

Cytomegalovirus retinitis following dexamethasone intravitreal implant

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ABSTRACT

Purpose: To describe a case of Cytomegalovirus (CMV) Retinitis in an immunocompetent patient following Dexamethasone Intravitreal Implant (DII).

Observations: Retrospective chart review of a single patient. An 80-year-old immunocompetent male presented with floaters in his left eye 10 weeks after his DII. He was noted to have a visual acuity of 20/1200 in his left eye and a panuveitis with CMV retinitis. The patient underwent a vitreous biopsy and given immediate intravitreal foscarnet and an ongoing management regimen of oral valganciclovir for two months. His vision improved to 20/200 and his CMV retinitis resolved.

Conclusion and Importance: DII can trigger CMV retinitis in immunocompetent patients.

1. Introduction

We present a rare case of cytomegalovirus (CMV) retinitis in an immunocompetent patient following dexamethasone intravitreal implant (DII, Ozurdex®) injection.

2. Case report

An 80-year-old immunocompetent, non-diabetic male presented with a two-week history of left eye floaters and irritation 10 weeks following DII injection for neovascular age-related macular degeneration (AMD). The patient had previously been treated for 8 years with intravitreal anti-VEGF (ranibizumab and aflibercept) and photodynamic therapy however the choroidal neovascularisation (CNV) had become refractory to these therapies with persistent exudation. The eye had previously been vitrectomised for a retinal detachment, resulting in a reduced half-life of intravitreal anti-VEGF. Although unconventional, DII had resulted in improvement in exudation, and 6 injections had been administered over the preceding 2 years. His past medical history included asthma, prior curative radiotherapy for prostate cancer with some residual mild renal impairment.

On examination his best corrected visual acuity had dropped to 20/1200 in his left eye (OS) from 20/160 on the previous review. The

intraocular pressure was 13 mmHg OS. The left eye revealed a mild ciliary flush, fine keratic precipitates, 3+ cells in the anterior chamber, a well-positioned posterior chamber intraocular lens, moderate vitritis and white retinitis associated with peripheral scattered retinal haemorrhages in the nasal and superior quadrants, posterior pole and inferior to the inferior retinal vascular arcade (Fig. 1A). Examination of the right eye was unremarkable.

A provisional diagnosis of viral retinitis was made and the patient underwent an urgent vitreous cavity pars plana biopsy with a 25-gauge needle which was positive for CMV on polymerase chain reaction (PCR). The specimen was negative for Herpes simplex virus, Varicella zoster virus, toxoplasmosis PCR and microbiological cultures. CMV serology revealed a positive IgG result and a negative IgM result for CMV. CMV DNA PCR on serum is not available at our centre. Syphilis and HIV serology were negative. No Systemic signs of CMV infection were found. Immediate medical treatment included intravitreal foscarnet 2.4mg in 0.1ml as well as oral valganciclovir at a reduced induction dosage of 450mg twice daily due to a prior history of renal impairment (serum creatinine of 122 µmol/L at baseline).

Following a two-month course of oral valganciclovir his vision improved back to 20/200 with resolution of the CMV retinitis (Fig. 1B). He did not require any further intravitreal foscarnet after the initial dose. He was referred to an immunologist, who performed a thorough

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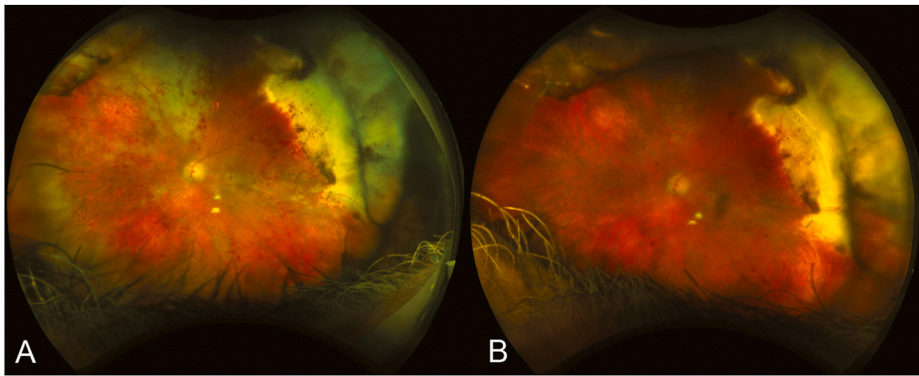


Fig. 1. A) Colour fundus photograph of the left eye on presentation demonstrating active CMV retinitis in the superior and nasal quadrants, posterior pole and inferior to the inferior retinal vascular arcade. The supero-temporal quadrant has a white scar from previous cryotherapy and laser applied during vitrectomy surgery for a retinal detachment 20 years prior. B) Following two months of intravitreal foscarnet and oral valganciclovir, there has been resolution of the CMV retinitis with mild residual pigmentary changes. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

systemic screen including exclusion of infectious causes, urine analysis, autoimmune serology including IgG subclasses and haematological screens. None of these screens revealed any abnormalities that could have predisposed this patient to any cellular or antibody immunodeficiency.

3. Discussion

CMV retinitis is one of the most common opportunistic ocular infections, usually seen in immunocompromised patients.^{1–3} Rarely, CMV retinitis can occur in immunocompetent patients.^{4–6} Presentation of disease in immunocompetent patients with CMV retinitis more frequently presents with a marked inflammatory response including vitritis, a finding also noted in this case.^{4,7} Recently, the use of localised intravitreal or periocular steroids agents, such as triamcinolone acetonide, has been suggested to be an additional risk factor in developing CMV retinitis in both immunosuppressed and immunocompetent patients.^{2,8} The advent of the DII (Ozurdex®) has helped treat macular oedema due to diabetes, posterior non-infectious uveitis, retinal vein occlusions and choroidal neovascularisation secondary to age-related macular degeneration.^{9,10} Steroids are known immunosuppressive agents that work through sequestering CD4 T cells alongside inhibiting the transcription of cytokines.¹¹ It is possible that the DII caused enough local immunosuppression to trigger retinal CMV infection.

A thorough MEDLINE and PubMed search revealed four cases in English print journals of patients that underwent DII and subsequently developed CMV retinitis.^{5,12–14} Two of these cases were patients who were systemically immunosuppressed due to underlying conditions such as a renal transplant and retinal vasculitis.^{13,14} A third case was described as being in an immunocompetent patient but they had a 25-year history of type 2 diabetes.¹² In the fourth case, the medical history of the patient was not clearly described, such that it is impossible to verify if the patient was definitely immunocompetent.⁵ In our case, systemic immunosuppression was definitively excluded by an immunologist. The patient's past medical history was not thought to be contributory.

One factor that may have contributed to the development of CMV retinitis is the patient's elderly age. Immunosenescence refers to the impaired ability of the body's immune system to respond to various triggers with increasing age.^{15,16} CD4 helper T cell proliferation reduces with age¹⁷ and there is an age associated increase in the prevalence CMV infections.¹⁸ Regardless, spontaneous CMV retinitis in immunocompetent patients is rare, and the DII is likely to be major contributing factor.

4. Conclusion

DII is a useful treatment for many forms of macular oedema, but CMV retinitis should be added to the potential side effects, even in the immunocompetent patient.

Patient consent

The patient has provided written consent for publication of their case in AJO.

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Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

Written consent to publish potentially identifying information, such as details or the case and photographs, was obtained from the patient(s) or their legal guardian(s).

Authorship

All listed authors meet the ICMJE criteria. We attest that all authors contributed significantly to the creation of this manuscript, each having fulfilled criteria as established by the ICMJE.

Declaration of competing interest

No conflict of interest exists.

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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