American Journal of Ophthalmology Case Reports 10 (2018) 189–191

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.elsevier.com/locate/ajoc

Case report

Two cases of cytomegalovirus panuveitis in immunocompetent patients

Masato Sakai[a], Hiroshi Takase[b], Kenichi Namba[a,*], Kazuomi Mizuuchi[a], Daiju Iwata[a], Susumu Ishida[a]

[a] Departments of Ophthalmology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan
[b] Department of Ophthalmology &Visual Science, Tokyo Medical and Dental University, Tokyo, Japan

ARTICLE INFO

Keywords:
Cytomegalovirus
Panuveitis
Immunocompetent
Intravitreal injection
PCR

ABSTRACT

Purpose: To report two cases of panuveitis in immunocompetent patients in which cytomegalovirus was involved.

Observation: Case 1 was a 46-year-old man who had a history of recurrent anterior chamber inflammations in his left eye. After Nd:YAG laser posterior capsulotomy, he developed panuveitis with vitreous haze and periphlebitis. Polymerase chain reaction (PCR) examination revealed the presence of cytomegalovirus (CMV) DNA in the anterior chamber (AC). He responded well to a series of intravitreal injections of ganciclovir (GCV). Case 2 was a 63-year-old woman who had a history of recurrent anterior uveitis in her left eye. Two years after cataract surgery, AC inflammation, diffuse vitreous haze, and periphlebitis had developed. CMV DNA was detected in the AC. Intravitreal injections of GCV and oral valganciclovir were administered, and ocular inflammation finally improved.

Conclusions: and importance: We experienced two cases of CMV panuveitis in immunocompetent adults, both of which responded well to anti-viral therapies.

1. Introduction

Cytomegalovirus (CMV) is known as a pathogen that usually causes retinitis in immunocompromised patients and iridocyclitis and/or corneal endotheliitis in healthy (immunocompetent) patients.[1–3] We report herein two cases of immunocompetent individuals who developed retinal vasculitis with panuveitis in which CMV was considered as a pathogenic microbe.

2. Findings

2.1. Case 1

A 46-year-old man had a history of recurrent anterior chamber inflammations with elevated intraocular pressure (IOP) > 30 mmHg in his left eye for seven years. He was initially diagnosed with Posner-Schlossman syndrome (PSS), and he had been well-controlled with topical betamethasone eye drops at first. However, the IOP gradually increased, therefore, he underwent cataract surgery with trabeculotomy. Thereafter the IOP was kept within normal range for three years. Due to the development of postoperative capsule opacity, Nd:YAG laser posterior capsulotomy was performed one year earlier. Thereafter, exacerbation of the anterior chamber inflammation and gradual development of vitreous opacity appeared. He received sub-Tenon injection of triamcinolone acetonide (STTA), and oral prednisolone (5mg/day). He was then referred to our hospital. He had not suffered from any systemic disease including diabetes.

At the first visit, the best-corrected visual acuity (BCVA) was 1.5 in the right eye (OD) and 0.7 in the left eye (OS). Intraocular pressure was 21 mmHg OD and 14 mmHg OS. With slit-lamp examination, 1 + flare and 2 + cells anterior chamber (AC) inflammation with keratic precipitates (KPs) was seen, the intraocular lens was well-located, and the posterior capsule was widely open OS. Fundus examination showed 2 + of vitreous haze (Fig. 1a) and sheathings of a part of peripheral retinal veins OS (Fig. 1b). Fluorescein angiography (FA) revealed leakages from the optic disk and retinal veins all over the fundus OS (Fig. 1c). There were no remarkable findings OD. Viral infection was suspected, and the patient then underwent AC paracentesis. A polymerase chain reaction (PCR) testing revealed the presence of CMV DNA (9.5×10^4 copies/mL) but neither herpes simplex virus nor varicella zoster virus. CMV antigenemia was negative, and blood tests for syphilis and tuberculosis were negative.

We started intravitreal injections of ganciclovir (GCV) at a dose of 0.4mg/0.05mL weekly. After one course of intravitreal injections of GCV (every week for eight weeks), AC cells and vitreous haze were reduced, and BCVA improved to 1.2 OS, while the CMV DNA copy

* Corresponding author. Department of Ophthalmology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, N15-W7, Kita-ku, Sapporo, 060-8638, Japan.
E-mail address: knamba@med.hokudai.ac.jp (K. Namba).

https://doi.org/10.1016/j.ajoc.2018.01.025
Received 22 March 2017; Received in revised form 9 October 2017; Accepted 10 January 2018
Available online 17 January 2018

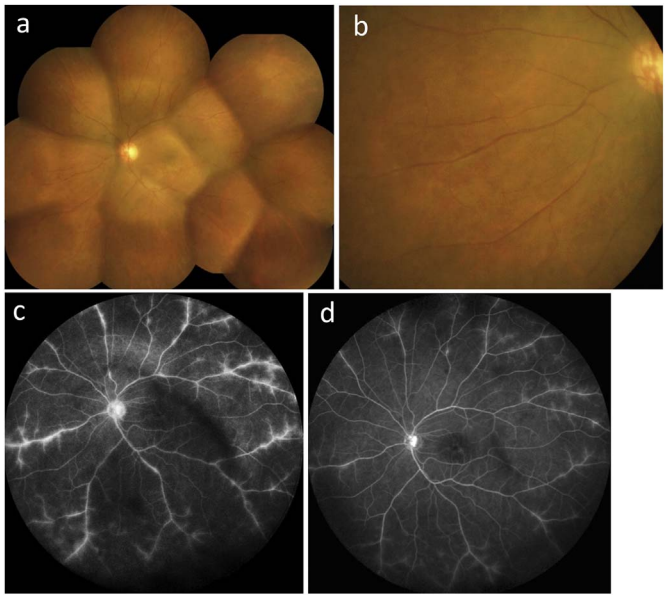

Fig. 1. Case 1. Clinical findings at the initial visit (a, b, c). Left eye showed 2 + of vitreous haze and sheathings of a part of peripheral retinal veins (a,b). Fluorescein angiography (FA) showed leakages from the optic disk and peripheral retinal veins (c). Leakages from retinal veins were decreased four months later from the end of the second intravitreal injections of ganciclovir (GCV) course(d).

number decreased to 9.3×10^3 copies/mL, although FA showed no difference compared to prior to the intravitreal injections of GCV. Administration of intravitreal injections of GCV was then stopped, and the patient was observed carefully.

The ocular inflammation was minimal for a while; however, four months later, it relapsed with 2 + of anterior chamber cells and 2 + of vitreous haze. BCVA decreased to 0.9 OS, and the CMV DNA copy number increased to 2.0×10^5 copies/mL. Another course of intravitreal injections of GCV (every week for eight weeks) was administered to the patient. At one month from the end of the second intravitreal injections of GCV course, anterior chamber cells and the vitreous haze were diminished, BCVA improved to 1.2 OS, and the CMV DNA copy number was at an undetectable level. After the second intravitreal injections of GCV course, monthly intravitreal injections of GCV administration was performed as maintenance therapy for four months. Meanwhile, no recurrences of ocular inflammations were seen, and FA showed a marked decrease in leakages from retinal veins (Fig. 1d). After the second series of intravitreal injections of GCV therapy, the patient has not shown any relapses for 13 months. The final BCVA was 1.2 OS.

2.2. Case 2

A 63-year-old woman had a history of recurrent anterior uveitis with elevated intraocular pressure OS for 18 years. She was initially diagnosed with PSS, and had been well-controlled with topical betamethasone eye drops. Cataract surgery was performed six years earlier. Four years earlier, diffuse vitreous opacity developed in addition to AC inflammation with elevated intraocular pressure. She was then referred to our hospital three years earlier. She had a history of type-2 diabetes of which the HbA1c was 7.0% controlled with oral hypoglycemic agents. She also had a history of breast cancer and she underwent mastectomy 17 years and 10 years ago. She had been in complete remission for 10 years.

At the first visit, her BCVA was 1.2 OD and 0.9 OS. Intraocular pressure was 18 mmHg OD and 16 mmHg OS. With slit-lamp examination, 2 + flare and 2 + cells AC inflammation with pigmented mutton-fat KPs was seen, and the intraocular lens was well-located OS

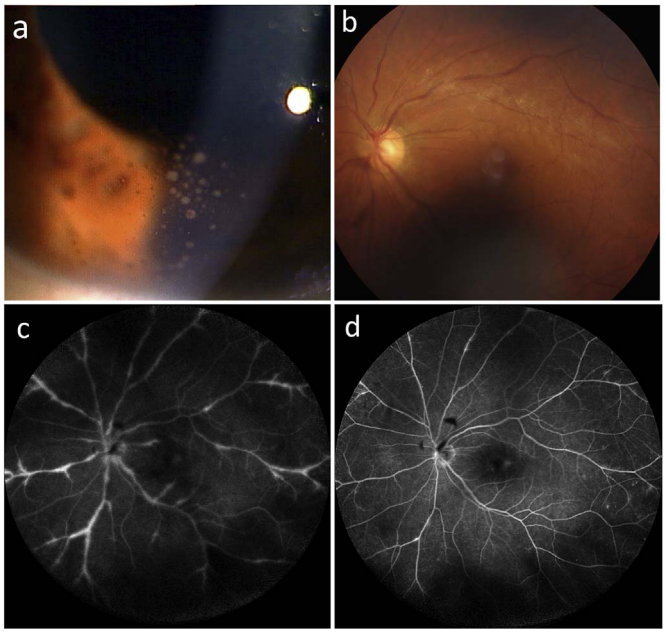

Fig. 2. Case 2. Clinical findings at the initial visit (a, b, c). Anterior chamber inflammation with pigmented mutton-fat keratic precipitates (a) and sheathings of a part of peripheral retinal veins (b) were seen. Fluorescein angiography (FA) showed leakages from the optic disk and peripheral retinal veins including arcade vessels (c). After antiviral therapies leakages were gradually diminished in FA (d).

(Fig. 2a). Gonioscopic examination showed a tent-shaped peripheral anterior synechia OS. Fundus examination showed sheathings of a part of peripheral retinal veins OS (Fig. 2b). There were no remarkable findings OD. FA revealed leakages from the optic disk and retinal veins all over the fundus OS (Fig. 2c). Although sarcoidosis was suspected from the granulomatous feature of the ocular findings, systemic workup did not support the diagnosis of sarcoidosis. CMV antigenemia was negative, and blood tests for syphilis and tuberculosis were negative. She was treated with topical betamethasone eye drops and 20mg of a STTA for four times; however, neither the anterior nor posterior intraocular inflammation responded to the treatment. The patient then underwent AC paracentesis, and PCR examination revealed the presence of CMV DNA (3.8×10^5 copies/mL) but neither herpes simplex virus nor varicella zoster virus.

We first performed intravitreal injections of GCV at a dose of 1mg/0.1mL once, but the patient refused to receive other injections to the eye. Instead, intravenous injections of GCV (5mg/kg) twice a day for two weeks were administered, followed by oral valganciclovir (900mg) once a day. Mutton-fat KPs and the vascular leakage shown by FA gradually improved (Fig. 2d), and FA findings completely disappeared 10 months later. The patient has not shown any relapses for 12 months. The final BCVA was 1.2 OS.

3. Discussion

We experienced two cases of immunocompetent adults who developed unilateral panuveitis featured with sheathings of retinal veins and dye leakages from the optic disk and retinal veins shown by FA. Both cases developed posterior intraocular inflammation after cataract surgery. Notably, the posterior intraocular inflammation of Case 1 developed right after Nd:YAG laser posterior capsulotomy. CMV DNA was detected in the aqueous humor in both cases, and the CMV DNA copy number decreased with treatment in Case 1. In addition, both cases responded to the antiviral therapy. These results suggested that CMV was involved in the pathogenicity of our cases.

The clinical entity of CMV-associated anterior segment inflammations is characterized as chronic iridocyclitis, high intraocular pressure

and/or corneal endothelial cell loss, and it has already been known that the some of the cases that have been diagnosed as PSS or Fuchs heterochromic iridocyclitis are positive for CMV DNA in the AC, indicating that they are actually CMV iridocyclitis and corneal endotheliitis.[2,3]

It is considered that our cases, previously diagnosed as PSS, are also truly CMV iridocyclitis, and CMV in the anterior chamber may have disseminated to the vitreous cavity. In both cases, cataract surgeries had been previously performed ahead of the onset of panuveitis. Additionally, in Case 1, panuveitis developed after Nd:YAG laser posterior capsulotomy. Cataract surgery and laser posterior capsulotomy may be a trigger of the dissemination of the virus.

There have been no reports that described posterior segment inflammation with CMV iridocyclitis in immunocompetent adults except one paper reported by Wong MH et al.[4] They reported that among 11 cases with CMV iridocyclitis, two cases presented cystoid macular edema, and one of them presented disk swelling, 1 + of vitreous haze, and vascular leakages in FA examination. Although there was no mention of laser posterior capsulotomy, both cases were pseudophakia, that is consistent with our present cases.

Of course, we cannot exclude the possibility that posterior segment inflammations undetected with funduscope may be accompanied in some patients with CMV iridocyclitis.

Our cases were obviously far from cytomegalovirus retinitis in that they had long history of antecedent iridocyclitis and no retinal exudates. Case 2 had a history of diabetes and history of breast cancer those are known as risk factors of cytomegalovirus retinitis, however, both disease were well controlled at the onset of the uveitis. In addition, local immunocompromised state can be a risk factor of CMV retinitis. Michael A et al. described a case who developed CMV retinitis after intravitreous injection of triamcinolone (IVTA) in an immunocompetent patient.[5] Indeed, both our cases had received neither STTA nor IVTA before the onset of uveitis.

It has not been revealed what cells are the host for CMV persisting in the vitreous cavity or retinal tissue. Although CMV is generally not a pathogenic microbe in immunocompetent people; however, anterior chamber-associated immune deviation (ACAID) may be considered to play a role in the pathogenic mechanism.[6] Once CMV migrate into the anterior chamber (the mechanism how to migrate has not been revealed yet), immune tolerance toward the CMV antigen is induced by the mechanism of ACAID, consequently anterior chamber and vitreous cavity become the favorable environment for the persistence of CMV infection, even in immunocompetent patients.

The patient of Case 1 responded well to a series of intravitreal injections of GCV therapy, which is commonly used for CMV retinitis. Considering that CMV retinitis is one of the symptoms representative of opportunistic CMV infections that develop in immunocompromised patients, systemic treatment with ganciclovir - as we performed in Case 2 - should be the principle therapy, and intravitreal injections of GCV should only be an adjunctive therapy. However, as regards CMV panuveitis that developed in immunocompetent patients, serum CMV antigen is theorized to be negative with infection localized in the eye. Therefore, intravitreal injection of GCV is considered to be the reasonable treatment in our current cases, and the CMV DNA copy number can be a good indicator of this disease activity.

Patient consent

Institutional review board approved this retrospective case report. Written informed consent was obtained from patients for publication of these case reports and any accompanying images.

Acknowledgements and disclosures

Funding

No funding or grant support.

Conflicts of interest

All of the authors have no financial disclosures.

Authorship

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

Acknowledgement

We appreciate Dr. Taro Kondo for performing intravitreal injections in Case 1.

References

1. Friedman AH, Orellana J, Freeman WR, et al. Cytomegalovirus retinitis: a manifestation of the acquired immune deficiency syndrome (AIDS). *Br J Ophthalmol.* 1983;67:372–380.
2. Koizumi N, Inatomi T, Suzuki T, et al. Clinical features and management of cytomegalovirus corneal endotheliitis: analysis of 106 cases from the Japan corneal endotheliitis study. *Br J Ophthalmol.* 2015;99:54–58.
3. Chee SP, Bacsal K, Jap A, et al. Clinical features of cytomegalovirus anterior uveitis in immunocompetent patients. *Am J Ophthalmol.* 2008;145:834–840.
4. Wong MH, Cheung GC, Chee SP. Posterior segment findings of ocular cytomegalovirus infection in immunocompetent patients. *Graefes Arch Clin Exp Ophthalmol.* 2014;252:1811–1816.
5. Saidel MA, Berreen J, Marqolis TP. Cytomegalovirus retinitis after intravitreous triamcinolone in an immunocompetent patient. *Am J Ophthalmol.* 2005;140:1141–1143.
6. Streilein JW, Masli S, Takeuchi M, et al. *The eye's view of antigen presentation.* vol. 63. 2002; 2002:435–443.