Treatment of Congenital Cytomegalovirus Retinitis With Intravitreous Ganciclovir

Cytomegalovirus (CMV) is the most common infectious congenital syndrome worldwide, occurring in 0.2% to 2.4% of all live births. While most newborns with congenital CMV are asymptomatic, long-term complications can include deafness, mental retardation, and vision loss. Active congenital ocular disease is rare, and systemic treatment is controversial. Herein, we describe a newborn with active CMV retinitis and optic neuritis for whom systemic treatment was withheld owing to risk of toxic effects. Faced with this dilemma, we...
administered intravitreous ganciclovir sodium. We present our findings regarding the possible efficacy and safety of this treatment in slowing disease progression.

Report of a Case. A premature infant with intrauterine growth restriction was born at 35 weeks' gestation weighing 1180 g. On day of life (DOL) 1, the ophthalmology department was consulted after microcephaly and intracranial calcifications were observed. Anterior segment examination findings were normal, but dilated funduscopic examination revealed extensive retinitis in both eyes with optic neuritis (Figure 1). Urine culture and polymerase chain reaction results confirmed CMV infection. Systemic ganciclovir treatment was recommended owing to optic nerve involvement.

Systemic ganciclovir treatment, however, was declined by the infectious disease consultants owing to risk of neutropenia. On DOL 4, intravitreous ganciclovir sodium (600 µg in 0.03-mL volume) was administered to each eye. Rapid and dramatic improvement of retinitis and optic neuritis was observed 3 days later. During the next 2 weeks, 2 additional injections were given in the right eye and 1 was given in the left eye. On DOL 25 (2 weeks following the last injection), retinitis recurred in both eyes. Systemic ganciclovir treatment was again recommended in the setting of recurrent CMV ocular infection and underlying central nervous system disease but was declined again by the infectious disease consultants. During the next 3 weeks, 3 and 4 more injections of intravitreous ganciclovir were given in the right and left eyes, respectively. By DOL 65, a total of 12 injections (6 per eye) had been administered (Figure 2). No ocular complications (cataract, retinal whitening, or inflammation) or systemic complications (neutropenia) were observed after any intravitreous ganciclovir treatment. At the most recent examination (on DOL 95), there was no sign of active disease in either eye.

Comment. To our knowledge, this is the first report of intravitreous ganciclovir treatment for active congenital CMV retinitis. We derived the dose (600 µg) from the standard adult dose (2 mg/0.1 mL) by adjusting for the smaller eye volume in the infant. The lack of observed complications and rapid response to each of 12 treatments support the safety of this dose.
In a 10-year prospective study by Coats et al that screened for congenital infections, only 1 immunocompetent newborn had active retinitis. Because the disease is considered to be self-limiting and systemic treatment can be harmful, treatment remains controversial. In 2003, the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group conducted a pharmacokinetic-pharmacodynamic study establishing a safe dose of intravenous ganciclovir in infants with CMV. A subsequent phase 3 randomized controlled study demonstrated the benefit of systemic ganciclovir therapy in reduction of hearing loss in congenital CMV infection with central nervous system involvement. While two-thirds of infants receiving treatment developed neutropenia, no deaths were related to the use of intravenous ganciclovir. Rapid resolution of CMV retinitis in immunocompetent infants has been reported with systemic ganciclovir treatment in 2 isolated cases. In our particular case, optic nerve involvement made complete remission unlikely with intravitreal ganciclovir treatment alone. Nevertheless, treatment temporarily arrested the disease and potentially reduced the degree of tissue damage.

The optimal treatment for congenital CMV retinitis remains unknown. Our case and those of others demonstrate that congenital CMV retinitis can persist for months after diagnosis before resolving spontaneously. Early treatment of active cases therefore is recommended to preserve vision. If systemic treatment is delayed or withheld owing to potential toxic effects, intravitreal treatment can be used as an adjunctive or alternative treatment to limit retinal and optic nerve damage. The results of our case may therefore assist the management of future cases.

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Incidence of Cytomegalovirus Retinitis in Patients With Human Immunodeficiency Virus Following Negative Initial Screening Examination Results

Cytomegalovirus (CMV) retinitis is an important cause of blindness among individuals with human immunodeficiency virus (HIV) and AIDS. While the prevalence has decreased in some countries owing to widespread antiretroviral therapy, CMV retinitis is still found in up to one-third of patients with HIV and AIDS in Southeast Asia. Screening for CMV retinitis is important for the prevention of blindness, but it is unclear how frequently patients should be rescreened after having negative results on an initial examination, especially in settings with good access to antiretroviral therapy.

Methods. In this retrospective study, we identified and reviewed the records of all patients with HIV seen for an initial screening examination for CMV retinitis at the Ocular Infectious Diseases Clinic, Chiang Mai University, Chiang Mai, Thailand, from July 6, 2006, to December 24, 2009. Collected data included diagnosis of CMV retinitis, age, sex, CD4 lymphocyte count, visual acuity, presence of HIV retinopathy, and treatment with antiretroviral drugs. We calculated the incidence of CMV retinitis in patients who initially had negative results on a screening examination, stratified by baseline characteristics. We used the Mantel-Haenszel rate ratio to assess for risk factors associated with incident CMV retinitis following negative results on an initial screening examination. Ethical approval was obtained from the Research Ethics Committee at Chiang Mai University and from the Committee for Human Research at the University of California, San Francisco.

Results. Of 597 patients with HIV identified, 469 patient records were available for review. On initial examination, 238 of these patients were diagnosed as having CMV retinitis and 22 had non–CMV retinitis pathological findings. Of the remaining 195 patients, 127 were examined at least once more. Seven of these patients were subsequently diagnosed as having CMV retinitis (incidence, 3.7/100 person-years; 95% CI, 1.8-7.8), 4 of whom developed bilateral disease. Retinitis in these 11 eyes was characterized by peripheral involvement (no optic disc or macular involvement in 10 eyes), small lesion size (<10% of retinal surface area in 6 eyes), and good visual acuity (≥20/40 in 6 eyes). The median time until diagnosis was 5.1 months (interquartile range, 2.3-27.8 months). At the time of diagnosis, all patients were receiving antiretroviral agents (median duration of therapy, 3.0 months; interquartile range, 1.0-16.3 months), although the self-reported CD4 lymphocyte count remained below 100/µL (to convert to ×10⁹ per liter, multiply by 0.001) in 5 patients.