Highly Active Antiretroviral Therapy-Associated Ptosis in Patients With Human Immunodeficiency Virus

We describe 2 patients with human immunodeficiency virus (HIV)/AIDS receiving highly active antiretroviral therapy with bilateral ptosis. In both cases, the ptosis developed during the course of the disease and its treatment. Each patient underwent surgical ptosis repair. A biopsy of the advanced levator complex, including the levator muscle, aponeurosis, and orbicularis oculi muscle, was obtained intraoperatively. This was compared with a similar biopsy taken from an HIV-negative control subject.

Report of Cases. Case 1. A 57-year-old man with a medical history of HIV/AIDS was referred for treatment of vision-impairing upper eyelid ptosis. He was treated for cytomegalovirus retinitis in his left eye 15 years prior to his initial visit to us. His HIV medications included lamivudine (Epivir; GlaxoSmithKline, Philadelphia, Pennsylvania) and didanosine (Videx; Bristol-Myers Squibb Co, New York, New York), both of which are nucleoside analogues similar to zidovudine, as well as fosamprenavir calcium (Lexiva; GlaxoSmithKline), which is a protease inhibitor. The patient had a CD4 lymphocyte count of 180/µL.

External examination revealed lipoatrophic facies and bilateral ptosis. Eyelid fissures measured 5 mm OD and 4 mm OS. Levator function was 10 mm OU. The patient underwent a bilateral levator resection.

Case 2. A 53-year-old man had a 17-year history of well-controlled HIV/AIDS. He reported the development of droopy eyelids over the past several years. The patient underwent an uncomplicated levator advancement procedure 5 years prior. His condition remained undercorrected. His HIV medications included enteric-coated didanosine (Videx EC; Bristol-Myers Squibb Co), tenofovir disoproxil fumarate (Viread; Gilead Sciences, Inc, Foster City, California), and abacavir sulfate (Ziagen; GlaxoSmithKline), all of which are nucleoside analogues similar to zidovudine, as well as nevirapine (Viramune; Boehringer Ingelheim Pharmaceuticals, Inc, Ridgefield, Connecticut), which is a nonnucleoside reverse transcriptase inhibitor. The patient demonstrated a CD4 lymphocyte count of 343/µL.

External examination demonstrated lipoatrophic facies and bilateral ptosis. Eyelid fissures measured 5 mm OU. Levator function measured 10 mm OU. The patient underwent a bilateral levator resection.

Comment. Myopathy associated with HIV was first described in the 1980s.1,2 This myopathy may manifest as an inflammatory myopathy with numerous inflammatory cells in sarcolemmal complexes (i.e., polymyositis) or less commonly as a type II muscle fiber atrophy or nemaline myopathy.3 Zidovudine and drugs of its class are indicated for the treatment of patients with AIDS. These drugs are dideoxynucleoside analogues that inhibit y-DNA polymerase, an enzyme found solely in the mitochondria. These drugs interfere with the replication of mitochondrial DNA and have been...
implicated as the cause of a mitochondrial myopathy associated with atrophic ragged-red fibers and marked myofibrillar alterations.\(^4^{,}\)\(^5^{,}\)

The histologic samples in this small case series depict findings similar to those described in the first reported cases of zidovudine-associated myopathy.\(^3^{,}\)\(^4^{,}\) Dalakas and colleagues\(^3^{,}\)\(^4^{,}\) studied muscle specimens of 15 patients treated with zidovudine. These specimens displayed the morphologic changes in muscle architecture consistent with mitochondrial pathology, ie, abundant ragged-red fibers. None of these changes were seen in the untreated control subjects. Moreover, the patients who had HIV-associated myopathy did not have these findings. Similarly, our patients had a higher density of ragged-red fibers (Figure 1) in comparison with that in the control subject (Figure 2). Increased staining of reduced nicotinamide adenine dinucleotide and succinate dehydrogenase and in numerous muscle fibers as well as electron microscopy results showing mitochondrial hyperplasia and hypertrophy in our cases also support a mitochondrial abnormality.

We report 2 cases of ptosis likely secondary to HIV and highly active antiretroviral therapy. This association is based on histopathologic findings consistent with the mitochondrial myopathy associated with these drugs. Given the utility of highly active antiretroviral therapy, it is not feasible for these patients to discontinue this treatment. However, identification of the ptosis is important to the understanding of the disease and the consequences of its treatment.

Rona Z. Silkiss, MD
Han Lee, MD, PhD
Vincent L. Gills Ray, MD

Correspondence: Dr Gills Ray, Department of Ophthalmology, California Pacific Medical Center, 2340 Clay St, Fifth Floor, San Francisco, CA 94115 (vgills@gmail.com).

Financial Disclosure: None reported.


**COMMENTS AND OPINIONS**

**Optic Nerve Sheath Hemorrhages, Increased Intracranial Pressure, and Retinal Hemorrhages in Central Nervous System Trauma**

Walsh\(^1^{,}\) established that optic nerve sheath hemorrhages (ONSH) arise at sites in the optic nerve sheath dura with rapid increases in intracranial pressure (ICP). He also established that retinal hemorrhages increased in prevalence proportional to the severity of the ONSH. Muller\(^2^{,}\) documented acute increased ICP as the cause of ONSH with retinal hemorrhage and orbital hemorrhage, confirming Walsh’s findings. Gilles\(^3^{,}\) reported the appearance and progression of retinal hemorrhages in the presence of sustained increased ICP. Albert’s ophthalmology textbook\(^4^{,}\) states that retinal hemorrhages that extend to the far periphery suggest venous occlusive disease. Emerson\(^5^{,}\) could find no support for the vitreous traction hypothesis and proposed that sustained venous stasis and leakage from retinal vessels can lead to elevated circular retinal folds. To date, biomechanical analysis and animal studies have failed to confirm the validity of the vitreous traction hypothesis. Consequently, any article seeking the pathogenesis of eye findings in brain injury must analyze the data correlating the duration of postinjury survival and the timing of eye examination with evidence of increased ICP before discounting increased ICP as the etiology of any eye findings. Kivlin\(^6^{,}\) fails to provide such analysis.

Cases 1 through 8 all had bilateral ONSH indicating sustained increased ICP before death.

Case 9 died the day of the injury with bilateral ONSH and only unilateral retinal hemorrhages, consistent with less sustained increased ICP prior to death than in cases 1 through 8.

Case 10 had no ONSH and no retinal abnormalities, suggesting no rapidly increased ICP prior to death.

Therefore, Kivlin’s\(^6^{,}\) findings do not confirm or even support the role of vitreous traction for eye findings in

Figure 2. Hematoxylin-eosin stain showing scant muscle fibers, with marked fibrosis in this patient with previous surgery (original magnification >200 in A, >400 in B). Succinate dehydrogenase stain showing increased staining in a few fibers (blue aggregates), indicating mitochondrial hyperplasia (original magnification >200 in C, >400 in D).