JAMA Ophthalmology Clinical Challenge

Bilateral Blurry Vision After a Liver Transplant

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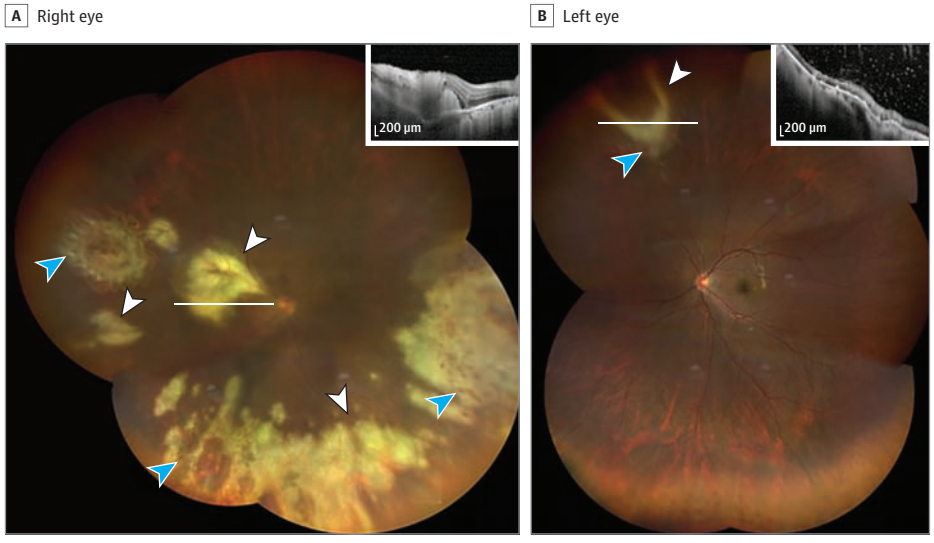

Figure 1. Bilateral necrotic lesions in the right eye (A) and left eye (B) at the first visit to the clinic. The white lines show the locations of the optical coherence tomography scans on the retina. Patches of yellowish full-thickness necrotic lesions were seen at the posterior pole and peripheral area of the retina (white arrowheads). Previous laser spots are present around areas of necrosis (blue arrowheads). Characteristic subretinal exudates are seen along the retinal pigmented epithelium layer, with intraretinal fluid at the yellow-white area.

A 31-year-old woman presented for evaluation of bilateral blurry vision over the past month. She experienced fulminant hepatic failure 3 months ago and underwent a liver transplant 2 weeks later. Postoperative pathological results showed hepatolenticular degeneration. Routine prophylactic antiherpes virus therapy had been applied for 2 weeks. Immunosuppressants, including tacrolimus and mycophenolate sodium, were applied for subsequent maintenance therapy. She noticed the onset of decreased vision in both eyes about 2 months after the liver transplant. Diagnosed with ocular herpes virus infection, she was given systemic valaciclovir and ocular laser retinopexy around areas of necrosis. Her vision was not improved and twice intravitreous injection of ganciclovir was added. However, vision was decreasing continuously.

At her presentation to our clinic, the best-corrected visual acuity was finger count in the right eye and 20/125 in the left eye. On slitlamp examination of both eyes, 1+ aqueous cells and 1+ flare were presented in the anterior chamber, while the dilated fundus examination showed mild inflammation in the vitreous. Extensive patches of yellowish necrotic lesions were seen at the peripheral retina of the right eye and 1 triangular necrotic lesion in the posterior pole (**Figure 1**A). A large annular necrosis was found in the peripheral retina of the left eye (Figure 1B).

WHAT WOULD YOU DO NEXT?

A. Find new microbial pathogens by intraocular fluid analysis to clarify the diagnosis

B. Increase the dose of ganciclovir for antiherpes virus

C. Add systemic steroids for the treatment of inflammation

D. Stop all immunosuppressants

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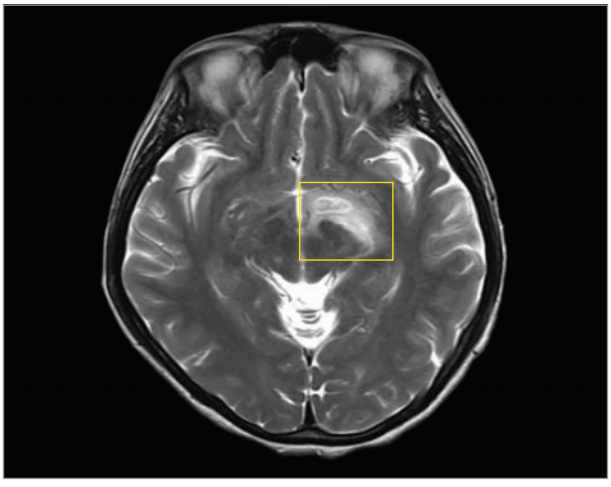

Figure 2. Magnetic resonance imaging (T1-weighted, gadolinium-enhanced) demonstrated an about 30.6 × 12.8 × 17.6-mm lesion with an enhanced annular edematous edge (yellow box) in the left dorsal thalamus.

Diagnosis

Toxoplasma retinochoroiditis

What to Do Next

A. Find new microbial pathogens by intraocular fluid analysis to clarify the diagnosis

Discussion

Herpes virus is not the only pathogen that could cause retinal necrosis. We acquired aqueous humor samples from the patient's right eye immediately for a pathogen test to clarify the diagnosis (choice A). Cytomegalovirus, herpes simplex virus, Epstein-Barr virus, and varicella-zoster virus DNA were 0 copies per mL, while 3.7×10^5 copies per mL of *Toxoplasma gondii* DNA was reported. Laboratory test results for HIV, syphilis, tuberculosis, and hepatic virus were negative. Thus, the diagnosis of toxoplasma retinochoroiditis was established. Since *Toxoplasma gondii* is neurotropic and could cause fatal central nervous system infection, we referred the patient for a magnetic resonance imaging scan of the brain. The results showed a large patchy lesion with an enhanced annular edematous edge in the left dorsal thalamus (**Figure 2**).

Increasing the dose of ganciclovir for antiherpes virus (choice B) or adding systemic corticosteroids (choice C) would not be the preferred answers because each had been applied at sufficient doses. Moreover, increasing systemic corticosteroids might increase the risk of other severe infections. Stopping immunosuppressants (choice D) risks transplant rejection.

Routine application of long-term immunosuppressive therapies after transplants can increase the risk of opportunistic infections. When there are necrotic changes in the retina, herpes viruses, especially cytomegalovirus, are common secondary infectious pathogens. Other possible infections include treponema pallidum, tuberculosis, and toxoplasmosis infection.

Gondii can cause serious damage. The seroprevalence is generally assumed to be about 20% to 30% worldwide.[1,2] In this case, toxoplasmosis did not present with a classic "lamplight in the fog" in association with the patient's immunosuppressed state. Some early reports of blurred vision in immunosuppressed patients were mostly diagnosed as virus associated.[3-5] In these cases, patients' vision remained in bad condition or even deteriorated to enucleation with continuous application of antivirus-only treatments.

Gondii is known for its neurotrophic characteristics.[6] In immunocompetent patients, the infection can cause mild manifestations and is usually self-limited. In immunocompromised patients, the parasite can reach anywhere in the central nervous system and can cause life-threatening brain damage.[7] Studies suggest that *gondii* invades the cerebral vascular endothelial cells either by increasing the migratory ability of immune cells or infecting the endothelial cells directly.[8] Once inside the brain, *gondii* can target the neurons primarily or can turn into a chronic infection.[8,9]

Patient Outcome

The patient was given antimicrobial drugs that target the *gondii*, including azithromycin and sulfamethoxazole-trimethoprim. Systemic immune suppressant dosage was decreased. The patient also started topical steroids for the treatment of ocular inflammation. Lesions in the eyes and the brain reacted to the systemic antitoxoplasma medications. One week later, the retinal necrotic lesions were stabilized. Best-corrected visual acuity had improved to 20/200 in the right eye and 20/63 in the left. Magnetic resonance imaging scan of the brain was normal 2 months later.

ARTICLE INFORMATION

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