Frequency of Lung Disease in Patients Diagnosed with Uveitis

Hatice Kılıç1, Asiye Kanbay2, Ayşegül Şentürk1, H. Canan Hasanoğlu2, Ayşegül Karalezli1, Fatma Yülek3, Can Ateş4

ABSTRACT

Objective: To identify the etiologic and demographic features of uveitis cases admitted to the Ankara Ataturk Education and Research Hospital in Turkey and to determine the frequency of lung disease in these cases.

Materials and Methods: The records of 140 uveitis cases followed up in our hospital were retrospectively examined. The patients underwent systemic and complete ophthalmologic examinations. Laboratory and radiological examinations were performed for the etiology of uveitis. The age and sex of the patients, anatomic localization, and the etiology of uveitis were evaluated.

Results: The mean age±standard deviation of 140 patients included in the study was 39.6±14.9 years. The proportion of female/male was 61 (43.6%)/79 (56.4%). The cases were put into 4 groups according to their anatomical localizations: anterior uveitis (48.6%; n=68), posterior uveitis (28.6%; n=40), panuveitis (31.1%; n=31), and intermediate uveitis (0.7%; n=1). Idiopathic uveitis accounted for the majority of all cases (n=69, 49.3%). Behcet’s disease was the second most common diagnosis (n=41, 29.3%), followed by uveitis associated with sarcoidosis (n=8, 5.7%). Anterior uveitis was the most common anatomical localization (n=68, 48.6%) and posterior uveitis followed it (n=40, 28.6%).

Conclusion: The etiologic distribution of uveitis varies with the geographical location. The most frequently seen form of uveitis in our clinic is idiopathic. Among diseases leading to uveitis and primarily affecting the lung, Behcet’s disease comes first and it is followed by sarcoidosis.

Keywords: Demography, lung, uveitis

INTRODUCTION

The uvea, which is the middle part of the eyeball, is rich in veins and pigments. The inflammation of the uvea is called uveitis. The anatomic classification of uveitis, made by the International Uveitis Study Group (IUSG) in 1987, is the most common classification (1). It is classified into anterior, intermediate, posterior, and panuveitis according to its involvement in the eye.

In anterior uveitis, primary inflammation occurs in the iris and ciliary body and is known as iridocyclitis. In posterior uveitis, primary inflammation occurs in the posterior segment of the eye, in the choroid or retina. It is called as retinitis, choroiditis, retinal vasculitis, or neuroretinitis. Primary inflammation is seen in the vitreous humor in intermediate uveitis. On the other hand, in panuveitis, the inflammation is detected in all intraocular structures and does not originate from only one region. If uveitis lasts for less than 3 months, it is limited uveitis. If it lasts for more than 3 months, it is defined as persistent uveitis (2).

Based on these explanations, uveitis is anatomically classified as anterior uveitis (iritis, iridocyclitis, and anterior cyclitis), intermediate anterior uveitis (pars planitis and posterior cyclitis), posterior uveitis (focal, multifocal, diffuse choroiditis, chorioretinitis, and retinitis neuroretinitis) and panuveitis (anterior chamber, vitreous, retina, and choroid) (2).

Uveitis is a complex intraocular inflammatory disorder that can develop due to many diseases. The diseases mentioned for the etiology of uveitis can differ among countries depending on the different ecological factors and socioeconomical conditions (3). Although all evaluations are often conducted for the detecting the etiology of uveitis, if its etiology cannot be found, it is defined as idiopathic uveitis. In about 40% of cases, systemic diseases account for uveitis. No clear data on the frequency of lung diseases in the etiology of uveitis are available for our country. There are only a limited number of studies on this issue (4-8).

In this study, we aimed to determine the incidence of lung diseases in patients diagnosed with uveitis in the outpatient clinic.
MATERIALS and METHODS

In this study, 140 patients who applied to the Ophthalmology Outpatient Department in Ankara Atatürk Research and Training Hospital and were diagnosed with uveitis between the years of 2004 and 2008 were included. The data of all these cases recorded in the files and system were retrospectively evaluated. Ethical approval was obtained from the Ankara Atatürk Training and Research Hospital Ethics Committee.

The patients admitted to the outpatient clinic were examined with regard to infectious and non-infectious causes. Routine biochemical parameters, chest X-rays, tests for viral causes, collagen tissue markers, and serological tests were ordered for all cases and their results were recorded (1). The patients were consulted by the Department of Thoracic Diseases.

For the diagnosis of sarcoidosis, additional tests for serum ACE level, calcium levels in blood and urine, purified protein derivatives (PPD) and acid-resistant bacilli (ARB) in the sputum, and computed tomography (CT) of the chest were performed. Computed tomography was performed for the cases with the finding reminding sarcoidosis in chest radiography. On the other hand, bronchoscopy was performed for the patients having significant findings with the appearance of icy glass or reticulonodular infiltration in the CT. Samples were taken with bronchoalveolar lavage and transbronchial biopsy. The diagnosis of sarcoidosis was established for patients whose clinical, radiological, and laboratory findings were consistent with sarcoidosis and whose transbronchial biopsy result revealed non-caseating granuloma.

All patients underwent systemic steroid treatment according to their clinical weights. Moreover, etiology-oriented treatment was given in cases with known etiology.

Statistical analysis
The data obtained were analyzed using SPSS 16.0 software (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, United States). The cases were grouped based on their etiologies. The incidence rates of etiological causes were determined according to anatomic localizations. The value of p<0.05 was accepted to be significant.

RESULTS

The mean age of 140 cases included in the study was 39.6±14.9 years. Of all cases, 43.6% (n=61) were females and 56.4% (n=79) were males. Demographic distributions of participants were evaluated with regard to age and gender (Table 1).

The cases were put into 4 groups according to their anatomic localizations. The incidence rates of anterior uveitis (n=68), posterior uveitis (n=40), panuveitis (n=31), and intermediate uveitis (n=1) were 48.6%, 28.6%, 31.1%, and 0.7%, respectively. The most common detectable cause of anterior uveitis was found to be Behcet’s disease at the rate of 14.3% (n=20). It was followed by sarcoidosis (3.6%; n=5) and then by ankylosing spondylitis (1.4%; n=2). The most common causes of posterior uveitis were revealed to be Behcet’s disease, toxoplasma, and being hepatitis B carrier, in that order.

Patients were grouped according to etiological causes (Table 2). With regard to underlying etiological causes, Behcet’s disease (29.3%; n=41) was ranked in the first place, sarcoidosis (5.7%; n=8) in the second place, and toxoplasmosis (2.9%; n=4) in the third place.

Moreover, the incidences of etiological reasons were determined according to anatomic localizations (Table 2). The most common detectable cause of anterior uveitis, posterior uveitis, and panuveitis was found to be Behcet’s disease, followed by sarcoidosis.

DISCUSSION

In this study, the patients diagnosed with uveitis mostly had idiopathic reasons which were followed by Behcet’s disease and then toxoplasma. Among lung diseases causing uveitis, Behcet’s disease was the most common disease at the rate of 29.3% (n=41) and sarcoidosis was the second most common one at the rate of 5.7% (n=8).

The disease of uveitis differs according to geographical regions. In a study conducted in Saudi Arabia, the frequency of tuberculosis was reported to be higher than that in Western countries (9, 10). Although a study carried out in our country revealed that the frequency of tuberculosis as 2% (n=1), tuberculosis was observed only in one case (0.7%) in our study (5).

When uveitis cases were evaluated according to the etiological distribution, the distribution of patients in this study was observed to be similar to that in previous studies (11, 12). Although idiopathic acute anterior uveitis was found in 48% of patients in a study conducted in Saudi Arabia, this rate was found to be 22.9% (n=32) in our study (5, 9). Among all cases, the rate of idiopathic uveitis was observed to be 49.3% (n=69).

The manifestation of uveitis can occur with many different signs according to the anatomical region of uveitis, the pathological pattern of inflammation that develops in uveitis, and its etiology. In the etiology of uveitis, endogenous reasons, including both infectious and non-infectious ones, are common. Bacterial, viral, parasitic, fungal, and other infections can be observed in association with infectious factors. Uveitis developing due to endogenous immune system and infectious factors vary depending on different cultures (9, 13). The forms of uveitis developing secondary to endogenous immune system include Behcet’s disease, sarcoidosis, and Vogt-Koyanagi-Harada syndrome (VKH). The prevalence of these causes differs in different populations depending on genetic and environmental factors (14). Vogt-Koyanagi-Harada syndrome is a disease frequently observed among African, African-American, Middle Eastern, and Spanish people (15). As expected, the rate of VKH was found to be high in a study carried out in Saudi Arabia (16). Behcet’s disease is common among the far eastern and Mediterranean countries. The highest incidence rates for this disease are seen in Turkey and Japan (17). On the other hand, the incidences of ocular toxoplasmosis and tuberculosis are higher in Saudi Arabia than those in the western countries (9). In a study conducted in the United States of America, the prevalence of tuberculosis uveitis was reported to be 0.2% in a series of 445 cases (18). On the other hand, in a series of 368 cases in England, no case with tuberculosis uveitis was found (19). The frequency of toxocariasis and histoplasmosis is lower in western country than those in the eastern ones.
In another study, uveitis after vaccination was observed in three cases [2 cases after measles-mumps-rubella vaccine (MMR) and 1 case after hepatitis-B vaccine].

In the study of Chavis et al. (10) conducted with 282 cases, VKH, Behcet’s disease, idiopathic vasculitis, toxoplasmosis, and idiopathic causes were reported to be the most common causes of uveitis. The frequency of ocular tuberculosis was found to be higher than in the Western countries in this study, too. Although vision findings are quite well in Behcet’s disease, patients with tuberculosis have severe eye diseases. In almost all of tuberculosis cases, complications, such as posterior synechia, secondary cataract, and chorioternal damage, develop after the establishment of diagnosis (10).

In Saudi Arabia, the most common infectious reason was found to be herpetic uveitis (9). However, in our study, the first most common factor was revealed to be toxoplasmosis at the rate of 2.8% (n=4) and the second most common was hepatitis-B at the rate of 2.1% (n=3).

The mean age of patients was 39.6±14.9 years. In the review of Nashtaei et al. (20), the data from the Middle East (35.2, 37.4) and Europe (39.1) were found to be similar.

The ratio of female/male was 0.77 in our study. Similar results were obtained in the studies conducted in Turkey (6, 7). Although the results were also similar in the Middle East, the ratio was found to be 1.02 in Europe (20). In another study carried out in Turkey, a similar ratio was detected as 1.01 (8).

In our study, the rate of granulomatous uveitis was found as 8.5%. Of cases, 5.7% (n=8) had sarcoidosis, 1.4% (n=2) had systemic lupus erythematosus (SLE), 0.7% (n=1) had tuberculosis, and 0.7% (n=1) had granulomatous uveitis. In developed countries, the causes of granulomatous uveitis include VKH and sympathetic ophthalmia in addition to sarcoidosis. In developing countries, tuberculosis and leprosy are also reported (9). In our study, the rate of non-granulomatous uveitis was 91.5%. This
The most common type of uveitis is acute anterior uveitis (AAU), and it is related to the HLA-B27 gene at the rate of 40-82%. Among seronegative spondyloarthropathies, ankylosing spondylitis (AS) should be mainly considered. Although 18-34% of patients with AAU are diagnosed with AS, approximately 25-40% of patients with AS develop AAU. Posterior uveitis can develop in SPA cases. Among seronegative SPAs, uveitis associated with psoriatic arthritis and inflammatory bowel diseases (IBD). Seronegative SPAs, is mostly in tendency to develop as chronic, bilateral, and posteriorly located especially in women. Uveitis is seen in 5% of IBD cases and in 7% of cases with psoriatic arthritis. In 50% of these patients who developed uveitis, HLA B-27 was found to be positive (4). Chronic anterior uveitis is less common than AAU, and it presents with juvenile idiopathic arthritis (JIA) and sarcoidosis more frequently.

One of the most frequent causes of uveitis is Behcet’s disease (BD). This disease is common in countries on the route of historical Silk Road, including Japan, Korea, Iran, and Turkey. Uveitis in cases with BD is a major finding. In our country, BD constitutes 32% of uveitis cases observed in reference centers. With regard to the frequency rates, anterior uveitis was reported at the rate of 56-79%, intermediate uveitis at the rate of 18-66%, posterior uveitis at the rate of 3-29%, and panuveitis at the rate of 29-41%. Ocular involvement is generally observed at the rate of 66-73% in Behcet’s disease. When ocular involvement occurs in male patients and under the age of 30 years, it develops a severe clinical course. Isolated anterior uveitis in BD cases is seen in 10% of patients and is more common in women than in men. Isolated anterior uveitis is mostly associated with HLA-B27 rather than BD (22).

Behcet’s disease mostly affects the skin and can also be involved in other systems, such as the lungs, cardiovascular, neurological, and gastrointestinal systems. The most frequent lung-associated adverse events are pulmonary artery aneurysm and pulmonary embolism. In our cases having uveitis associated with Behcet’s disease, these events were detected. The diagnosis is made in accordance with the criteria described for Behcet’s disease by the International Study Group in 1990: basic diagnostic criterion is oral ulceration, which must be accompanied with 2 or more findings, including genital ulceration, ocular findings, skin lesions, and positive pathergy test. Inflammatory eye disease usually develops after oral ulceration. In our case, Behcet’s disease was found in 29.3% (n=41) of cases. Of these cases, 14.3% (n=20) were AAU, 10% (n=14) were posterior uveitis, and 5% (n=7) were panuveitis (22).

Table 2. The causes of uveitis according to anatomical localization

<table>
<thead>
<tr>
<th></th>
<th>Anterior (%)</th>
<th>Posterior (%)</th>
<th>Panuveitis (%)</th>
<th>Intermediate (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic</td>
<td>32 (22.9)</td>
<td>17 (12.1)</td>
<td>19 (13.6)</td>
<td>1 (0.7)</td>
<td>69 (49.3)</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>5 (3.6)</td>
<td>2 (1.4)</td>
<td>1 (0.7)</td>
<td></td>
<td>8 (5.7)</td>
</tr>
<tr>
<td>Behcet’s disease</td>
<td>20 (14.3)</td>
<td>14 (10.0)</td>
<td>7 (5.0)</td>
<td></td>
<td>41 (29.3)</td>
</tr>
<tr>
<td>Scleromalacia</td>
<td>0</td>
<td>0</td>
<td>1 (0.7)</td>
<td></td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>B₁₂ deficiency</td>
<td>0</td>
<td>0</td>
<td>1 (0.7)</td>
<td></td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>EBV</td>
<td>0</td>
<td>0</td>
<td>1 (0.7)</td>
<td></td>
<td>1 (0.7)</td>
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<tr>
<td>Herpes</td>
<td>0</td>
<td>0</td>
<td>1 (0.7)</td>
<td></td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Hepatitis B carriage</td>
<td>1 (0.7)</td>
<td>2 (1.4)</td>
<td>0</td>
<td></td>
<td>3 (2.1)</td>
</tr>
<tr>
<td>Toxoplasma</td>
<td>1 (0.7)</td>
<td>3 (2.1)</td>
<td>0</td>
<td></td>
<td>4 (2.9)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>0</td>
<td>1 (0.7)</td>
<td>0</td>
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<td>1 (0.7)</td>
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<tr>
<td>Breast cancer</td>
<td>0</td>
<td>1 (0.7)</td>
<td>0</td>
<td></td>
<td>1 (0.7)</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1 (0.7)</td>
<td>0</td>
<td>0</td>
<td></td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>2 (1.4)</td>
<td>0</td>
<td>0</td>
<td></td>
<td>2 (1.4)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>1 (0.7)</td>
<td>0</td>
<td>0</td>
<td></td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Granulomatous uveitis</td>
<td>1 (0.7)</td>
<td>0</td>
<td>0</td>
<td></td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Hydatid cysts</td>
<td>1 (0.7)</td>
<td>0</td>
<td>0</td>
<td></td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>CMV</td>
<td>1 (0.7)</td>
<td>0</td>
<td>0</td>
<td></td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>SLE</td>
<td>2 (1.4)</td>
<td>0</td>
<td>0</td>
<td></td>
<td>2 (1.4)</td>
</tr>
<tr>
<td>Total</td>
<td>68 (48.6)</td>
<td>40 (28.6)</td>
<td>31 (22.1)</td>
<td>1 (0.7)</td>
<td>140 (100)</td>
</tr>
</tbody>
</table>

SLE: Systemic Lupus Erythematosus; CMV: Cytomegalovirus; EBV: Epstein-Barr Virus
The frequency rate of ocular involvement in sarcoidosis is 25-50%. It can be an initial finding in about 5% of the cases or it can present during the course of the disease. Because ocular involvement generally develops as asymptomatic in cases, routine, detailed ophthalmologic examination should be performed in patients with sarcoidosis. AAU is the most common type of involvement in sarcoidosis. It generally develops bilaterally and is useful in the differential diagnosis of SPAs. Moreover, posterior uveitis, retinal vasculitis, and conjunctivitis can be observed. The presence of yellow perivascular exudates, which is rarely encountered, supports the diagnosis of sarcoidosis. In our study, sarcoidosis was detected at the rate of 5.7% (n=8). Of these cases, 5 (3.6%) were AAU, 2 were posterior uveitis, and 1 was panuveitis (23).

The most frequent lesions in systemic lupus erythematosus (SLE) are retinal vascular lesions. Retinopathy usually appears as cotton-wool spots with or without hemorrhages and can be seen in the absence of hypertension. It is generally observed in patients with a high level of antiphospholipid antibody. In our study, the frequency of SLE was 1.4% (n=2) (24, 25). The levels of antiphospholipid antibody were normal in these cases.

CONCLUSION

Uveitis is a disease that occurs with inflammation in various parts of the eyeball. Moreover, it is a symptom of a systemic disease in 50% of cases. In consultations performed by pulmonologists for uveitis, the geographical region of the inflammation should be taken into consideration, particularly for infectious causes. Underlying reasons should be investigated and the cases in Turkey should be evaluated with regard to BD, tuberculosis, and sarcoidosis in detail.

Ethics Committee Approval: Ethics committee approval was received for this study.

Informed Consent: Written informed consent was not obtained due to retrospective nature of the study.

Peer-review: Externally peer-reviewed.

Authors’ Contributions: Conceived and designed the experiments or case: HK, AK, AŞ, HCH, AK, FY. Performed the experiments or case: HK, AK, AŞ, HCH, AK, FY. Analyzed the data: HK, HCH, AK, FY, CA. Wrote the paper: HK. All authors have read and approved the final manuscript.

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