Clinical Features and Diagnosis of Anterior Segment Inflammation Related to Cytomegalovirus in Immunocompetent African, Asian, and Caucasian Patients

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Short title: Clinical features and diagnosis of anterior uveitis related to Cytomegalovirus in immunocompetent patients

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Abstract

Objective:

To report the clinical features and treatment outcomes in immunocompetent patients with anterior segment inflammation (ASI) related to human cytomegalovirus (HCMV) depending on their ethnic origin.

Material and Methods:

Multicenter retrospective study of 38 patients with at least one test, either HCMV-positive PCR or GWc.

Results:

Features of Posner-Schlossman syndrome were observed in 50% of the eyes, Fuchs heterochromic iridocyclitis in 13% of the eyes, chronic nonspecific anterior uveitis in 21% of the eyes, and corneal endotheliitis in 18% of the eyes. PCR and GWc were positive for HCMV in 50% and 96.2% of the eyes, respectively. Glaucoma was diagnosed in 50% of eyes. Treatment was oral valganciclovir in about half of the patients. Other treatments were intravenous ganciclovir and/or ganciclovir topical ointment and/or intravitreal ganciclovir.

Conclusions:

No obvious association of specific clinical features with individual ethnicity could be identified. We found a high rate of glaucoma in all ethnic groups. There was a delay in diagnosis and specific treatment of HCMV in most patients.

Introduction

Human cytomegalovirus (HCMV) infections of the anterior segment can present as corneal endotheliitis or hypertensive anterior uveitis or both.[1] The pathophysiology of HCMV anterior segment infection involves a latent HCMV infection in myeloid progenitor cells with intermittent viral reactivation from activated macrophages or dendritic cells. It produces a CD4+ and CD8+ T-cell immune response.[2] Inflammation of the trabecular meshwork cells could be the main mechanism underlying intraocular pressure (IOP) elevation.[3] In HCMV infections, an enormous variety of different virus strains exist, with a wide variety of possible genotypic combinations throughout the whole virus genome.[4,5] Moreover, different authors have described the detection of mixed-genotype infections with different HCMV strains in transplant recipients.[5] It is technically possible to describe the geographic and phylogenetic origin of the strains involved and now to sequence the entire genome of these viruses and, based on genomic comparison, draw virological conclusions.[6]

HCMV-associated uveitis most often presents with raised IOP, such as Posner-Schlossman syndrome (PSS), Fuchs heterochromic iridocyclitis (FHI), or uveitic glaucoma. The presence of coin-shaped keratic precipitates (KPs) in corneal endotheliitis strongly suggests an HCMV origin with a reported positive predictive value ranging from 70% to 91%.[1,7] Typically, coin-shaped KPs have been described as medium-sized KPs arranged in a circumferential pattern with localized corneal edema.[7] The clinical features were previously described as being quite different depending on the geographical origin of patients with HCMV anterior uveitis. A trend for more FHI-like presentations with diffuse stellate KPs has been reported in Asian patients. Comparatively, European patients commonly present with chronic hypertensive anterior uveitis with fewer KPs that are brown in color and have an inferior location.[8,9]

We present herein the clinical characteristics, evaluation of viral diagnostic methods, and outcomes of patients from different ethnic groups (Africans, Asians, and Caucasians) who attended specialized uveitis centers in Paris, France, and were diagnosed with HCMV anterior uveitis.

Materials and methods

Patients and Methods

This was a retrospective cohort study of patients examined at four uveitis clinics (Quinze-Vingts National Eye Hospital (CHNO), Pitié-Salpêtrière (PS) Hospital, Kremlin-Bicêtre (KB) Hospital, and Rothschild Ophthalmological Foundation) from January 2000 to December 2015. This study was conducted in accordance with the tenets of the Declaration of Helsinki. We identified patients with a new diagnosis of HCMV-related anterior segment inflammation.

The diagnosis of CMV uveitis was established based on the presence of suggestive clinical features identified through a review of the recent literature. The diagnostic criteria for CMV anterior uveitis used in this study were as follows (patients had to satisfy criteria 3 and at least one criteria 1 and one criteria 4):

1. Clinical signs suggestive of CMV uveitis, including the following:

a. anterior uveitis: sectorial iris atrophy[10,11] or high IOP without iris abnormalities[11]; eyes with concurrent CMV posterior segment inflammation (vasculitis, retinitis, optic neuritis) were excluded.
b. keratouveitis with corneal endotheliitis and coin-shaped KPs;
c. brown active-appearing KPs[12];
d. PSS[10,11,13];
e. FHI[14];

2. Unilateral chronic anterior uveitis or recurrent hypertensive anterior uveitis[15];
3. Exclusion of other uveitic entities, where relevant, based on clinical manifestations of disease and ocular sample results when performed: *herpes simplex virus* type 1, HSV1), type 2 (HSV2), and varicella-zoster virus (VZV);
4. Investigations that document the CMV:

a. Demonstration of CMV by GWc from ocular fluid (aqueous humor [AH]);
b. Positive polymerase chain reaction from ocular fluid for CMV.

We reviewed patient files to collect the following data: demographic information, clinical

features, diagnosis, treatment, and outcomes. Only cases of immunocompetent patients were included.

Ophthalmologic examination included clinical features of the disease activity, IOP measurement, and best-corrected visual acuity (BCVA) at initial presentation and the last follow-up. We converted BCVA to a visual acuity (VA) score based on the logarithm of the minimum angle of resolution (LogMAR).

There was no difference in the access to healthcare among patients of the different ethnicities, or the demographic distribution of patients who were seen at each hospital. Furthermore, there was no difference in the access to medication or to diagnostic testing. The 4 specialized uveitis centers in Paris are public hospitals and part of the French universal healthcare system.

Sample collection and analysis

All patients had laboratory evaluation regardless of the type of uveitis (complete blood count, erythrocyte sedimentation rate, C-reactive protein, tuberculin skin test, syphilis serology, and chest x-ray or chest CT scan) followed by more complex investigations based on the ophthalmologic findings**.** An AH tap for virus detection was performed in cases with chronic uveitis or severe uveitis resistant to treatment. AH was tested for rubella in two patients. Four patients had serology testing for HIV and results of HIV testing were negative. No other specific clinical investigations were done to assess immunocompetency. No past history of immunodeficiency was reported for the patients included.

AH samples (0.02–0.1 mL) were obtained under sterile conditions under topical anesthesia (tetracaine 0.5% eye drops) and sent to a laboratory for analyses. Samples were divided under a sterile laminar flow cabinet and aliquots were stored in coded sterile DNA-free microfuge tubes at −80°C for qPCR.

The following tests were performed on AH in order to detect viral pathogens (HSV, VZV, HCMV):

1. Enzyme-linked immunosorbent assay (ELISA) for virus-specific antibody (spIgG) detection in AH and serum (SER) in order to assess the Goldmann-Witmer coefficient (GWc).

This coefficient is calculated as the ratio of antibody levels: AH-spIgG/AH-total IgG versus SER-spIgG/SER-Total IgG. We consider a ratio >4 as confirmation of local antibody production against the viral agent. A ratio between 2 and 4 is interpreted with regard to the clinical features.

2. Polymerase chain reaction (PCR) for detection of viral genome in AH was performed at the CHNO using the nucleic acid extraction of the patient's sample and analyzed using the R-gene® kit and NucliSENS® easyMag® (bioMérieux®, Marcy l'Etoile, France) following the manufacturer's instructions. This technology is based on magnetic silica particles that capture nucleic acids. The total nucleic acid was extracted from 25–100 µL of AH and recovered in 100 µL of elution buffer. DNA amplification was performed in 96-well plates using Applied Biosystems 7500 Fast Real-Time PCR System or Applied Biosystems ViiA 7 Real-Time PCR System ViiA7 (ThermoFisher, Villebon-sur-Yvette, France), depending on the laboratory. Briefly, for each patient's sample, 10 µL of the total nucleic acid extract was amplified in a dedicated well of the 96-well plate, each well containing 15 µL of reaction mixture. For each sample, the quality and efficiency of both steps, extraction and amplification, were checked using an internal quality control supplied in the R-gene® kit mixed with the sample. The PCR results were expressed qualitatively.

qPCR was performed in all three centers. The GWc test was performed at the CHNO and KB hospital laboratories if a sufficient volume of AH was collected.

qPCR in the PS Hospital's laboratory was performed as described elsewhere[16] and expressed qualitatively for samples collected before 2006 and quantitatively for samples collected after 2006. The GWc test was performed when the PCR result was negative but there was a strong clinical suspicion of HCMV (such as PSS).[16]

The sensitivity of the two real time PCR assays methods, was 10 copies/ sample.[16]

Classification for uveitis

The anatomical classification of uveitis and the grading scheme for the anterior chamber cells was based on the international recommendations from the International Uveitis Study Group criteria.[17] All patients had a complete workup to exclude any other cause of anterior uveitis.[18]

If a patient had more than one PCR and/or GWc test done, a positive result would count if any one test was positive.

Disease relapse was defined as a recurrent episode of uveitis separated by ≥3 months of inactivity without treatment. The number of uveitis relapses and the duration of uveitis were recorded. Improved activity of uveitis was defined as a two-step decrease in the SUN (Standardization of Uveitis Nomenclature) grade or improvement to grade 0.[17]

Statistical analysis

The Fisher tests and chi-squares were performed using GraphPad Prism version 8.0.0 for Windows (GraphPad Software, San Diego, CA, USA; www.graphpad.com).

Results

The results are presented in Table 1.

Demographics:

Thirty eight eyes of 38 patients (unilateral presentation in 100% of the cases) were included. The male to female (M/F) ratio was 21/17. With regard to their ethnic origin, 15 patients were Europeans, 8 were Sub-Saharan Africans, 4 were North Africans, 10 were Southeast Asians and one was Indian. Four patients had serology testing for HIV and results of HIV testing were negative. No past history of immunodeficiency was reported for the patients included, except one patient who was diagnosed with a moderate CD8 deficiency (272/mm^3; n>600). One patient was using topical cyclosporine 1% eye drops for prevention of corneal graft rejection.

The mean age at presentation of the first symptoms was 43 years (range, 11–85 years). The mean duration between initial presentation and diagnosis of HCMV infection was 67.5 months (range, 1–182 months). The mean follow-up period from the time of diagnosis until the last visit was 28 months (range, 6–120 months).

Clinical features:

Nineteen out of 38 eyes (50%) were categorized as PSS (32% in African patients, 26% in Asian patients, and 42% in Caucasian patients), five (13%) as FHI (40% in African, 20% in Asian, and 40 in Caucasian patients). Seven (18%) had chronic unspecified anterior uveitis (14% in African, 58% in Asian, and 28% in Caucasian patients**)**, and seven (18%) were diagnosed with corneal endotheliitis (43% in African, 14% in Asian, and 43% in Caucasian patients).

Anterior chamber activity: Anterior chamber inflammation was labeled as 0.5 to 1+ in 30 out of 38 eyes (79%) and 2–3+ in two eyes (5%). There was no inflammation in six eyes (16%). None of the eyes had posterior synechiae. KPs were present in 37 out of 38 eyes (97%). The KPs presented as follows: white or grey in 25 eyes (65.8%), brown in 11 eyes (29%); granulomatous in 28 eyes (including six eyes with a typical coin-shaped feature) (76%); and nongranulomatous in 10 eyes (including five eyes with stellate KPs in FHI) (21%). Most KPs were granulomatous and white/grey (65.8% in total: 50% in African, 65% in Asian, and 86% in Caucasian patients). Other characteristic features were: iris atrophy (5/38 eyes, 13%), heterochromia (4/38 eyes, 11%), Busacca iris nodules (1/38 eyes, 3%), coin-shaped KPs (6/38 eyes, 16%), and cornea edema (17/38 eyes, 45%).

In unspecified anterior uveitis (*n*=7 eyes), we observed diffuse brown KPs in two eyes, and white/grey granulomatous KPs in four eyes including one with a typical coin-shaped feature. One eye had no KPs. In corneal endotheliitis, KPs presented as white or brown granulomatous (two eyes) including one with a typical coin-shaped feature, fine and brown in the lower cornea (two eyes), and white, fine, and diffuse (two eyes). One eye had no KPs.

Visual acuity: The mean best-corrected visual acuity (BCVA) was 0.62 ± 0.79 LogMAR at initial presentation and 0.64 ±0.95 LogMAR at the final visit (*p*-value = 0.8).

Complications

High IOP was noted in 87% of the patients at initial presentation (*n*=33/38). Mean IOP during the first acute episode was 32.5 ± 14.6 mmHg compared with the mean IOP of 17.3 ± 7.9 mmHg at the final visit. Besides the acute episodes, we found a chronically increased IOP between

inflammatory episodes in 47% (*n*=18/38) of the eyes that required antiglaucoma treatment. Gonioscopy revealed an open angle in all patients except in one with peripheral anterior synechiae. At the final visit, the mean difference in the cup/disk ratio between the two eyes was 0.53 ± 0.27 versus 0.40 ± 0.20 for inflamed eyes and fellow eyes, respectively (Δ= 0.13, 95% CI: 0.05–0.2; *p*=.001, paired *t*-test).

Nineteen eyes (50%) were diagnosed with glaucoma. Glaucoma resulting from ASI was found in all ethnic groups (*p*=.097) and was not related to any presenting ocular features (*p*=.007, chi-square tests). There was no difference in the time to diagnosis of CMV from presentation of uveitis between patients with or without glaucoma (73 months, range, 1–180 months vs 55 months, range, 0–182) (*p*=.520).

Nine eyes (24%) underwent filtering surgery (four trabeculectomies, two Ahmed valve implantations, and three nonpenetrating deep sclerectomies). The mean time between initial presentation and filtering surgery was 102 ± 65 months (range, 23–288 months).

We analyzed the use of anti-HCMV treatments (topical, IV and intravitreal ganciclovir, or oral valganciclovir) and the rate of efficacy to reduce an acute or chronic elevation in IOP. No significant reduction of IOP was noted in the 19 patients with HCMV-induced glaucoma (*p*= .133, chi-square statistic). Five patients out of the nine who had glaucoma surgery were on anti-HCMV treatment when the surgery was scheduled.

Filtration surgeries were performed because of persistent elevated IOP ≥40 mmHg despite maximal topical and oral antiglaucoma treatment.

Overall, one patient developed corneal decompensation and one patient presented with CMV endotheliitis in the context of failed penetrating keratoplasty.

Fifteen (53%) out of the 28 phakic eyes presented with or developed a cataract during the follow-up. Twelve eyes (40%) underwent cataract surgery with implantation of an intraocular lens.

Laboratory tests: Some patients had multiple PCR and/ or GWc when relapse or mild improvement. The number of diagnostic testings (PCR & GWc) is presented in Table 2.

The probability of the first and second PCR being positive for CMV was 53% (18/34) and 42.8%

(3/7), respectively. The corresponding numbers for the GWc were 96.2% (25/26) and 100% (3/3), respectively. Figure 1 shows the agreement between PCR and GWc positive results.

We analyzed the differences between three groups (PCR positive vs PCR negative, GWC positive vs GWC negative, or both PCR and GWC positive) in terms of patient characteristics (age, duration of symptoms before anti-HCMV treatment). No discernible differences between the groups were observed for mean age (p=.0281 for PCR positive vs PCR negative, p=.0.497 for GWC positive vs GWC negative and p=.461 for both PCR and GWC positive, t-test,).
We noted no difference in disease duration between patients with positive and negative PCR results in AH samples (58 months, range, 0–182 months vs 71 months, range, 0–192 months (p=.689, non parametric Mann Whitney test).
We did not compare positive PCR and GWC rates among European, Asian, and African patients since the patients were retrospectively included in one of the centers based on positive PCR results.
Among the 6 patients with quiet AC and KPs, PCR was positive 3 out of 6 patients and GWC was positive for the 4 of them who had this test done.

Treatment:

Oral valganciclovir (900 mg twice daily for 3 weeks followed by valganciclovir 450 mg twice daily for 1 to several months) was the main treatment modality used in this study. This regimen was used in 22 patients (58%). One patient received a maintenance dose of valganciclovir once daily. The other treatments used were intravenous ganciclovir (n=7 patients, 18%) and/or ganciclovir topical ointment (n=7 patients, 18%) and/or intravitreal ganciclovir (n=2 patients, 5%). Fourteen patients (37%) received no specific antiviral treatment. When PCR was positive for HCMV, 94% (17/18 patients) of the patients received specific antiviral drugs. Only 38% of patients (10/26) received treatment when GWc was positive.

Nineteen patients had received previous antiviral treatment that was ineffective in controlling the inflammatory episodes (oral famciclovir: two patients; oral valacyclovir: 18 patients; intravenous (IV) acyclovir: three patients, and oral acyclovir: two patients). The mean duration of antiviral treatment (oral ganciclovir, topical, intraocular, or intravenous ganciclovir) was 17 (0.5–72) months. The mean duration of treatment was 18 months (range, 0.5–36 months) with oral

valganciclovir and 22 months ± (1–26 months) with ganciclovir topical ointment.

The mean number of uveitis relapses was 4.5 (range, 1–10; SD ± 2.61) before oral valganciclovir. The mean number of uveitis relapses was 1.08 (range, 0–7; SD ± 1.05) during oral valganciclovir treatment (p=.0036). Three patients presented with relapses ≤ 1 month after discontinuation of oral valganciclovir.

There was no association between the efficacy of anti-HCMV treatment in reducing the number of uveitis relapses and the type of uveitis (p=.450). There was no association between the efficacy of anti-HCMV treatment and the number of previous episodes (≤3 or >3) (p=.035) or the disease duration (≤12 months or >12 months) prior to anti-HCMV treatment (p=.071) (chi-square). We did data exploration to identify possible determinate factors on number of previous episodes. Univariate analysis did not identify any significant factor. There was no association between the number of ASI relapses (≤3 versus >3) versus 1/ the mean age of patients (p=.314, t-test), 2/ ethnicity (either African, Asian or Caucasian) (p=.492137, chi-square statistic), 3/ presence or absence of glaucoma (p=.736, chi-square statistic), and 4/ anti-HCMV treatment (p=.253, chi-square statistics).

Of note patients were also treated with prednisolone eye drops.

Discussion

In this study, acute HCMV anterior uveitis presented as PSS in most cases. The PSS form was previously reported in about 60–80% of HCMV-related anterior uveitis cases, mostly in European patients.[5,14] We also observed the PSS form as being frequent in Asian patients (45%) as well as in African (50%) and Caucasian patients (53%). This contrasts with other studies in Asian populations from Singapore reported by Chee et al. in which patients presented with typical characteristics of FHI.[14] However, the series from Hong Kong by Kam et al. studied eyes with HCMV endotheliitis that were labeled as anterior uveitis (70%) and PSS (40%) prior to HCMV confirmation.[19] In the present study, FHI was found in 17% African, 9% Asian, and 13% Caucasian patients.

In accordance with the typical description of HCMV anterior uveitis, the KPs reported in the

present study were white or grey in 66% of the cases regardless of the patients' ethnic background. Brown KPs were noted in 29% of patients from all ethnic groups, instead of being the hallmark of European patients as previously reported.[7]

Overall, 87% of our patients suffered from hypertensive uveitis at initial presentation with a mean IOP of 32 mmHg. Besides the acute episodes, we found a persistently increased IOP between inflammatory episodes in about half the eyes. Likewise, in their series of HCMV endotheliitis from Hong Kong, Kam et al. observed that during the initial years, a significant proportion of these patients present with brief episodes of hypertensive anterior uveitis, which show rapid response to treatment with topical corticosteroids.[19] In later years, the condition becomes chronic despite prolonged use of topical corticosteroids. In the present study, glaucoma was found in 40–67% of cases regardless of the patients' ethnicity. Hypertensive uveitis as well as corneal endotheliitis seem to be the hallmark of HCMV uveitis in other reports.[20-22] However, it was noted in only 18% of patients from all ethnic groups in our study (25% African, 9% Asian, and 20% Caucasian patients). In contrast, HCMV endotheliitis is relatively less frequent in Europe[8,22-24] compared to the series reported from Asia.[6,19,20,25]

The main limitations of this study are that even if the overall number is high, given the rarity of the disease, the number of subjects per group is small and the statistical power therefore remains weak for showing minor differences. The same type of argument could also explain certain similarities with the data from other countries because they generally include a restricted number of patients. Moreover, confocal microscopy was not performed in our series of patients for the 'owl's eye morphology' (i.e., "large corneal endothelial cells with an area of high reflection in the nucleus surrounded by a halo of low reflection") which is a characteristic sign seen in Cytomegalovirus infections.[26]

In earlier studies, different authors also investigated whether there was a correlation between a particular HCMV genotype and the clinical expression or virulence of all HCMV-related diseases in immunosuppressed patients. HCMV has a large collection of genes dedicated to subjugating host immune systems, such as the UL40 Signal peptide.[27,28] Some of these variable genes encode envelope glycoproteins, such as the glycoproteins gB, gH, gN, and gO. Other highly variable genes used for genotyping are located in the UL/b' region and *RL11* genes. It is presumed that

viruses with different *gB* genotypes have different cell tropisms. In this context, contradictory results have been reported in studies that demonstrated that the *gB* genotype 2 was found more frequently in the eye during HCMV retinitis in AIDS patients,[31] although this was not confirmed by others.[5,30,31] It was hypothesized that the genotype influences the severity of HCMV-related disease and the extent of sequelae. Some studies investigated the impact of different *UL144* and *gN* genotypes among strains on fetal damage after congenital infection, and discrepant results were obtained, indicating that perhaps variants of these genes could be related to the outcome of fetal infection.[5,32,33] To our knowledge, no studies on HCMV genotypes in anterior uveitis have been conducted in immunocompetent patients. Another possible source of bias in establishing correlations between HCMV genotypes and clinical data may be the relationship between distinct HCMV genotypes and the host's HLA status, which, because of the differential presentation of polymorphic peptides specific to a particular HCMV genotype, could have an effect on the immunological response of the individual host.[28-34]

Another limitation of this study is that we could not determine the number of years some of our patients had been living in France. The Asian and African patients in this series are a priori French – possibly for several generations. They retain all or some of the initial genetic code and were infected with viral strains in France. However, various studies have shown that no significant associations of individual virus genotypes with specific geographic areas can be identified, although the local incidence of individual genotypes may differ.[5,34] Most genotypes determined so far are probably distributed worldwide.[5,32,34-41]

In this study, a long period of time was observed (67 months) between symptom onset and diagnosis of HCMV infection. In France, when the condition becomes chronic after each episode, HCMV anterior uveitis is diagnosed by aqueous tap analysis, mainly using GWc testing. We believe that this is because the majority of the patients had either delayed presentation and/or diagnosis and the tests were done at later stages of each episode. PCR is usually positive in the early stages of the disease, whereas GWc remains positive at later stages of the disease due to sustained IgG production.

To our knowledge there is limited information currently available about the immunoglobulin locally produced in CMV uveitis and how long CMV GWC will stay positive after one episode of anterior uveitis. It has been shown for herpes virus encephalitis that antibodies to herpes virus persist in CSF and the serum/ CSF antibodies ratio remained altered during the follow-up of 29 to 36 months.[42,43] If kinetics of CMV antibodies are similar in the aqueous and the CSF, GWC could not be used as indication for the termination of anti-viral treatment. It can be used for initiation of anti-viral treatment, though. Aqueous humor albumin would be a sensitive indicator of the function of the blood retinal barrier to unsure that kinetics of aqueous CMV and simultaneous measurement of albumin levels would be interesting in assessing ocular activity on treatment.

Other studies showed that combining PCR and GWc was helpful to confirm the diagnosis.[24,44]

We suggest that an aqueous tap should be performed when the clinical features such as increased IOP with coin-shaped KPs and localized corneal edema are suggestive of HCMV infection.

Currently, there are no guidelines for treatment of uveitis related to HCMV in immunocompetent patients.[45] A previous study showed that ganciclovir topical ointment is effective in preventing relapses,[21,46] whereas oral valganciclovir seems more useful to treat acute episodes.[47,48] We showed here that oral valganciclovir is effective as treatment of acute manifestations and in reducing the number of relapses. However, the use of anti-HCMV treatments did not reduce acute or chronic IOP elevation.

Contrary to the recent study by Kam et al., oral valganciclovir was preferred as the initial treatment in the present study (over ganciclovir ointment).[19] However, these authors reported that even if topical ganciclovir was started in all patients as the initial preferred treatment because of the absence of systemic adverse effects and low cost, both topical and oral antiviral treatments were necessary during later stages of the disease. A recent study reported that ganciclovir levels in the AH were below the 50% inhibitory dose (ID_{50}) for HCMV replication, following topical application of ganciclovir gel 0.15%.[49] The preferential concentration of the ganciclovir gel in solid ocular tissue can explain the clinical improvement seen in these eyes, and this form of ganciclovir therapy seems to be tolerated. The treatment option, topical 2% ganciclovir solution as induction and maintenance treatment for CMV iritis, is gaining attention recently.[50,51]

Therefore, the choice of therapy (oral or topical), can also be based on factors such as cost and availability.

In summary, this study showed that HCMV-related anterior uveitis can present with variable clinical features. We did not observe a typical presentation related to patients' ethnic origin. Aqueous tapping should be done as soon as possible in patients who are referred for management of hypertensive anterior uveitis after failure of treatment with acyclovir or topical corticosteroids in order to administer antiviral medication targeting HCMV.

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