Mortality in Patients With AIDS-Related Cytomegalovirus Retinitis in Myanmar

To the Editor—Retinitis is the most common clinical manifestation of human

immunodeficiency virus (HIV)–related cytomegalovirus (CMV) disease, but there is irrefutable clinical [1] and autopsy [2] evidence that AIDS-related CMV retinitis is only part of a systemic infection. By virtue of this association with systemic disease, CMV retinitis both predicts and contributes to mortality [3], and systemic anti-CMV therapy improves patient survival [4].

In high-income countries, systemic anti-CMV treatment has always been the standard of care, but in middle- and low-income countries, systemic anti-CMV treatment is rarely available because of cost. In the few settings that provide diagnosis, patients with retinitis receive local anti-CMV treatment (ganci-clovir eye injection), combined with antiretroviral therapy (ART) [5]. This approach can prevent blindness in the involved eye, but ignores systemic disease.

We investigated all-cause mortality of HIV patients with active CMV retinitis in Yangon, Myanmar, where trained HIV clinicians diagnose CMV retinitis by indirect ophthalmoscopy and provide intraocular ganciclovir injections, but where systemic anti-CMV treatment was not available.

Consecutive patients with active CMV retinitis were retrospectively analyzed for all-cause mortality. All patients were offered complete medical care including ART. An ophthalmologist with expertise in CMV retinitis regularly visited and monitored diagnostic accuracy.

Twenty-six of 94 (28%) patients with CMV retinitis died. In 19 patients for whom information was available, 13 of 19 (68%) died within 3 months of diagnosis of CMV retinitis, and all 19 died within 6 months. Sixteen of 94 (17%) patients were lost to follow-up.

Cytomegalovirus was one of the 3 unusual infections that occurred in all 5 patients in the 5 June 1981 Centers for Disease Control and Prevention report marking the beginning of the AIDS epidemic. That report established that CMV infection is a systemic disease: 1

patient died with CMV pneumonia; another had biopsy proven CMV esophagitis [6]. At this time there is a substantial burden of CMV retinitis in Southeast Asia, no apparent reduction over the past decade, little information about mortality, and virtually none about extraocular CMV disease [7].

We document a 28% mortality rate associated with a diagnosis of CMV retinitis, similar to cryptococcal meningitis mortality [8], and believe that the actual mortality rate in our CMV retinitis cohort was higher as most patients lost to follow-up in this setting are likely to have died. Where information is available, patients with CMV retinitis who did not survive typically died within months (13 of 19 patients died within 3 months), also consistent with prior data showing early mortality in patients with CMV retinitis [9].

To improve management of CMV retinitis, we must provide early diagnosis by indirect ophthalmoscopy screening for all new patients who first enter the healthcare system with a CD4 count <100 cells/µL as part of the initial physical examination; in addition, treatment for all patients with CMV retinitis must include systemic therapy with valganciclovir for at least 3 months, combined with intraocular ganciclovir injection for the first 2 weeks to promptly stop progression of retinitis, as well as to preserve this technique for patients who may become cytopenic from valganciclovir or otherwise require an alternative therapy [10].

Note

Potential conflicts of interest. All authors: No potential conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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References

- Yust I, Fox Z, Burke M, et al. Retinal and extra ocular cytomegalovirus end-organ disease in HIV-infected patients in Europe: a EuroSIDA study, 1994-2001. Eur J Clin Microbiol Infect Dis 2004; 23:550-9.
- Brantsaeter AB, Liestel K, Goplen AK, Dunlop O, Bruun JN. CMV disease in AIDS patients: incidence of CMV disease and relation to survival in a population-based study from Oslo. Scand J Infect Dis 2002; 34:50-5.
- Deayton JR, Sabin CA, Johnson MA, et al. Importance of cytomegalovirus viraemia in risk of disease progression and death in HIV-infected patients receiving highly active antiretroviral therapy. Lancet 2004; 363:2116–21.
- Jabs DA, Ahuja A, Van Natta M, Dunn JP, Yeh S; for the Studies of the Ocular Complications of AIDS Research Group. Comparison of treatment regimens for cytomegalovirus retinitis in patients with AIDS in the era of highly active antiretroviral therapy. Ophthalmology 2013; 120:1262–70.
- Teoh SC, Ou X, Lim TH. Intravitreal ganciclovir maintenance injection for cytomegalovirus retinitis: efficacy of a low-volume, intermediate-dose regimen. Ophthalmology 2012; 119:588–95.
- Centers for Disease Control and Prevention. Pneumocystis pneumonia—Los Angeles. MMWR Morb Mortal Wkly Rep 1981; 30: 250–52.
- Ford N, Shubber Z, Saranchuk P, et al. Burden of HIV-related cytomegalovirus retinitis in resource-limited settings: a systematic review. Clin Infect Dis 2013; 57: 1351–61.
- Bicanic T, Wood R, Meintjes G, et al. High-dose amphotericin B with flucytosine for the treatment of cryptococcal meningitis in HIV-infected patients: a randomized trial. Clin Infect Dis 2008; 47:123-30.
- Balo KP, Amoussou YP, Bechetoille A, et al. Cytomegalovirus retinitis and ocular complications in AIDS patients in Togo. J Fr Ophthalmol 1999; 22:1042–6.
- Heiden D, Saranchuk P, Tun NN, et al. We urge WHO to act on cytomegalovirus retinitis. Lancet Global Health 2014; 2: e76-7.

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