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Rapidly Progressive Neovascular Glaucoma Associated with Atypical Cytomegalovirus Retinitis: A Case Report

Dear Editor,

Cytomegalovirus (CMV) retinitis is a vision-threatening disease that is often accompanied by human immunodeficiency virus (HIV) infection and systemic immunosuppression. Previous studies have reported neovascular complications caused by HIV-related CMV retinitis. However, little is known about CMV retinitis with immunocompetent and neovascular glaucoma. To the best of our knowledge, this is the first report of neovascular glaucoma (NVG) in atypical CMV retinitis caused by intravitreal triamcinolone acetonide injection (IVTA).

A 59-year-old male patient with peripheral T cell lymphoma and diabetes presented with decreased visual acuity 4 months after IVTA due to pseudophakic cystoid macular edema. The patient was HIV-negative, and his last chemotherapy was completed a year prior. His visual acuity was 20 / 60. The left eye had 1+ anterior chamber and vitreous cells with an open angle on gonioscopy. Whitish retinal infiltrations of the retina and diffuse arterial vascular sheathing were found (Fig. 1A).

A presumptive diagnosis of vitreoretinal lymphoma and CMV retinitis was made, and vitreous and aqueous sampling were performed. CMV polymerase chain reaction test was positive, the leukocyte count was within normal limits (4,700 cell/mm^3) and the brain magnetic resonance imaging and positron emission tomography-computed tomography revealed no abnormal findings. Fluorescent angiography (FAG) showed no delay in filling time of early phase in the area except of a wide capillary nonperfusion and late phase leak in the infiltration area (Fig. 1B). The diagnosis was CMV retinitis.

Intravitreal ganciclovir (2 mg/0.04 mL) injection was started and 15 days after the first injection, a new vessel was observed in the iris with uncontrolled intraocular pressure (32 mmHg) and the visual acuity dropped to 20 / 1,000 due to corneal edema. Therefore, intravitreal bevacizumab injection was performed, and the neovascularization of the iris improved after 2 weeks of intravitreal bevacizumab injection and intraocular pressure decreased to 16 mmHg. Seven ganciclovir injections were administered over a month, and the patient had oral valganciclovir for 3 weeks. Compared to the wide FAG performed 3 months previously, extensive areas without perfusion were identified in the affected eye, while the perfusion status was relatively good in the fellow eye, and the patient underwent panretinal photocoagulation (Fig. 1C-1F). At the final follow-up, 10 months after presentation, visual acuity remained at 20 / 60 in the treated eye.

The patient in this case was HIV-negative, relatively immunocompetent with a white blood cell count of 4,700 mm^3 and had completed chemotherapy a year previously. CMV retinitis developed unilaterally 4 months after IVTA. There have been reports of CMV retinitis occurring after intraocular steroid injection in immunocompetent patients. In these studies, CMV retinitis occurred 3 to 7 months after intraocular injection [1,2]. A local reduction in immunity caused by steroids may have caused CMV retinitis as in these previous studies.

Regarding the neovascular complications arising from HIV-related CMV retinitis, it was thought that immune recovery and HIV microangiopathy cause retinal capillary nonperfusion [3]. There are also increasing reports of neovascular cases of CMV retinitis in patients without HIV. Schneider et al. [4] reported five cases of CMV retinitis in patients with HIV, of whom two developed neovascularization of the iris and two developed neovascularization elsewhere. Although it was not as fast as acute retinal necrosis caused by Herpes simplex virus and Varicella zoster virus, the patients exhibited necrotizing retinitis, occlusive vasculitis, and vitritis, which the authors referred to as "chronic retinal necrosis." CMV spread was considered limited due to the patients' immunocompetency, however, immunologic tissue damage occurred, leading to retinal

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vascular changes.

In our case, during CMV retinitis treatment with an antiviral agent, the nonperfused area increased, and NVG occurred within a few weeks. There have been previous reports that patients with non-HIV-related CMV retinitis may have higher rates of neovascular complications [4,5]. Unlike typical CMV retinitis, panretinal occlusive vasculitis was severe in our patient. As the nonperfusion area increased even more after aggressive antiviral treatment, the increase in the immune response caused by the antiviral agent may have affected this. Further research is needed to understand the underlying mechanisms.

In summary, this study is the first report of NVG in atypical CMV retinitis caused by IVTA. In patients without HIV, CMV retinitis can develop even in patients with normal systemic immunity. If CMV retinitis occurs in

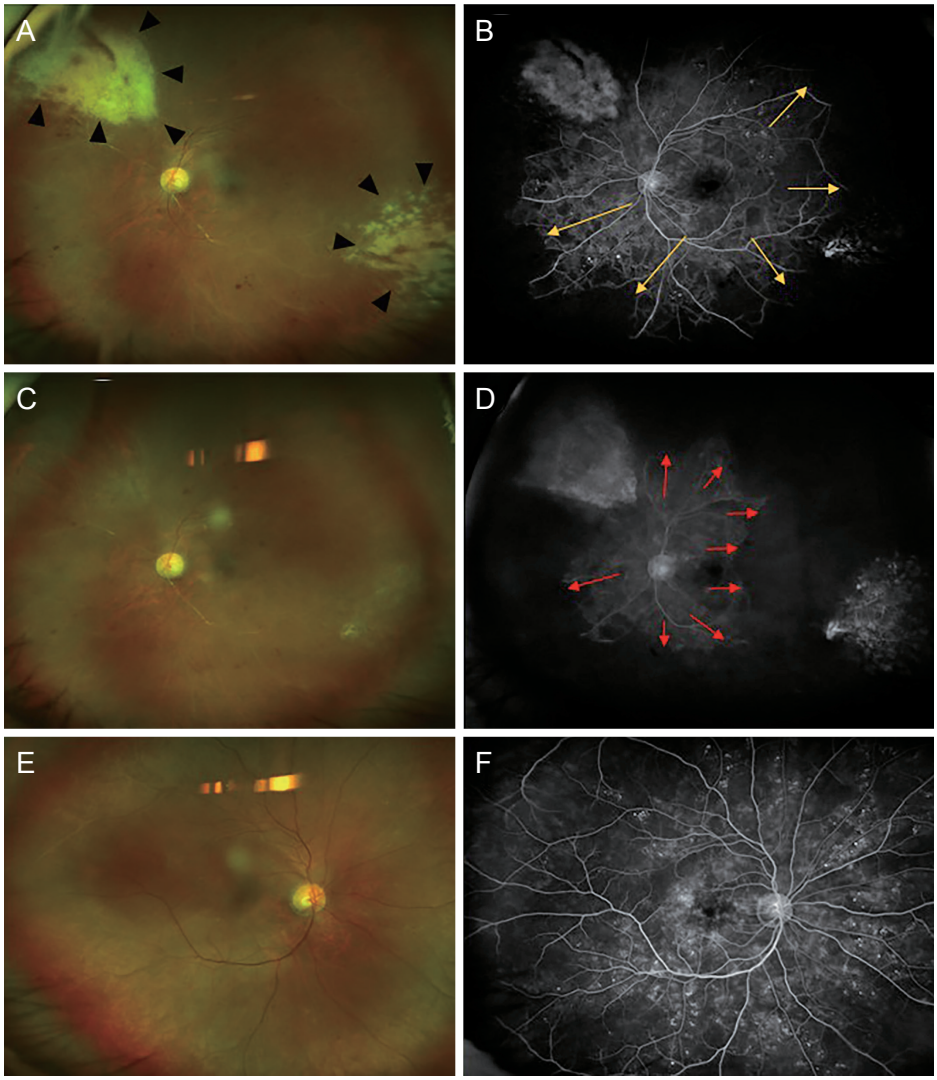

Fig. 1. Changes of retinal capillary nonperfusion area and status of contralateral eye. Wide-field fundus photography and late phase of fluorescent angiography at (A,B) 4 months after intravitreal triamcinolone acetonide injection and 3 months after initiation of (C,D) antiviral therapy and (E,F) contralateral eye. (A) Note the foci of retinitis (black arrowheads) associating retinal whitening, hemorrhages, vascular sheathing, and generalized retinal vascular narrowing in the 10 o'clock and 4 o'clock positions. (B) The granular hyperfluorescence in the 10 o'clock and 4 o'clock positions is seen (yellow arrows). (C) The size of retinal infiltration markedly decreased. Retinal vascular narrowing and hemorrhage are seen. (D) The granular hyperfluorescence at the area of retinitis in the 10 o'clock and 4 o'clock positions is seen. The capillary nonperfusion area (red arrows) was further expanded. (E,F) In the contralateral eye, some retinal hemorrhages were observed, and there were no suspicious findings such as dye filling time delay or nonperfusion area on the wide fluorescent angiography. The patient provided written informed consent for publication of the research details and clinical images.

ischemia-vulnerable conditions, neovascular complications may occur rapidly, even if antiviral therapy is appropriately performed. Therefore, it could be helpful that patients with non-HIV-related CMV retinitis should be closely monitored with anti-vascular endothelial growth factor treatment and panretinal photocoagulation in mind.

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