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# Bilateral Toxoplasma Retinochoroiditis Simulating Cytomegalovirus Retinitis in an Allogeneic Bone Marrow Transplant Patient

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A 36-year old female with acute myelogenous leukemia presented with a sudden decrease in vision one month following bone marrow transplantation (BMT). She had been taking multiple immunosuppressants to treat her recently-developed graft-versus-host-disease (GVHD). Visual acuity was 20/60 in her right eye and 20/25 in her left. Ophthalmic examination revealed mild inflammatory reaction in both the anterior chamber and the vitreous of both eyes, as well as densely opaque yellow-white infiltrates with well-demarcated borders in the posterior retina of both eyes. She was originally diagnosed as CMV retinitis, but treatment with ganciclovir failed to improve her ocular condition. Subsequent work-up, including serology and brain MRI, led to a diagnosis of combined ocular and cerebral toxoplasmosis. After 6 weeks of antiparasitic therapy, her retinal lesions became inactive and her cerebral lesions improved.
Immunosuppressed patients with necrotizing retinochoroiditis should be suspected of having toxoplasmosis. Accurate differentiation between this condition and CMV, and early intervention with the appropriate treatment may be critical to preserve the best vision.


**Key Words:** Bone marrow transplantation, Toxoplasmic retinochoroiditis

## Case Report

A 36-year-old woman who had undergone allogeneic bone marrow transplantation (BMT) for acute myelogenous leukemia (M4) 2 months previously was referred with a complaint of decreased vision for 2 days.

Since BMT, she had been under multiple regimens including intravenous ciprofloxacin, fluconazole and acyclovir as a prophylaxis for bacterial, fungal and herpes viral infections. For the prophylaxis for Pneumocystis pneumonia, monthly inhalation of pentamidine (a dose of 300mg in a nebulizer) was used and trimethoprim/sulfamethoxazole was not given. She also had been taking methylprednisolone (1.9 mg/kg, daily), cyclosporine (1.4 mg/kg, daily) and mycophenolate mofetil (7.1 mg/kg, daily) for the treatment of BMT-induced graft-versus-host-disease (GVHD).

Ophthalmic examination revealed visual acuity of 20/60 in the right eye and 20/25 in the left. There were mild cellular reactions in the anterior chambers and vitreous humors of both eyes. Densely opaque, yellow-white curvilinear infiltrates of 2 disc area size were observed with a small satellite lesion at the posterior retina of her right fundus. A similar infiltrate was also identified temporal to the macula in her left eye (Fig. 1). No retinal hemorrhage was found. Blood test showed positive CMV antigenemia (12/200,000 WBC). Necrotizing retinitis in the posterior pole with CMV antigenemia in this immunocompromised patient prompted us to make diagnosis of CMV retinitis. However, despite 2 weeks treatment with intravenous ganciclovir (2.5 mg/kg daily, dose adjusted to her glomerular filtration rate), her retinal lesion worsened and new satellites appeared (Fig. 2). In addition her vision had decreased to 20/400 in the right eye, and 20/60 in the left.

A subsequent blood test revealed the negative conversion of CMV antigenemia, but showed positive for serum toxoplasmosis antibody (both IgM and IgG by ELISA). At this time, the patient's mental status changed for the worse and a brain imaging was performed. The finding of multifocal, ill-defined nodular enhancing lesions in cerebral, cerebellar hemispheres and basal ganglia was consistent with toxoplasmic involvement of CNS (Fig. 3). The cerebrospinal fluid analysis was normal in cell counts, protein and glucose and the CSF culture for fungus and bacteria were all negative.

With a presumed diagnosis of concomitant toxoplasmic

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* This study was presented at the combined meeting of Club Jules Gonin and the Retina Society, Oct 2006, as a poster.

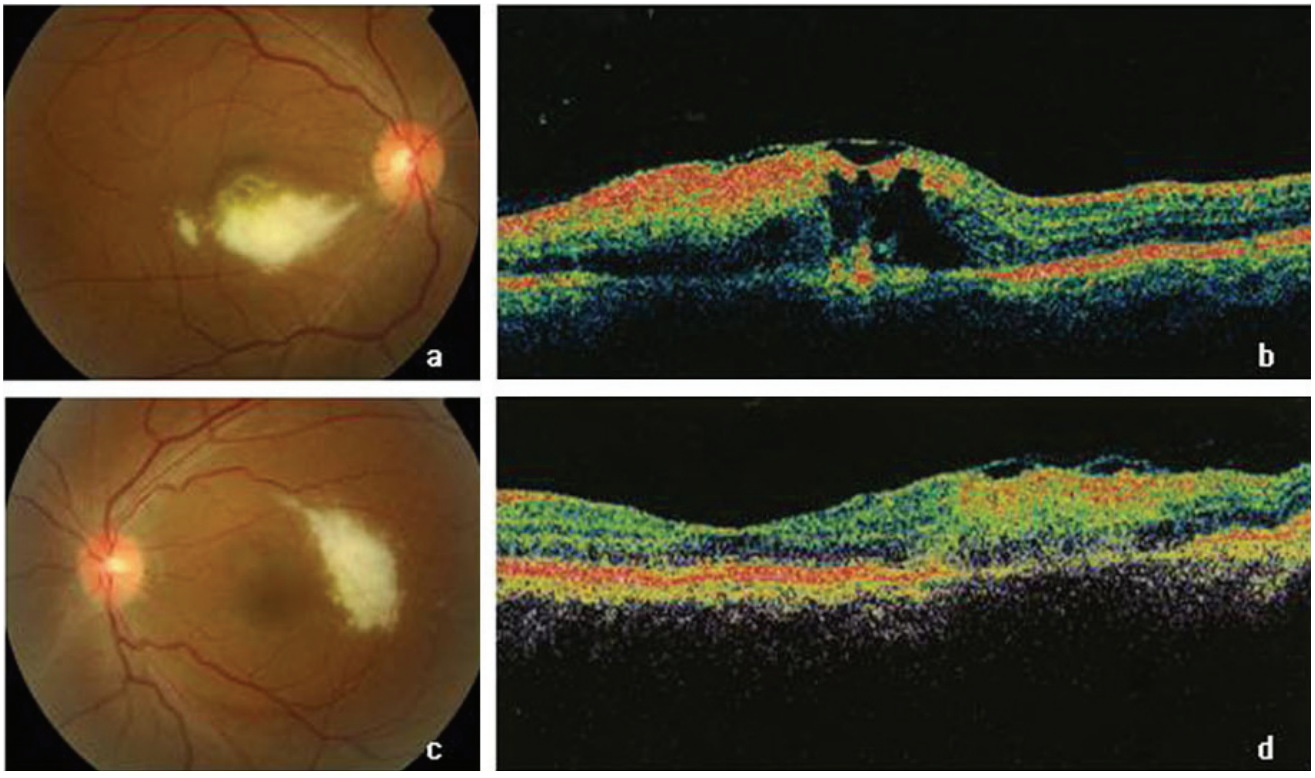


**Fig. 1.** Fundus photographs and optical coherence tomography (OCT) at presentation in the patient's right (a, b) and left (c, d) eyes. Her visual acuity was 20/60 in the right eye and 20/25 in the left eye.

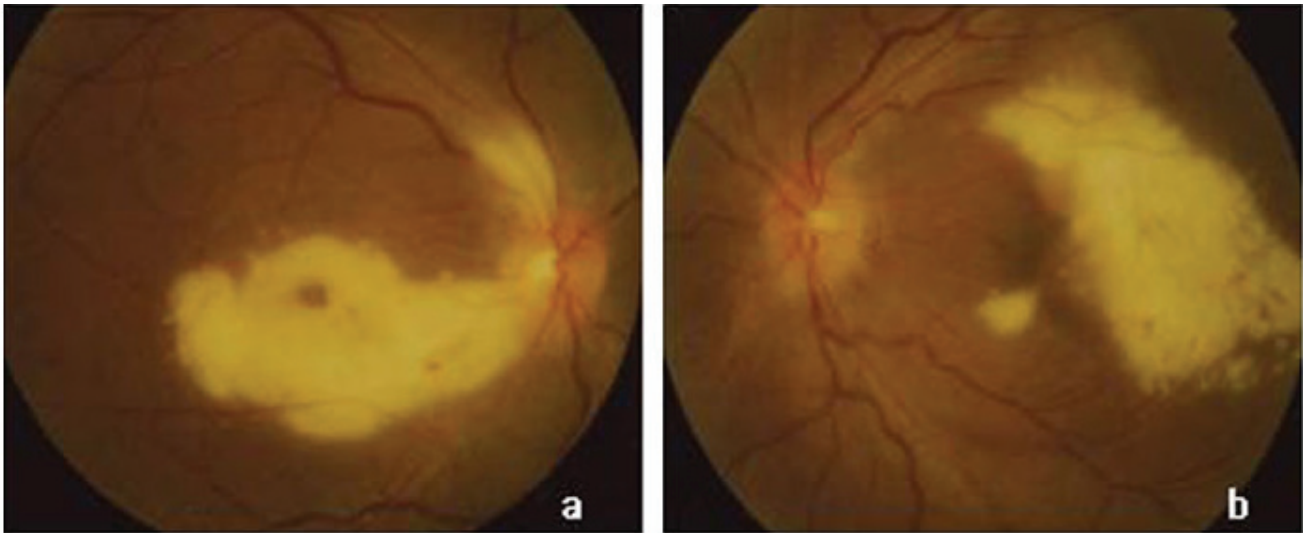


**Fig. 2.** Fundus photographs of both eyes 2 weeks after the initiation of intravenous ganciclovir (a, b). Her visual acuity had decreased to 20/400 in the right eye and 20/60 in the left eye.

retinochoroiditis and encephalitis, trimethoprim/sulfamethoxazole 5 mg/kg PO BID and clindamycin 600 mg PO QID were started. One week later, the cellular reaction in her anterior chambers and vitreous cavities had disappeared, and the size and thickness of her retinal infiltrates were decreased markedly. Brain MRI showed improvement as well. The inflammatory retinal lesion became inactive following six weeks of therapy; however her right vision failed to improve because of macular involvement (Fig. 4). Visual acuity at the last follow-up was 20/400 in the right eye and 20/80 in the left eye. Brain MRI taken after 6 weeks of therapy showed little evidence of any lesions. At four months after discontinuation of treatment, there was no evidence of ocular or intracranial recurrence.

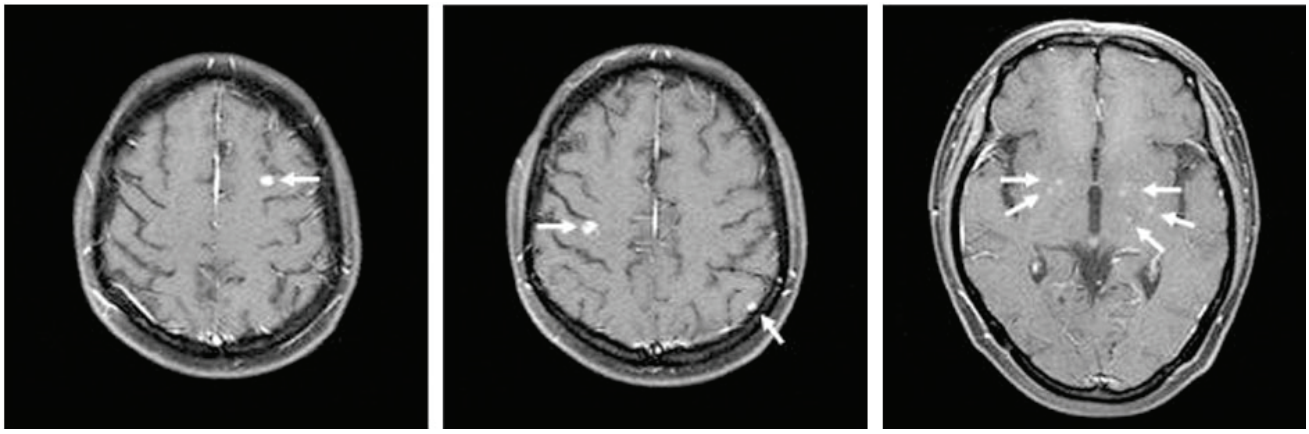

**Fig. 3.** Magnetic resonance imaging of the brain showing multifocal, ill-defined nodular enhancing lesions in both cerebral hemispheres and basal ganglia.

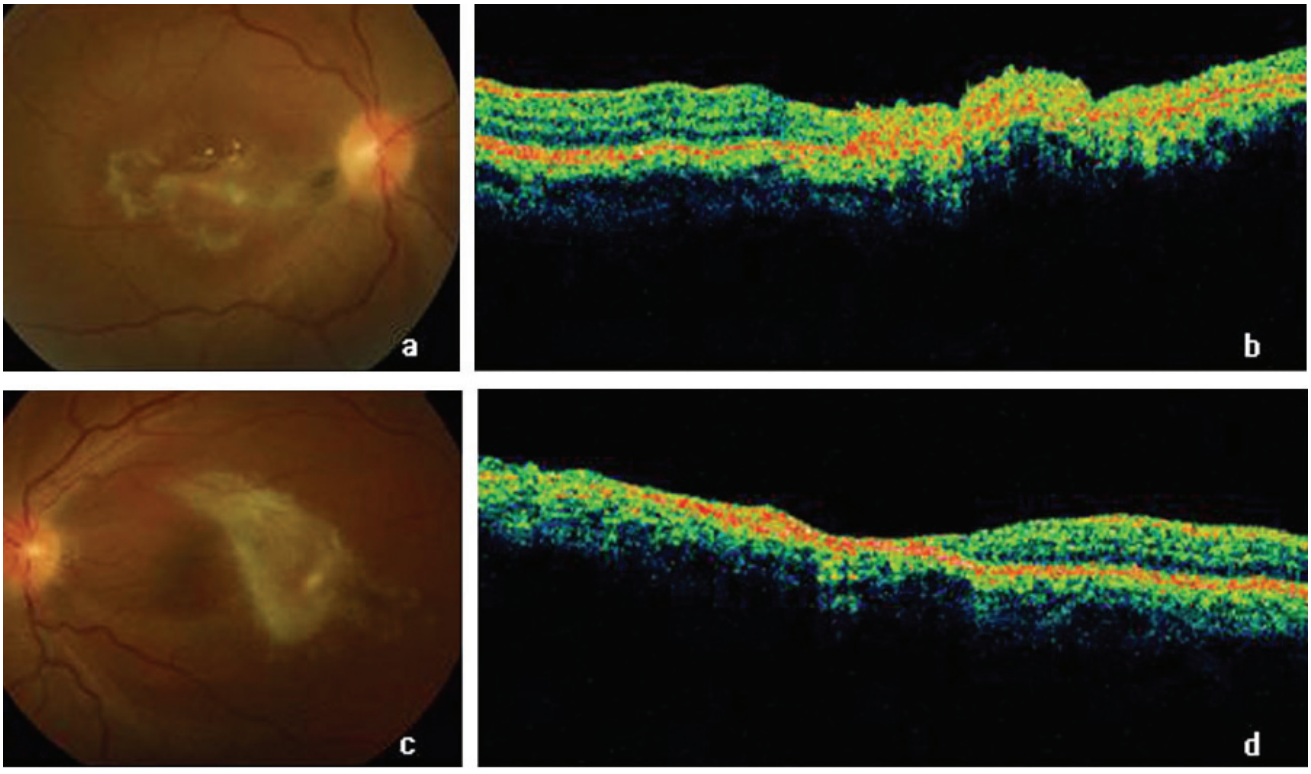


**Fig. 4.** Fundus photographs and OCT of right eye (a, b) and left (c, d) after 6 weeks of antiparasitic therapy. Her visual acuity remained poor due to the formation of epiretinal membrane and atrophy of her neurosensory retinas.

## Discussion

In this study, we have described one interesting case of toxoplasmic retinochoroiditis simulating CMV retinitis with concurrent cerebral toxoplasmosis after allogeneic BMT. In our case, positive serum toxoplasma serology, no use of trimethoprim/sulfamethoxazole as a prophylaxis for Pneumocystis pneumonia after BMT, exacerbation of the condition after intravenous ganciclovir treatment, apparent good response to antiparasitic therapy and concurrent encephalitis with multiple nodular brain lesions suggested toxoplasmosis.

Differential diagnosis of necrotizing retinochoroiditis in immunocompromised hosts has been challenging.[1-4] Compared with CMV retinitis, toxoplasmic retinochoroiditis has clinical features of mild to moderate inflammatory reactions in the anterior chambers and vitreous, an absence of retinal hemorrhages, and opacified retinas that appear thicker and more densely white-yellow. In addition, the borders of the lesions are better defined and smoother in contour. While CMV has become the most frequent cause of necrotizing retinochoroiditis since the advent of AIDS, other

causes such as toxoplasmosis or herpes should be considered as a possible pathogen. Therefore, one should perform serum toxoplasma serology in such patients, especially when exacerbation of the condition was noted following intravenous ganciclovir treatment like in our case.

Our case holds additional several interesting characteristics: 1) development of retinal hemorrhage during the aggravation phase, 2) concurrent encephalitis which has rarely been reported in non-AIDS ocular toxoplasmosis cases, and 3) bilateral simultaneous involvement unlike most cases which are either unilateral or sequentially bilateral.[1,3,4]

Toxoplasmosis in the immunocompromised including BMT patients was known to be usually through reactivation of latent infection.[5] Because IgM for toxoplasmosis could last for several years and we had not performed the serology test for toxoplasmosis in both the patient and the donor before BMT, it is difficult to assume the accurate routes of infection. However, primary infection via donor marrow or transfusion also could be a possible mode of infection considering her positive toxoplasmosis IgM.

In conclusion, toxoplasmic retinochoroiditis in immunosuppresed patients is very different from that in immunocompetent patients, and can be easily confused with CMV retinitis. Toxoplasmosis should be considered as a pathogen for the necrotizing retinochoroiditis in immunocompromised patients with anti-CMV therapy failures. High index of suspicion is essential to make an accurate differential diagnosis.

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