Presumed Choroidal Atypical Tuberculosis Superinfected with Cytomegalovirus Retinitis in an Acquired Immunodeficiency Syndrome Patient: A Case Report

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Background: To report an unusual case of multifocal choroidopathy with uveitis and cytomegalovirus (CMV) retinitis in a patient with acquired immunodeficiency syndrome (AIDS) after initially presenting with pulmonary tuberculosis (Mycobacterium kansasii).

Case: Slit-lamp biomicroscopy and indirect ophthalmoscopic examination were done. Vitreous biopsy, pars plana vitrectomy, and retinal biopsy were performed. Computer tomography scan, magnetic resonance imaging and biopsy of the brain were also carried out.

Observations: Multiple yellowish-white, round, slightly elevated subretinal pigment epithelium lesions were noted in areas devoid of the atrophic retina of previous CMV infection. Anterior uveitis and vitritis were also noted. Vitreous, retina, and brain biopsy did not offer any clue for diagnosis. The visual acuity improved later, along with recovered immunity under the anti-tuberculosis medications and the cocktail therapy for AIDS.

Conclusions: Combined CMV retinitis and atypical tuberculosis chorioretinitis, although rare, can develop in the patients with AIDS. Systemic dissemination of atypical tuberculosis infection should be responsible for the choroidopathy in this patient. Jpn J Ophthalmol 2002;46:463–468 © 2002 Japanese Ophthalmological Society

Key Words: Acquired immunodeficiency syndrome, atypical tuberculosis, choroidopathy, cytomegalovirus retinitis, human immunodeficiency virus.

Introduction

Patients with the acquired immunodeficiency syndrome (AIDS) often have decreasing T4 subsets of lymphocytes, and they are at high risk of developing multiple opportunistic infections and a variety of malignant neoplasms. As the number of patients infected with the human immunodeficiency virus (HIV) increases, the clinical spectrum of eye disease associated with immunosuppression continues to expand. Here we report a case of an HIV-infected patient with pulmonary tuberculosis (TB) and cytomegalovirus (CMV) retinitis presumed to be superinfected with atypical TB choroidopathy.

Case Report

This 36-year-old male patient had been diagnosed with AIDS in May 1997. He was admitted to the Chang Gang Memorial Hospital due to pneumonia (Mycobacterium kansasii) on November 8, 1997. The absolute CD4 cell count was 19 cells/mm³. A triple drug regimen of Isoniazid (oral administration of 300 mg once a day), Rifampicin (oral administration of 450 mg once a day), and Ethambutol (oral administration of 800 mg once a day) combined with cocktail therapy (Lamivudine, oral administration of 150 mg twice a day; Ritonavir, oral administration of 400 mg twice a day; and Zidovudine, oral administration of 100 mg three times a day) had been administered to this patient since that time.

Ophthalmologic examination was requested in June 1998 because of the progressive blurred vision in the right eye for 2 to 3 weeks. The CD4 cell count
at that time was 0.2 cells/mm$^3$. Visual acuity (VA) was 20/250 OD, and 20/25 OS. The slit-lamp examination demonstrated extensive fine keratic precipitates in both eyes and cells in the anterior chambers (grade 3). The pupil reaction of the eyes was sluggish. The fundus of the right eye showed a low-grade vitritis and yellowish-white, full-thickness necrotizing retinitis with hemorrhage along the inferior nasal vascular arcades. Splinter hemorrhage was present in the superior-temporal quadrants. Marked macula edema and disc swelling were also noted. The left eye revealed multiple granular appearing white dots with varying amounts of retinal hemorrhage along the superior nasal and temporal retinal vessel. Under the impression that he had CMV retinitis, he was admitted and intravenous injection of Gancyclovir (250 mg, intravenously every 12 hours) was given for 14 days. The patient was lost to follow-up for 4 months.

The patient returned to our clinic in October 1998 because of the deterioration of vision in his left eye (20/250 OD and 20/100 OS). The anterior segment in both eyes contained mild, fine keratic precipitates. Ophthalmoscopic examination of the right eye showed mild vitreous opacity. Atrophic retina and vessel sheathing were noted at the inferior-nasal side where CMV retinitis had been identified previously. Multiple yellowish, round, subretinal pigment epithelial (sub-RPE) lesions had developed in the superior-temporal area (Figure 1). The left eye revealed moderate vitreous opacity and retinal edema (Figure 2). Gancyclovir was suggested again, but the patient refused treatment. One month later, the VA was 20/200 OD and hand-motion only OS. There was still some low-grade uveitis in the anterior chambers. Vitreous haze blurred the right retina (Figure 3). The yellowish sub-RPE lesions previously noted had become round atrophic spots and new sub-RPE lesions extended more peripherally (Figure 4). The fundoscopic examination of the left eye showed severe vitreous opacity and some sub-RPE yellowish-white lesions similar to that found in the right eye. CMV retinitis was noted on the nasal side, but unknown superinfection was highly suspected. Fluorescein angiography (FAG) of the right eye showed numerous window defects at the round atrophic spots. The yellowish-white sub-RPE lesions showed late stage staining. Marked leakage from the disc was noted.
in the left eye at the late stage (Figure 5). Retinal and vitreous biopsy was suggested, but the patient refused the operation because of his poor general condition.

The patient returned to our clinic in February 1999 because of poor VA: hand-motion 10 cm for both eyes. The absolute CD4 cell count was 26 cells/mm$^3$. There was still marked vitreous haze and the optic discs were moderately pale. Newly developed CMV retinitis was found beneath the macula in the right eye and above the macula in the left eye (Figure 6). In the left eye, the yellowish-white sub-RPE lesions superior to the arcade noted previously had become round, confluent atrophic spots (Figure 7). FAG the right eye showed mild fluorescein dye leak-

Figure 5. The new yellowish-white subretinal pigment epithelial lesions showed late-stage staining (November 13, 1998).

Figure 6. Newly developed cytomegalovirus retinitis was found beneath the macula with yellowish-white subretinal pigment epithelial lesions in peripheral area (February 9, 1999).

Figure 7. Yellowish-white subretinal pigment epithelial lesions superior to the arcade noted previously became round, confluent atrophic spots, and dense vitreous opacity was noted (February 9, 1999).
to provide a diagnosis. Serologic assay for IgG and IgM antibodies against toxoplasmosis was negative. The vitreous cytology and retina biopsy failed to offer any clue for definite diagnosis due to insufficient specimen. The VA improved to 20/2000 OD and 20/1000 OS after the vitrectomy and the vitreous opacity decreased with low dose steroid (Prednisolone 10 mg twice a day) treatment for 2 weeks. According to the patient’s statement, his VA improved after his general condition had improved. Anti-TB drugs were still prescribed because the sputum culture showed *Mycobacterium kansasii*. Cocktail therapy against AIDS was given once again.

Brain computer tomography (CT) arranged in July 1999 showed that the previous brain lesions had disappeared and only multiple old infarctions remained (Figure 10). The CD4 cell count was 266 cells/mm³. His vision continued to improve with the maintenance treatment of anti-TB medication and cocktail therapy against HIV for over 2 years. His immunity partially recovered; multiple old infarctions were noted.

On his last visit on June 18, 2000, his immunity was partially recovered with CD4 cell count 248 cell/mm³. There was still mild vitreous opacity in both eyes with atrophic retinal scars. His VA was 20/60 in both eyes.

**Discussion**

The complex clinical signs and symptoms of the various intraocular infections in patients with AIDS have presented diagnostic challenges to ophthalmologists. The ocular abnormalities that occur among patients with AIDS have been divided into four categories: (a) a noninfectious microangiopathy seen most often in the retina, (b) ocular opportunistic infections, (c) ocular adnexal neoplasm, and (d) neuro-ophthalmic manifestations. CMV retinitis is the most common ocular opportunistic infection among patients who are HIV-positive, occurring with an estimated lifetime cumulative incidence of between 10 and 40%. Various other intraocular opportunistic infectious diseases include toxoplasmosis retinochoroiditis, TB choroidopathy, and histoplasmosis choroidopathy, cryptococcosis, herpes simplex, herpes zoster, and ocular syphilis. Clinical signs of CMV retinitis are well-established and easily recognized as a full-thickness retinal opacity associated with hard exudates and hemorrhages. The infection typically spreads along one of the major vascular arcades. Because of the severe immunosuppression of the patients, there is a minimal amount of overlying vitre-
uous inflammation. CMV infection in the peripheral retina shows granular white opacity of the retina with minimal or no retinal hemorrhage.\textsuperscript{11,12} In our case, in addition to CMV retinitis, there was moderate vitreous opacity and multiple yellowish-white sub-RPE lesions, which are not in the clinical presentation of CMV retinitis.

The toxoplasmosis retinochoroidopathy lesion is characterized by full-thickness necrosis with densely opaque yellowish-white appearance and well-demarcated smooth border.\textsuperscript{13,14} which is different from the yellowish-white sub-RPE lesions seen in our case. Moreover, the serologic assay for IgG and IgM antibodies against toxoplasmosis was negative for our patient, although the results may be negative in profoundly immunosuppressed patients.\textsuperscript{15} Although central nervous system (CNS) lesions are part of the clinical spectrum in toxoplasmosis infection, our patient improved without any anti-toxoplasmosis agent. This made the diagnosis of toxoplasmosis less likely.

In addition to toxoplasmosis, the most common CNS lesions in patients with AIDS are malignant lymphoma.\textsuperscript{16–19} However, the multiple cystic lesions in CNS were not a characteristic finding of CNS lymphoma. The examinations of CSF, biopsy of brain and retina also failed to establish a diagnosis. Moreover, the CNS lesions healed without chemotherapy or radiotherapy. All these made the diagnosis of malignant lymphoma unlikely.

Pneumocystic carinii is the most common systemic opportunistic infection in AIDS.\textsuperscript{20} However, ocular involvement is relatively rare. Fundus changes characteristic of pneumocystic carinii choroiditis consist of slightly elevated, plaque-like, yellowish-white lesions located in the chorioids with minimal vitritis. Fluorescence angiography typically shows hypofluorescence in the early phases. Because there was no systemic pneumocystic carinii infection and the patient’s condition improved without anti-pneumocystic carinii treatment; the diagnosis of pneumocystic carinii choroiditis is not likely.

Croxatto et al first noted bilateral multiple cotton wool spots and two small yellowish-white choroidal nodules with indistinct borders in the nasal macula and superior-temporal quadrant of the right eye in an HIV-infected patient with atypical TB infection.\textsuperscript{21} Blodi et al presented a case of presumed choroidal TB infection in an HIV-infected patient with extensive anterior uveitis. A secluded pupil and multiple yellowish-white sub-RPE lesions with anterior uveitis have been noted.\textsuperscript{22} Lewallen et al reported the retinal finding in Malawian patients with AIDS; interestingly, they described a patient with pulmonary TB and retinitis characterized by a yellow, necrotic retina with hemorrhages in the midperiphery, mild vitreous haze, and tractional posterior retinal detachment.\textsuperscript{23} DiLoreto et al\textsuperscript{24} noted a case of a solitary, nonreactive choroidal tuberculoma in a patient with AIDS. There was no associated inflammation, exudate, hemorrhage, or serous retinal detachment. FAG showed late hyperfluorescence in a staining pattern. The mass quickly regressed with anti-TB therapy.\textsuperscript{24} Muccioli et al\textsuperscript{25} reported a case of AIDS with neurologic involvement caused by Mycobacterium tuberculosis. There was a yellow-white chorioretinal infiltration with indistinct borders and mild vitritis in the right eye.\textsuperscript{25} The neurologic condition became normal and ophthalmologic examination disclosed a best-corrected VA of 20/20.

Examination of the fundus showed a healed lesion without vitritis after anti-TB drug therapy for 3 months. Recillas-Gispert et al\textsuperscript{26} described a case of chorioretinitis secondary to Mycobacterium tuberculosis in AIDS. The eye showed a normal papillary response, keratic precipitates inferiorly, and cell and flare in the anterior chamber. Funduscopic examination revealed vitritis with hemorrhagic retinitis in the posterior pole, white cuffing of the nasal vessels, and some atrophic, slightly pigmented chorioretinal areas.\textsuperscript{26}

Bodaghi and Lehoang stated that the TB-associated intraocular involvement in patients with normal immunity showed granulomatous, with mutton-fat keratic precipitates, iris granulomas, and posterior synechiae. Choroidal infection is the most common ocular manifestation during dissemination of bacillus via the blood stream because of its high level of blood supply and oxygenation. Vitritis can be associated with vasculitis, retinal vein occlusion with subsequent retinal ischemia, and macular edema.\textsuperscript{27} All the cases reported above were caused by Mycobacterium tuberculosis, which was different from the case we present caused by Mycobacterium kansasii. Although the clinical findings were not reminiscent of the cases reported previously, as we know, a variety of presentations are possible in intraocular TB infection. TB in AIDS patients is characterized by atypical features such as cutaneous anergy to purified protein derivative skin testing, diffuse pulmonary infiltrates, and extrapulmonary disease. Our patient’s VA, ocular and CNS lesions improved under anti-TB treatment and cocktail therapy, along with partially recovered immunity. This made the diagnosis of TB choroidopathy likely.

References


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