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Case report

Real-time polymerase chain reaction in recurrent cytomegalovirus anterior uveitis

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ABSTRACT

Purpose: Cytomegalovirus (CMV) has been reported to cause anterior uveitis in the immunocompetent people. Recurrence of this viral uveitis poses a mangement dilemma. With real-time polymerase chain reaction(PCR), it is possible to confirm the clinical diagnosis. We report a case of recurrent CMV anterior uveitis documented by real-time PCR.

Observations: A 42 year old man developed PCR proven CMV anterior uveitis. It resolved with oral and topical antivirals but recurred after ten months. The recurrence was controlled by restarting the oral antivirals. Real-time PCR was used to sequentially document the inital infection, the subsequent resolution and the recurrence of the infection.

Conclusions and Importance: Real-time PCR is a useful tool in the management of CMV anterior uveitis.

1. Introduction

Hypertensive anterior uveitis is known to be caused by Herpes group of viruses and Cytomegalovirus(CMV) is an emerging cause of uveitis amongst the immunocompetent people.The patients present with acute recurrent or chronic anterior uveitis along with ocular hypertension or corneal endothelitis. Review of reports[1,2] have shown that these eyes have been treated with a variety of antivirals, including systemic gancyclovir or valgancyclovir, gancyclovir gel or intravitreal injections of gancyclovir, with variable outcomes. Regardless of the modes of delivery of antivirals, all had recurrences. DNA analysis of the anterior chamber fluid can give a definitive diagnosis. PCR analysis of intraocular fluids may detect minimal amounts of viral DNA, making it a powerful and rapid diagnostic method.[3,4] Real-time PCR-based tests may provide additional information on viral load, disease activity and response to therapy.[5] We report a case of CMV DNA positive recurrent hypertensive anterior uveitis.

2. Case report

A 42 year old Asian Indian male came with complaints of redness and blurred vision in both eyes for four years. He was being treated with topical steroids along with topical prostaglandin analogues, timolol and brimonidine and oral acetazolamide. His vision was 6/6, N6 in both eyes. Anterior chamber was quiet. There were large keratic precipitates in central cornea in both eyes and a few coin shaped keratic precipitates (Fig. 1). The iris showed mild diffuse atrophy in both eyes The intraocular pressure (IOP) was within normal limits with antiglaucoma medications.Gonioscopy did not show any trabercular precipitates. Fundus examination showed suspicion of early glaucomatous changes in both discs.The Humphrey Visual Fields were normal in both eyes. Anterior chamber tap was done and the nested Polymerase Chain Reaction (PCR) from the aqueous was positive for CMV DNA. The quantitative real-time PCR detected 660 copies/mL of DNA(Fig. 2). He was given oral Valgancyclovir 900mg twice daily along with topical steroids and topical anti glaucoma medications ofdorzolamide, timolol and brimonidine. The prostaglandin analogues and oral acetazolamide were stopped. On review after one month, he was asymptomatic, the intraocular pressures were normal in both eyes and there was no anterior chamber or vitreous inflammation(Fig. 1). The PCR for CMV was repeated from the aqueous and it was negative. He was asked to continue the topical antiglaucoma medications and tapering doses of the topical steroid along with gancyclovir gel ointment and oral valgancyclovir 450mg twice daily. On followup, after four months from starting the treatment he was asymptomatic, however there was mild anterior chamber reaction in both eyes. The vitreous remained quiet and the IOP was normal. The real time PCR from the aqueous for CMV was negative (Fig. 3). He was asked to continue ganciclovir gel and the topical steroids. The subsequent follow-up showed a normal IOP with quiet anterior segment. However ten months from the first presentation

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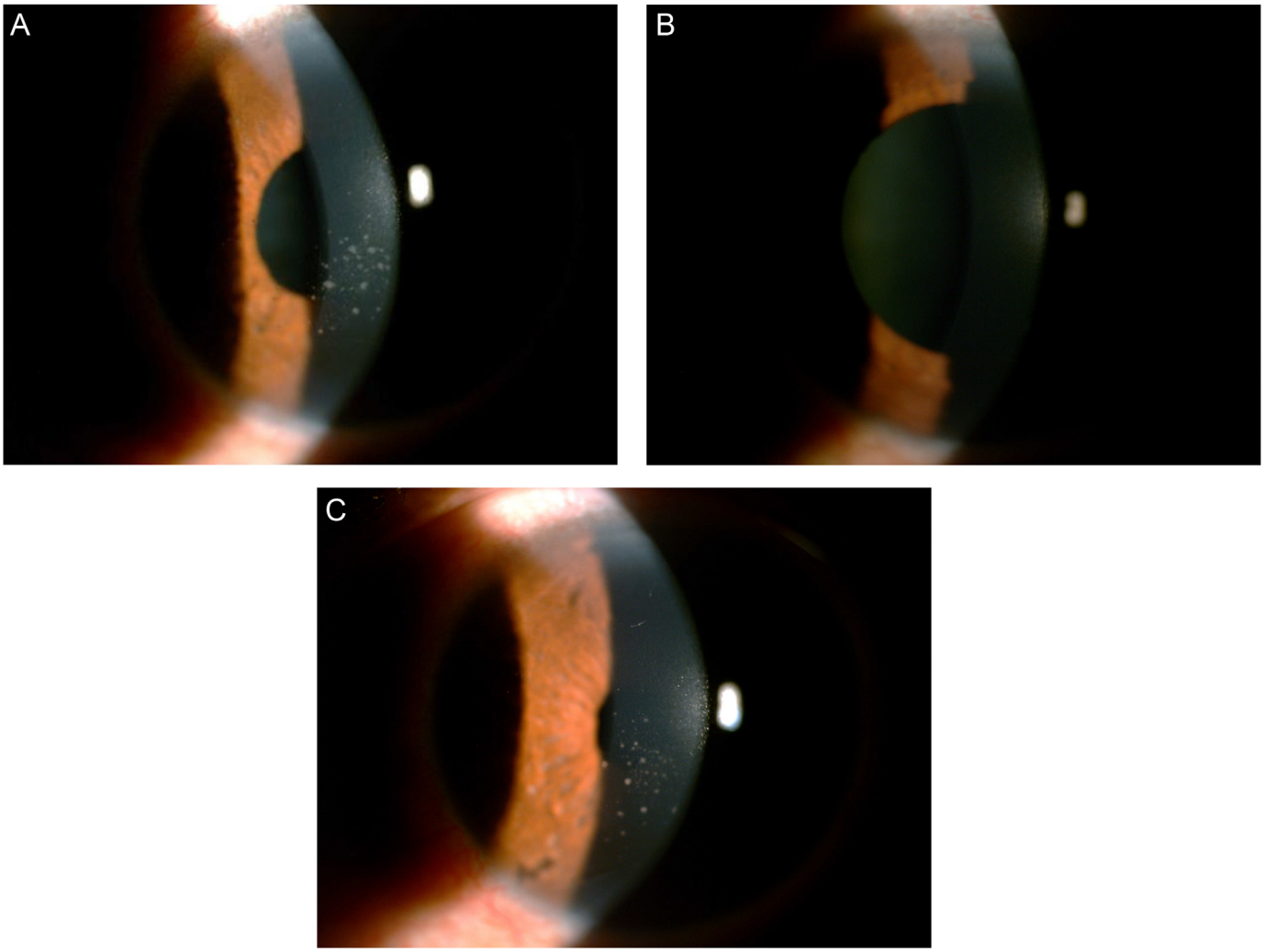

Fig. 1. Large keratic precipitates seen in the central cornea of the left eye at the first visit.b)slit lamp photograph of the left eye in remission.c)slit lamp photo of the left eye during recurrence with high copies of viral DNA in real time PCR.

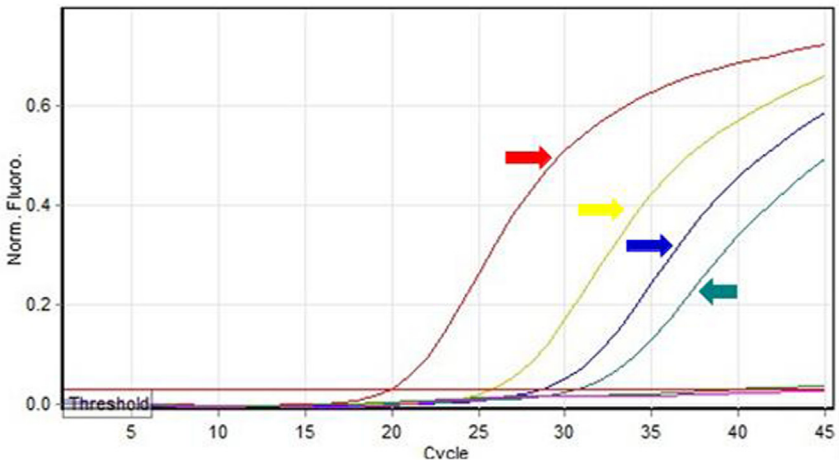

Fig. 2. Real time polymerase chain reaction report showing exponential rise in viral DNA copies suggestive of active replication of Cytomegalovirus along with defined standards: Standard 1/S1 (red arrow), Standard 3/S3 (yellow arrow), standard 4/S4 (Blue arrow) and test sample (SN No 1798/17: green arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

there was recurrence of inflammation in the anterior chamber with 1 + cells in the anterior chamber and keratic precipitates in both eyes. The number and size of the keratic precipitates which re-appeared were not significantly more than during the first insult (Fig. 1).The patient was using ganciclovir gel, topical steroids and topical antiglaucoma medications. The IOP was normal in both eyes.The real-time PCR from the aqueous was repeated and it was positive for CMV with 42,000 copies/mLof DNA (Fig. 4).The IOP increased progressively and oral acetazolamide had to be added. He was restarted on oral valgancyclovir 900mg twice daily and continued the gancyclovir gel ointment and steroid eyedrops. The anterior chamber inflammation subsided and the intra ocular pressure was controlled with topical medication. He was asked to continue a maintenance dose of 450mg of oral valgancyclovir twice a day and gancyclovirgel.

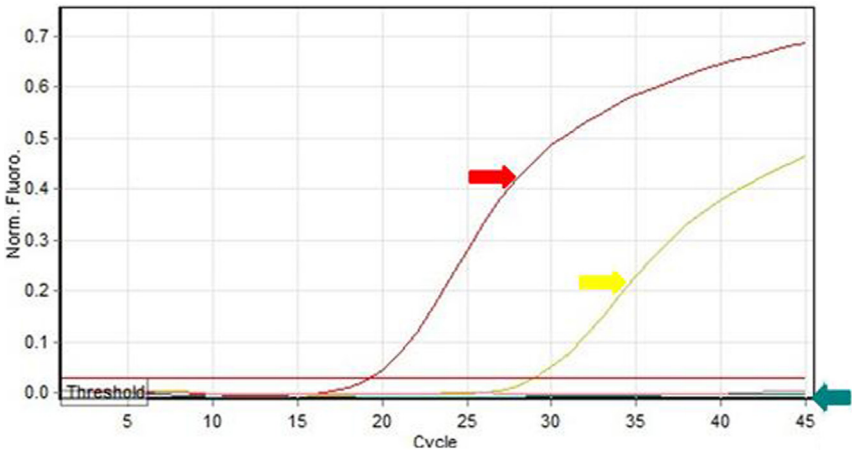

Fig. 3. Real time polymerase chain reaction report for detection of load of Cytomegalo virus along with defined standards: Standard 1/S1 (red arrow), Standard 4/S4 (yellow arrow), and test sample negative for CMV RTPCR (SN No 2282/17: green arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

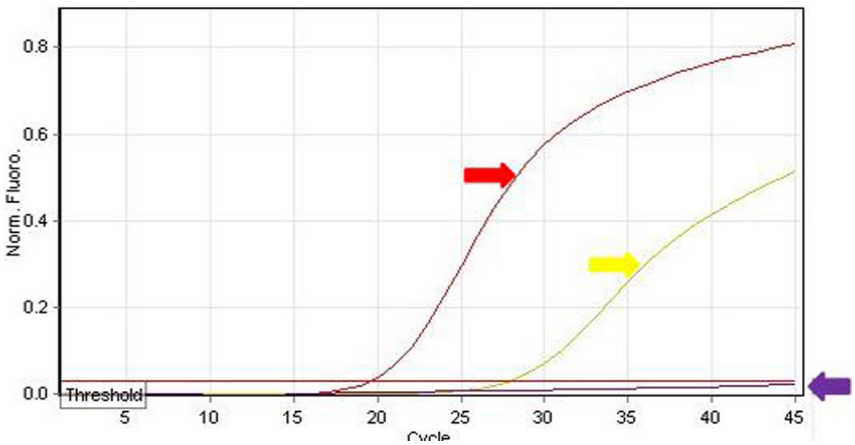

Fig. 4. Real time polymerase chain reaction report showing increase in viral DNA copies suggestive reactivation of Cytomegalo virus along with defined standard: Standard 1// S1 (red arrow), test sample (SN No 1228/18: yellow arrow) and negative control (purple arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3. Discussion

CMV anterior uveitis affects the Chinese and Japanese population more often, however there are few reports in Indians as well.[6,7] Recurrence of CMV anterior uveitis sometimes poses a management dilemma. With the use of real-time PCR it is possible to document a response to therapy as well as the recurrence.[8] Our case is unique in its use of real-time PCR which turned negative after treatment and then turned positive again with recurrence, thereby confirming our clinical diagnosis.

CMV anterior uveitis with a risk of visual loss from glaucomatous damage are given antiviral therapy. The various modes of delivery of antivirals range from sytemic gancyclovir, valgancyclovir, intravitreal gancyclovir and gancyclovir gel.[1,2] However there is a high rate of recurrence regardless of the mode of delivery of the antiviral. The reason for this could be that gancyclovir is virostatic and hence it fails to eliminate the CMV infection completely. After the primary infection, CMV is not eradicated and it establishes life-long infection in its host, and many factors such as the underlying viral load or various viral immune evasion mechanisms can contribute to reactivation.[9] Other possible reasons for CMV reactivation might include the development of various CMV immune evasion mechanisms, such as the expression of viral genes that inhibit Natural Killer cells recognitionand cytotoxicity and the prevention of $CD8^+$ and $CD4^+$ T-cell recognition via major histocompatibility Class I and II processing pathway downregulation.[10] Although CMV anterior uveitis has relapses, use of gancyclovir gel has been reported to have a lesser recurrence,[1] due to its high levels in the iris, after application in the form of ointment. Our patient responded to the oral valgancyclovir and was on a maintenance therapy with gancyclovir gel which has lesser potential for adverse effects with longterm use compared to systemic gancyclovir and gancyclovir implant.Besides, the duration of maintenance with oral valgancyclovir still remains undefined. In one case, there is a report of valgancyclovir being continued for 12 months[2] to prevent recurrences, but after a quiescent period of one year, when the drug was discontinued, the uveitis relapsed. There is also a report of a relapse of uveitis while on maintenance dose of oral valgancyclovir, but responded to an increase in dosage to the induction levels.[2] In our patient, mild anterior uveitis recurred after four months, but the IOP was controlled with one drug and the inflammation reduced with the gancyclovir gel and the topical steroids. However, later, gancyclovir gel alone was not enough to control the uveitis and it required theaddition of oral valgancyclovir in induction doses to control the inflammation and the IOP. We have continued oral valgancyclovir after discussing the risk and benefits with the patient.

To conclude, although gancyclovir gel is effective as a maintenance drug, patients who have recurrences while on it, may need a longer course of oral valgancyclovir to limit the progressive visual loss and glaucomatous damage. Also, this study showed that real-time PCR testing is useful for detecting CMVDNA in uveitic eyes allowing for a more accurate treatment and a better prognosis in patients with CMV anterior uveitis.

Patient consent

Availed.

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Conflicts of interest

The following authors have no financial disclosures: VGR, MKJ, JB.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajoc.2019.100470.

References

1. Chee SP. Jap A Cytomegalovirus anterior uveitis : outcome of treatment. *Br J Ophthalmol.* 2010;94:1648–1652.
2. Van Boxtel LA, van der Leilij A, van der Meer J, et al. Cytomegalovirus as a cause of anterior uveitis in immunocompetent patients. *Ophthalmology.* 2007;114:1358–1362.
3. De Groot-Mijnes JDF, Rothova A, Van Loon AM, et al. Polymerase chain reaction and Goldmann-Witmer coeffi- cient analysis are complimentary for the diagnosis of infectious uveitis. *Am J Ophthalmol.* 2006;141(2):313–318. https://doi.org/10.1016/j.ajo.2005.09.017.
4. Shoughy SS, Alkatan HM, Al-Abdullah AA, El-Khani A, De Groot-Mijnes JD, Tabbara KF. Polymerase chain reaction in unilateral cases of presumed viral anterior uveitis. *Clin Ophthalmol.* 2015;9:2325–2328. https://doi.org/10.2147/OPTH.S93655.
5. Scheepers MA, Lecuona KA, Rogers G, Bunce C, Corcoran C, Michaelides M. The value of routine polymerase chain reaction analysis of intraocular fluid specimens in the diagnosis of infectious posterior uveitis. *Sci World J.* 2013;2013. https://doi.org/10.1155/2013/545149 545149.
6. Babu K1, Kini R, Philips M, Subbakrishna DK. Clinical profile of isolated viral anterior uveitis in a South Indian patient population. *Ocul Immunol Inflamm.* 2014 Oct;22(5):356–359.
7. Kumar A, Singh MP, Gupta A, Bansal R, Sakia UN, Ratho RK. Viral etiology of anterior uveitis in immunocompetent patients in North India. *Int J Infect Dis.* 2016;45S 1–477.
8. SANTOS Fabio Felipe dos, et al. Real-time PCR in infectious uveitis as an alternative diagnosis. *Arq Bras Oftalmol.* 2011;74:258–261.
9. Jackson SE, Mason GM, Wills MR. Human cytomegalovirus immunity and immune evasion. *Virus Res.* 2011;157(2):151–160.
10. Jackson SE, Redeker A, Arens R, et al. CMV immune evasion and manipulation of the immune system with aging. *GeroScience.* 2017;39 273.