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Herpetic Uveitis: An Experience from a Tertiary Referral Center in Bulgaria

Gueorgui Markov^{1*}, Rozalia Hristova¹, Nikolina Andonova¹, Iva Petkova¹, Yani Zdravkov¹, Alexander Oscar¹

¹Clinic of Ophthalmology, University Hospital Alexandrovska, Medical University-Sofia, Bulgaria

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*Corresponding author:

Gueorgui Markov

E-mail address:

dr.georgimarkov@gmail.com

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ABSTRACT

Introduction: The human Herpesviridae have been described as a leading cause of infectious uveitis. The most common manifestations are keratouveitis and iridocyclitis. The diagnosis is usually made on clinical grounds. The present therapy is based upon the inhibition of viral replication and the use of anti-inflammatory medications. **Methods:** A descriptive study was conducted on the records of 206 patients with uveitis from the Clinic of Ophthalmology at University Hospital Alexandrovska, Sofia, Bulgaria. The study period was from January 2012 until August 2019. The diagnosis was based on the clinical exam and, when necessary, on specialized testing – PCR on aqueous humor or vitreous material. We used descriptive statistical methods. **Results:** Out of 206 patients with intraocular inflammation, 46 (22.3%) were diagnosed with herpetic uveitis. Of them, 35 (76.1%) had anterior uveitis, 7 patients (15.2%) had panuveitis, and 4 patients (8.7%) had posterior uveitis. The mean age was 45.3 years. The leading complications were ocular hypertension, corneal leucoma, retinal detachment, and cataract. Antiviral therapy with acyclovir or valaciclovir, alone or with corticosteroids, was used in all groups. **Conclusion:** The herpesviruses are important causative agents of infectious uveitis. In our study, non-granulomatous, hypertensive anterior uveitis was the most common clinical entity. There were also a few patients with posterior and panuveitis. VZV was the most common etiologic agent. The panuveitis cohort had the worse prognosis for visual acuity, mostly as a result of retinal detachment. The posterior uveitis presented most frequently as focal retinochoroiditis with a good prognosis.

1. Introduction

The human Herpesviridae have been described as a leading cause of infectious uveitis.¹⁻³ The most common manifestations are keratouveitis and iridocyclitis.² The most frequent etiologic agents from the group have been Herpes simplex type 1 (HSV-1), Varicella zoster virus (VZV), and cytomegalovirus (CMV).⁴ The diagnosis is usually made on clinical grounds and can be further corroborated by specialized testing on aqueous humor or vitreous material, using polymerase chain reaction (PCR) or determination of local antibody production by the Goldmann-Witmer coefficient.⁴ Prompt diagnosis and

accurate management of the infection are crucial as it may lead to blinding complications – decreased corneal transparency, glaucoma, retinal detachment, chorioretinal atrophy, occlusive vasculitis, and optic neuropathy. The present therapy is based upon the inhibition of viral replication and the use of anti-inflammatory medications.^{5,6} The purpose of the present study is to describe the epidemiologic, clinical, and therapeutic characteristics of our patients with herpetic uveitis.

2. Methods

This research was a descriptive study on the records of 206 patients with uveitis from the Clinic of Ophthalmology at University Hospital Alexandrovska, Sofia, Bulgaria. The study period was from January 2012 until August 2019. The follow-up period was from 3 months to 7 years. The diagnosis was based on the clinical exam and, when necessary, on specialized testing- PCR on aqueous humor or vitreous material. All patients had signed informed consent. An ethical board review was not required for the present study.

3. Results

Out of 206 patients with intraocular inflammation, 46 patients (22.3%) were diagnosed with herpetic uveitis. Of them, 35 (76.1%) had anterior uveitis, 7 patients (15.2%) had pan-uveitis, and 4 patients (8.7%)-posterior uveitis. Of the patients with anterior uveitis (Figure 1), 20 were female (57%), and 15 – were male (43%). The mean age was 55 years (range from 18 to 83). The inflammation was unilateral in all cases (100%). The uveitis had an acute course in 19 (54.3%), a chronic course in 11 (31%), and a recurrent course

in 5 (14.3%) of the patients. Etiologically, VZV was accountable for 10 of the cases (28.6%), HSV-1 in 7 (20%), and CMV in 3 (8.6%). In 15 cases (43%), the cause could be either VZV or HSV. There was associated dermatitis in 10 patients (28.6%). Keratouveitis was observed in 12 cases (34.3%), and sclerouveitis in 1 patient (2.9%). The iridocyclitis was non-granulomatous in 27 patients (77.2%) and granulomatous in 8 patients (22.8%). The final best-corrected visual acuity (BCVA) varied from 0.02 to 20/20, most commonly 20/20 in 26 cases (74.3%).

There were various complications in this study; ocular hypertension in 15 patients (43%); corneal leucoma in 7 patients (20%); ptosis of the upper eyelid in 4 patients (11.4%); cataract in 4 patients (11.4%), iris atrophy in 3 patients (8.6%), paralytic mydriasis in 2 patients (5.7%); postherpetic neuralgia in 2 patients (5.7%); posterior synechiae in 1 patient (2.9%), macular oedema in 1 case (2.9%), and branch arterial occlusion in 1 case (2.9%) with CMV. The therapy included acyclovir in initial doses up to 4000 mg daily, valaciclovir – up to 3000 mg daily, ganciclovir gel – up to 5 times daily, and corticosteroids by various routes of administration – topical, periocular, and systemic.

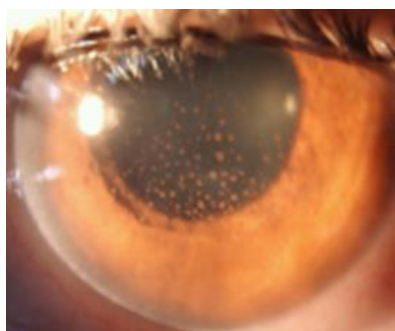


Figure 1. A slit-lamp photograph of a patient with granulomatous herpetic iridocyclitis.

Out of the patients with posterior uveitis (Figure 2), 2 were female (50%), and 2 patients were male (50%). The mean age was 40 years. The uveitis was unilateral in all cases, and the clinical course was always acute. The final BCVA ranged from LP to 20/20 in 1 patient

(25%) with LP due to retinal detachment in a patient with CMV, 2 patients (50%) with 20/30 due to chorioretinal scarring, and one with 20/20. The clinical picture was focal retinochoroiditis in 3 patients (75%) and of multifocal retinochoroiditis in 1 (25%).

The complications that we observed were chorioretinal atrophy in 2 patients (50%) and retinal detachment in 1 patient (25%). The identifiable risk factors were contact with a patient with systemic varicella in one case and concomitant labial herpes in another. The

therapy was conducted with acyclovir up to 4000 mg daily, alone or with systemic prednisolone, valaciclovir up to 3000 mg daily with prednisolone in 1 patient, and with indomethacin in another.



Figure 2. Fundus photograph of a patient with focal VZV retinochoroiditis.

In the panuveitis cohort (Figure 3), there was 3 female (43%) and 4 male patients (57%). The mean age was 41 years. The risk factors were untreated HIV in 1 patient and diabetes mellitus in another. Etiologically VZV was found in 5 of the cases (71.4%), HSV in 1 patient (14%), and CMV in 1 patient (14%). The uveitis was unilateral in 4 (57%) and bilateral in 3 cases (43%). There were 2 patients (28.6%) with dermatitis; in 1 patient, the distribution of the ophthalmic nerve, and in another was thoracic zoster. Both patients with dermatitis and panuveitis were immunocompromised. The process was non-granulomatous in 6 cases (86%) and granulomatous in 1 patient (14%). There was

associated keratouveitis in 2 patients (28.6%). The retinitis was necrotizing in 5 patients (71.4%) and non-necrotizing in 2 cases (28.6%). The BCVA ranged from NLP to 20/100. The observed complications included: retinal detachment in 5 (71%) patients, ocular hypertension – in 4 (57%), preretinal membranes – in 3 (43%), cataracts – in 3 (43%), diffuse chorioretinal atrophy – in 1 (14%). The treatment was commenced with acyclovir up to 4000 mg or valaciclovir up to 3000 mg, alone or with systemic prednisolone, and with pars plana vitrectomy with silicone tamponade and endolaser in 4 cases with retinal detachment.



Figure 3. Fundus photograph of a patient with necrotizing VZV panuveitis.

4. Discussion

Out of all patients with uveitis, we had herpetic etiology in 44 (22.3%). The mean age varied greatly in the anterior uveitis group, but it was much lower in the posterior and panuveitis cohorts. Etiologically, VZV was the most frequent infectious agent in all groups, which has been shown in other studies as well.²

The cases with anterior uveitis had a predominantly acute clinical course and unilateral involvement, which corresponds with the findings of other researchers.^{2,4} The uveitis was most frequently non-granulomatous and complicated with ocular hypertension. Elevated intraocular pressure has been the most frequent complication reported in the literature.⁷ Keratitis was not an uncommon feature. There were also 7 patients (20%) with residual corneal leucomas. Nevertheless, the prognosis for recovery and normal visual acuity was excellent.

The posterior uveitides were also acute and unilateral. The clinical picture was most commonly that of focal retinochoroiditis. The lesions were in the macular area or along the major vascular arcades, which is what has been described in other studies.⁸ The prognosis was relatively good, and most patients responded to treatment with antivirals and anti-inflammatory medications. Only one patient ended up with a BCVA at the level of PPLC due to a retinal detachment.

The outcomes were worse in the panuveitis group, especially in the necrotizing variety (acute retinal necrosis), where BCVA at the end of the follow-up period was at most 20/100, which corresponds to other published reports.^{9,10} The percentage of bilateral involvement was high. Retinal detachment, along with ocular hypertension, were the most frequent complications.^{9,10}

In all cohorts, the conservative treatment was carried out with antiviral medications – acyclovir or valaciclovir, alone or in combination with corticosteroids, as it has been recommended.^{5,6} In one case, we also used systemic indomethacin. Surgical

treatment was necessary for 4 patients with panuveitis and retinal detachment.

5. Conclusion

The herpesviruses are important causative agents of infectious uveitis. In our study, non-granulomatous, hypertensive anterior uveitis was the most common clinical entity. There were also a few patients with posterior and panuveitis. VZV was the most common etiologic agent. The panuveitis cohort had the worse prognosis for visual acuity, mostly as a result of retinal detachment. The posterior uveitis presented most frequently as focal retinochoroiditis with a good prognosis. Antiviral therapy with acyclovir or valaciclovir, alone or with corticosteroids, was used in all groups.

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