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Blurred Vision After a Kidney Transplant

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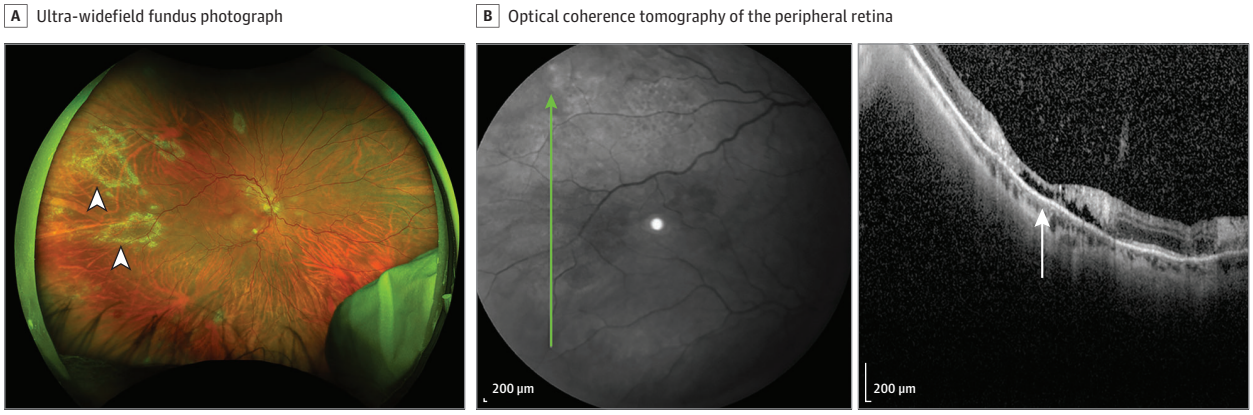

Figure 1. Ultra-widefield fundus photograph and optical coherence tomography of a necrotic retinal lesion in the right eye demonstrating (A) multiple cotton wool spots along the arcades with retinal lesions in the temporal periphery (arrowheads) and (B) a cross-section through a temporal lesion along the superior arcade showing full thickness retinitis (arrow).

A patient in their mid-30s with a medical history of deceased donor kidney transplant, cytomegalovirus (CMV) colitis, and CMV viremia with documented resistance to foscarnet and ganciclovir (*UL97* and *UL54* gene mutations) presented with new-onset floaters in both eyes. The patient was taking systemic immunosuppression but recently stopped taking maribavir because of concerns about resistance and was transitioned to cidofovir and CMV immune globulin. On clinical examination, the visual acuity measured 20/25 OD and 20/20 OS. Motility, visual fields, and anterior segment examination were normal. Dilated fundus examination revealed tortuous vasculature, multiple cotton wool spots along the arcades and periphery, and granular, hypopigmented retinal lesions without hemorrhage in the macula and temporal periphery in both eyes (**Figure 1**A). Optical coherence tomography showed localized areas of full-thickness retinitis (Figure 1B). CMV titers indicated viremia at 2.24 million IU/mL. Despite the patient's documented *UL97* and *UL54* mutations, a series of 5 biweekly intravitreal injections of foscarnet and ganciclovir were performed given their vision-threatening lesions. Retinal pathology failed to improve, and the patient eventually refused additional intravitreal therapy because of pain and transiently decreased vision after each injection.

WHAT WOULD YOU DO NEXT?

- **A.** Observation with systemic cidofovir and CMV immune globulin
- **B.** Multivirus-specific cytotoxic T lymphocytes (CTLs)
- **C.** Continued foscarnet and ganciclovir intravitreal injections
- **D.** Leflunomide initiation

Quiz at jamacmelookup.com

Diagnosis

***UL97*- and *UL54*-resistant CMV retinitis**

What to Do Next

B. Multivirus-specific cytotoxic T lymphocytes (CTLs)

Discussion

Treatment of CMV retinitis is a challenging situation in patients who have undergone transplant because they require long-term immunosuppression and therefore must also receive ongoing antiviral therapy for an increasingly resistant virus. The option of systemic cidofovir and CMV immune globulin or continued treatment with intravitreal ganciclovir and foscarnet would be suboptimal, as no significant improvement was seen using these medications in the context of documented mutations in the *UL97* and *UL54* genes. A mutation in the *UL97* gene confers resistance to ganciclovir and valganciclovir, while mutation in the *UL54* gene confers resistance to ganciclovir, valganciclovir, foscarnet, and cidofovir.[1-3] Furthermore, the patient did not tolerate biweekly intravitreal injections because of pain and transient vision changes. Leflunomide would be an option; however, in the context of the patient's high viral load, resistance would likely develop quickly, resulting in only a transient effect.[4]

Cytotoxic T lymphocytes are a novel therapy for CMV retinitis that is refractory to available therapies. A type of immunotherapy,

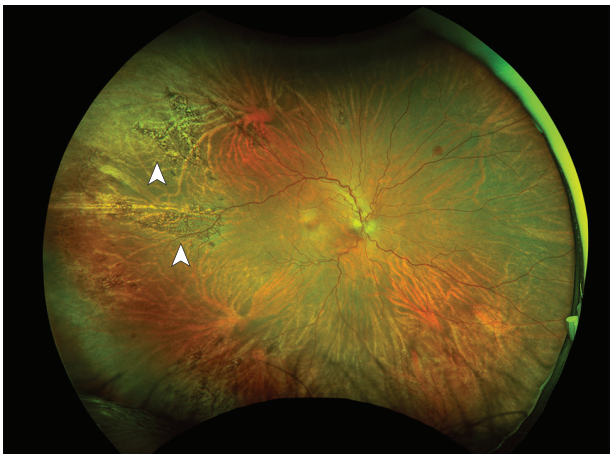

Figure 2. Ultra-widefield fundus photograph of the right eye after multivirus-specific cytotoxic T-lymphocyte therapy demonstrates resolution of active cytomegalovirus retinitis and cotton wool spots with residual areas of partially pigmented scarring (arrowheads).

CTLs involve adoptive transfer of donor T cells to provide a virus-specific immune response to clear infection.[5] This patient received posoleucel, a multivirus-specific T-cell therapy, with dramatic improvement in both retinal findings (**Figure 2**) and CMV titers (2.24 million IU/mL to 14 700 IU/mL) 1 month after the first infusion. There was complete resolution of active retinitis with residual scarring. Visual acuity remained stable at 20/20 OD and 20/25 OS.

There have been a handful of cases in the literature on outcomes of CMV retinitis treated with CTL therapy.[5-7] Gupta et al[5] presented a series of 7 patients treated with CMV-specific T cells in which 90% of eyes achieved disease resolution and 80% had stable or improved visual acuity. Prior to CTL therapy, all patients had progressive retinitis despite systemic and intravitreal antiviral therapy. Three patients had *UL97* mutations, and 1 patient had a *UL54* mutation. Underlying immunosuppression was secondary to stem cell transplant in 4 patients, AIDS in 2 patients, and kidney transplant in 1 patient.[5] Treatment was well tolerated in the limited sample size with no cases of immune recovery uveitis, 1 case of cystoid macular edema, and 2 cases of retinal detachment.[5] In addition to ocular adverse effects, systemic adverse effects of CTL therapy described in the oncology literature can include cytokine release syndrome, immune effector cell-associated neurotoxicity syndrome, and cytopenias.[8] Compared with the series from Gupta et al,[5] we used multivirus-specific T-cell therapy rather than CMV-specific T cells.

Patient Outcome

The patient returned 8 weeks after their initial diagnosis (6 weeks after the first infusion) with decreased vision. Best-corrected visual acuity was 20/70 OD and 20/60 OS. Optical coherence tomography showed new subretinal fluid under the fovea in both eyes, and retinal thickness had increased (right eye: 273 to 336 µm; left eye: 273 to 324 µm). CMV lesions in both eyes remained inactive. Unfortunately, before any additional testing could occur, the patient rapidly declined from complications of posttransplant lymphoproliferative disorder and transitioned to hospice. The patient's decreased vision could represent an adverse effect of CTL therapy or cidofovir, but the critically ill status of the patient precluded definitive diagnosis. Overall, CTL therapy is a promising novel therapy that requires further investigation, ideally with prospective trials, to evaluate its role in the treatment for CMV retinitis.

ARTICLE INFORMATION

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