in Isfahan showed that the major etiologies of posterior uveitis were infectious (88.4%), idiopathic (4.7%), and Behçet's disease (1.4%). Likewise, the most common etiology for posterior uveitis was toxoplasmosis (90.7%) (3). Infectious etiologies were also responsible for 50% of posterior uveitis in Mashhad (22). In another study by Soheilian et al, it was concluded that toxoplasmosis (54.5%), Eales disease, and toxocariasis were the most common causes of posterior

uveitis in Tehran (9). In a study designed by Rahimi and Mirmansouri in Shiraz, the most common causes of posterior uveitis were toxoplasmosis (42.1%) and Behçet's disease (15.7%) (4). According to European and the Middle East studies, toxoplasmosis Was also the most frequently reported cause of posterior uveitis in Amsterdam (23), Italy (24) and Saudi Arabia; for example, in a recent study in Saudi Arabia, toxoplasmosis (46%) was the most common cause of posterior uveitis (16). In the same vein, in another study in Saudi Arabia, toxoplasmosis (56.9%) and presumed tuberculous uveitis (23.1%) were also the most frequent posterior uveitis cases (8). The incidence of toxoplasmosis as the main cause of posterior uveitis showed a large variation in the ranges of 38.3% to 90.7% in different studies (3,7,8,16). In addition, *Toxoplasma* was the main cause of posterior uveitis in Tunisia and Egypt (7,14). Similarly, it was the main cause of infectious uveitis in Iraq (17). In a recent study in Turkey, *Toxoplasma* and herpetic uveitis were also found to be the most common infectious type of uveitis (25). In a study carried out by Ghavidel et al, *Toxoplasma gondii* was also the most common pathogen of infectious uveitis in children (26). In addition, in another study carried out on children in Iran, toxoplasmosis and toxocariasis were the most prevalent infectious uveitis (10). The JIA (juvenile idiopathic arthritis) and toxoplasmosis have been reported to be the main forms of uveitis in children in Turkey (27). However, tuberculosis was the major cause of infectious uveitis in children in north India (28). In the present study, 84.2% of the patients had non-granulomatous posterior uveitis. Generallynon-granulomatous uveitis occurs more than granulomatous in all types of uveitis (2,3). An associated systemic disease was found in 20.8% of the patients in this study. Behçet (8.3%), VKH (4.2%), and TB (3.3%) were the most frequent systemic diseases. In this study, the frequency of complications in each etiologic group was evaluated. Macular scar had the highest incidence (15%) followed by the macular edema (5.8%). Moreover, 18.3% of the active toxoplasma retinochoroiditis lesions were found to be located in macular areas. According to this finding, a large proportion of patients with posterior uveitis had macular toxoplasmosis and severe and permanent visual loss because of the resultant macular scar. It is well established that most cases of ocular toxoplasmosis are acquired (29). About 2% of infected people with *T. gondii* in the United States may have ocular involvement which is even more probable in other countries such as Brazil (29,30). Development of an effective vaccine for cats (as the definitive host that excrete millions of oocysts after ingesting bradyzoite or tissue cyst) and assessing its implementation is a research priority (31).

Limitations of the Study

The limitations of this study include retrospective nature and the small sample size. Future epidemiological researches should be conducted to cover a large number of patients in order to determine the risk factors for intraocular inflammation.

Conclusion

Toxoplasma gondii was also found to be the most common pathogen of posterior uveitis. In addition, the present study indicated that macular scar was the most common complication of posterior uveitis which was mostly related to the toxoplasma retinochoroiditis. Further studies are needed to evaluate the effects of genetic factors on the pathogenesis of posterior uveitis in the northwest of Iran.

Conflict of Interests

Authors have no conflict of interests.

Ethical Issues

This study was approved by research council of Tabriz University of Medical Sciences (with an ethical code of IR.TBZMED.REC.1397.085).

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