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 management 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 initial 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 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. Real-time PCR-based tests may provide additional information on viral load, disease activity and response to therapy. 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 acute recurrent or chronic anterior uveitis along with topical steroids and 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. 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 trabecular 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. He was given oral Valgancyclovir 900mg twice daily along with topical steroids and topical antiglaucoma medications of dorzolamide, timolol and brimonidine. The prostaglandin analogues and oral acetazolamide were stopped. On review after one month, he was asymptomatic, the IOP was normal in both eyes and there was no anterior chamber or vitreous inflammation. The PCR for CMV 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. 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
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/mL of 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 intraocular pressure was controlled with topical medication. He was asked to continue a maintenance dose of 450mg of oral valgancyclovir twice a day and gancyclovir gel.
3. Discussion

CMV anterior uveitis affects the Chinese and Japanese population more often, however there are few reports in Indians as well.\textsuperscript{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.\textsuperscript{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 systemic gancyclovir, valgancyclovir, intravitreal gancyclovir and gancyclovir gel.\textsuperscript{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.\textsuperscript{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 recognition and cytotoxicity and the prevention of CD8\textsuperscript{+} and CD4\textsuperscript{+} T-cell recognition via major histocompatibility Class I and II processing pathway downregulation.\textsuperscript{10} Although CMV anterior uveitis has relapses, use of gancyclovir gel has been reported to have a lesser recurrence,\textsuperscript{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\textsuperscript{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.\textsuperscript{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 the addition 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 CMV DNA 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

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Authorship

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

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Appendix A. Supplementary data

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