Management challenges of bilateral eye cytomegalovirus (CMV) retinitis in a patient with HIV and multidrug-resistant virological failure: A case report

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SUMMARY

Introduction: Cytomegalovirus (CMV) retinitis is a major cause of vision loss in patients with advanced Human Immunodeficiency Virus (HIV) infection, particularly those with virological failure. Case Presentation: We report a 29-year-old male, an ex-intravenous drug user, diagnosed with HIV in August 2023. He initiated antiretroviral therapy (ART) but developed progressive virological failure with a peak viral load of 1.53 million copies/mL and a declining CD4 T-lymphocyte count from 44 to 24 cells/μL. He was also diagnosed with disseminated tuberculosis and Mycobacterium avium complex (MAC) infection. Ophthalmic evaluation in February 2024 revealed right eye (RE) Zone 1 and left eye (LE) Zone 2 CMV retinitis with vitritis. Initial treatment with oral valganciclovir resulted in partial resolution. In September 2024, reactivation occurred, requiring intravenous and intravitreal (IVT) ganciclovir. In February 2025, he developed macula-off retinal detachment in the LE, which required surgical intervention. Discussion: CMV retinitis in immunocompromised individuals is challenging, particularly in the setting of ART resistance and limited antiviral access. Early antiviral IVT may prevent structural complications. Conclusion: Vigilant monitoring, prompt re-treatment, and multidisciplinary care are essential in preserving vision in complex CMV retinitis cases.

INTRODUCTION

Cytomegalovirus (CMV) retinitis is the most common opportunistic ocular infection in patients with advanced HIV infection and typically occurs in individuals with profound immunosuppression (CD4 <50 cells/μL).[1,3] Despite the advent of effective antiretroviral therapy (ART), CMV retinitis remains a significant cause of vision loss, especially in resource-limited settings or among individuals with poor ART adherence or resistance.[2-3] Prompt diagnosis and treatment are critical to prevent irreversible vision loss and ocular complications such as retinal detachment. We present a case of bilateral CMV retinitis in a patient with ART failure and multidrug-resistant Human Immunodeficiency Virus (HIV), complicated by reactivation and retinal detachment.

CASE PRESENTATION

A 29-year-old male, diagnosed with Human Immunodeficiency Virus (HIV) in August 2023, was referred to ophthalmology in February 2024 for evaluation of progressive visual symptoms. He was an ex-intravenous drug user and had been started on first-line antiretroviral therapy (ART) consisting of Tenofovir, Lamivudine, and Efavirenz in accordance with Malaysian guidelines. The treatment course was complicated by virological failure with rising HIV viral loads (875,290 copies/mL in January 2024, 284,403 copies/mL in April 2024, and 1.53 million copies/mL in July 2024), accompanied by progressive CD4 decline from 44 cells/μL in January 2024 to a nadir of 24 cells/μL in July 2024. Resistance testing revealed broad resistance to nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs), with the exception of zidovudine (AZT), prompting ART regimen modification in August 2024.[5] The ART regimen was subsequently switched to tenofovir/emtricitabine in combination with lopinavir/ritonavir (Kaletra).

He also had disseminated Mycobacterium tuberculosis (MTB) and Mycobacterium avium complex (MAC) infection. Anti-tuberculosis (anti-TB) therapy was initially commenced but temporarily withheld owing to drug-induced liver injury (DILI). Following stabilisation of liver function, anti-TB therapy was resumed with isoniazid, rifampicin, and ethambutol (HRE) in combination with ciprofloxacin. The regimen was subsequently modified to isoniazid, levofloxacin, and ethambutol (HLE) owing to significant drug–drug interactions between rifampicin and protease inhibitor-based ART (lopinavir/ritonavir). ART adherence prior to admission was suboptimal. Following resistance testing, ART optimisation was undertaken in coordination with the infectious disease team. Potential drug interactions, particularly with rifampicin-based anti-tuberculosis therapy, were carefully monitored. He was also on levetiracetam for seizure disorder.

On ophthalmic evaluation, his visual acuity was 6/9 right eye (RE) and 6/12 left eye (LE). Anterior segment examination demonstrated bilateral endothelial dusting and anterior chamber inflammation. Fundus examination revealed right eye (RE) peripapillary flame-shaped haemorrhages with exudates, granular retinitis, and vitritis involving zone 1. LE showed granular retinitis with vitritis in zone 2 (Figure 1). He was diagnosed with RE zone 1 and LE zone 2 CMV retinitis. The diagnosis of CMV retinitis was established clinically, based on characteristic confluent retinal haemorrhages and

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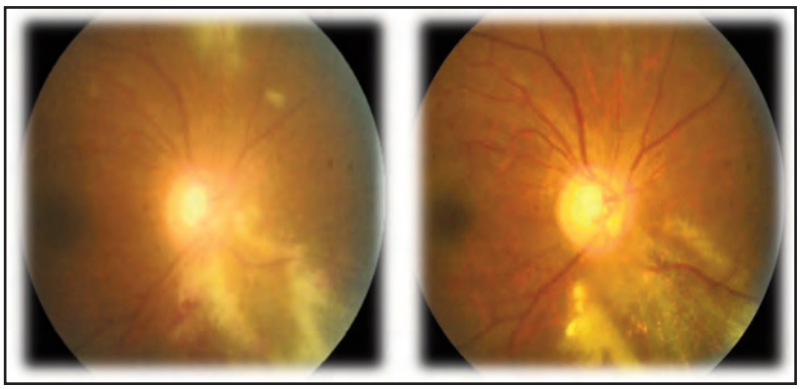

Fig. 1: Shows the fundus view at initial presentation with active CMV retinitis, characterised by granular retinal lesions * and vitritis (right), and fundus appearance two months after treatment initiation, showing resolving vitritis and retinitis (left)

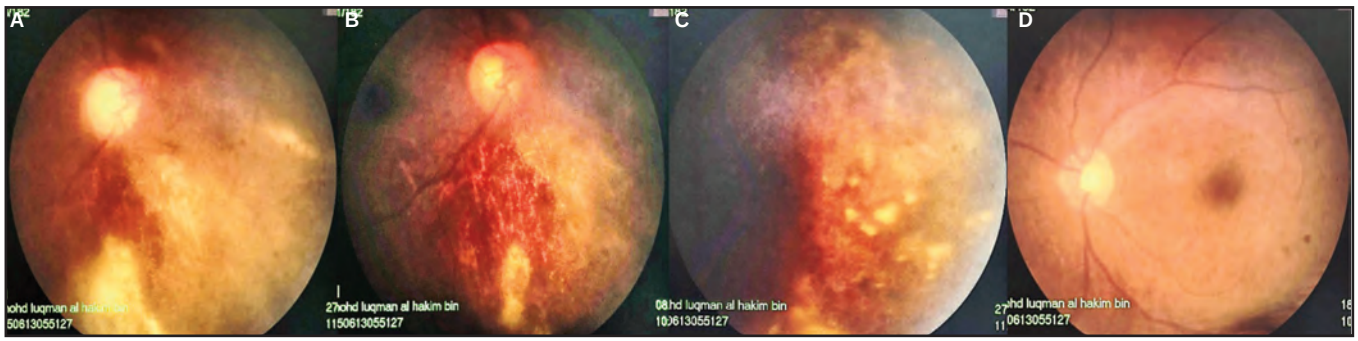

Fig. 2: (A, B) Shows the fundus view of the RE during reactivation of CMV retinitis characterised by inferior vitritis and wedge-shaped retinitis involving Zone 1(C) Shows the fundus view of the LE during reactivation of CMV retinitis characterised by dense vitritis*, retinitis, and fibrotic changes from 1–4 and 10–11 o'clock and (D) LE fundus post treatment 3 months

retinal whitening with granular borders in the setting of profound immunosuppression, with a nadir CD4 count of 44 cells/µL. Ocular fluid polymerase chain reaction (PCR) was not performed as the clinical features were classical. HIV retinopathy was considered less likely, as the lesions were progressive rather than limited to microvascular changes. There were no choroidal granulomas or occlusive vasculitis suggestive of ocular tuberculosis.

Topical corticosteroid (Gutt Maxitrol, both eyes [BE], four-hourly), cycloplegic (Gutt atropine 1%, BE, once daily), and anti-glaucoma medication (Gutt timolol 0.5%, BE, twice daily) were commenced to control anterior segment inflammation and secondary elevated intraocular pressure of 24 mmHg in both eyes. Systemically, oral valganciclovir 900 mg twice daily was administered for two weeks as induction therapy, followed by once-daily maintenance dosing for a further two weeks.

The patient was evaluated clinically for extraocular CMV involvement. There were no gastrointestinal, pulmonary, or neurological symptoms suggestive of systemic CMV disease. At the time of presentation, both intravenous (IV) and intravitreal (IVT) ganciclovir were unavailable at the treating centre owing to logistical and resource limitations. Given the absence of systemic CMV involvement and local drug availability constraints, induction therapy with oral valganciclovir was initiated. Oral valganciclovir is an accepted induction agent for CMV retinitis in the absence of systemic involvement, achieving systemic drug exposure comparable to intravenous administration. Vision improved to 6/9 bilaterally, with resolving retinitis after 2 months.

Seven months following his first presentation, the patient re-presented with bilateral floaters. Visual acuity remained 6/9 in BE. Slit-lamp examination demonstrated fine keratic precipitates and anterior vitreous cells bilaterally. Fundus exam showed reactivation features: the RE had inferior vitritis and wedge-shaped retinitis involving Zone 1 (Figure 2, A, B), while the LE showed dense vitritis, retinitis, and fibrotic changes from 1–4 and 10–11 o'clock (Figure 2, C). CD4 count dropped to 24 cells/µL, and HIV viral load remained high (1.53 million). He was treated with IV ganciclovir 300 mg BD and BE IVT ganciclovir injections (RE: 9 doses; LE: 5 doses). IVT ganciclovir (2 mg/0.05 mL) was administered weekly as induction therapy. The RE required a total of nine injections owing to slower resolution of zone 1 retinitis with persistent active borders, whereas the LE received five injections following earlier lesion inactivity and clinical improvement. Following IVT therapy, both eyes demonstrated a gradual reduction in retinal whitening and haemorrhages, with decreased vitritis. The retinitis borders eventually became inactive, with residual retinal scarring. A 21-day IV regimen was completed, followed by ongoing ophthalmic and infectious disease surveillance.

In February 2025, approximately five months later, the patient presented with progressive blurring of vision bilaterally, with visual acuity in the LE reduced to hand movements temporally. Anterior segment was unremarkable. Fundus examination of LE revealed inferior rhegmatogenous retinal detachment (RRD) from 4 to 8 o'clock with macula off. The patient underwent pars plana vitrectomy, endolaser photocoagulation, and silicone oil tamponade. Intraoperatively showed subtotal RRD with a retinal break at 8 o'clock and hyperpigmented scar at 2 o'clock. Postoperatively, the retina remained flat with silicone oil in situ, and visual acuity in the LE improved to counting fingers at 3 feet.

DISCUSSION

This case is noteworthy due to the presence of documented multidrug antiretroviral therapy (ART) resistance with virological failure, limited access to antiviral therapy, and the development of macula-off retinal detachment despite treatment. Although Cytomegalovirus (CMV) retinitis is a well-recognised opportunistic infection in advanced HIV, this case warrants reporting due to the presence of documented multidrug antiretroviral therapy (ART) resistance with virological failure, limited access to intravenous (IV) and intravitreal (IVT) antiviral therapy, and the development of macula-off retinal detachment despite treatment. These factors highlight contemporary management challenges in resource-limited settings.

CMV retinitis is most commonly observed in patients with CD4 counts below 50 cells/μL. The patient demonstrated poor viral suppression despite ART, likely secondary to antiretroviral resistance. This immunocompromised state predisposed him to severe bilateral CMV retinitis with reactivation.

This case illustrates several management challenges in CMV retinitis, particularly in patients with ART failure and significant systemic comorbidities. The absence of timely access to IVT therapy at initial presentation may have contributed to reactivation and eventual retinal detachment.[4] Reactivation rates are higher in patients with inadequate immune recovery or ongoing viraemia.

Furthermore, delayed ART optimisation owing to resistance patterns may prolong immunosuppression, increasing the risk of opportunistic infections and complications such as CMV reactivation. Differentiating between CMV reactivation and immune recovery uveitis remains a diagnostic challenge, particularly in patients recently transitioned to new ART regimens.

IVT ganciclovir is the treatment of choice for zone 1 retinitis, typically in combination with systemic antiviral therapy.[4] The patient responded well to a combination of IV and IVT ganciclovir during reactivation. Retinal detachment is a recognised complication of CMV retinitis, occurring particularly in eyes with extensive necrotic involvement. In the present case, the left eye (LE) developed macula-off RRD despite ART optimisation. During serial follow-up, peripheral retinal necrosis was closely monitored; no identifiable retinal breaks were detected to warrant prophylactic barrier laser treatment. Despite apparent clinical quiescence, structural retinal thinning likely predisposed the eye to delayed detachment.

At initial presentation, the LE demonstrated relatively milder zone 2 involvement compared with the right eye (RE), and both eyes received identical systemic antiviral therapy. The only difference in management was the number of intravitreal ganciclovir injections, which was determined by clinical response. Despite the milder initial presentation, the LE subsequently developed RRD. Retinal detachment in CMV retinitis is primarily attributable to necrotic retinal thinning and delayed atrophic break formation, rather than initial disease severity alone. Even eyes with apparently controlled retinitis remain structurally vulnerable; detachment may occur despite adequate antiviral therapy.

Multidisciplinary coordination between ophthalmology, infectious disease, and HIV care providers is crucial for early detection, systemic immune optimization, and timely ocular management.

CMV retinitis remains a significant cause of visual morbidity in the setting of advanced HIV infection. This case illustrates the potentially aggressive course and risk of reactivation and retinal detachment in patients with inadequate immune recovery. Early diagnosis, appropriate systemic and intravitreal antiviral therapy, and multidisciplinary care are essential for optimising visual outcomes.

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