Unusual presentation of more common disease/injury

Severe enophthalmos and lagophthalmos secondary to HIV-associated lipoatrophy

Jennifer Edith De Niro, Rona Z. Silkiss

Ophthalmology Department, California Pacific Medical Center, San Francisco, California, United States

Correspondence to Dr Jennifer Edith De Niro, Jennifer_DeNiro@yahoo.com

Summary

HIV-associated lipoatrophy has been closely linked to the use of the thymidine nucleoside reverse-transcriptase inhibitors stavudine and zidovudine. The lipoatrophy can have severe psychological effects and is associated with increased risk of metabolic disorders and cardiovascular disease. The authors present a case of a 45-year-old HIV-positive man who presented with severe bilateral enophthalmos (recession of the eyes) and lagophthalmos (inability to fully close the eyes) from orbital fat atrophy. He had taken zidovudine for 8 years and stavudine for 13 years. Cessation of the causative drugs usually does not result in noticeable improvement of the lipoatrophy. Placement of bilateral orbital floor implants decreased our patient's orbital volume and substantially improved his eyelid function and cosmetic appearance.

BACKGROUND

A syndrome of progressive lipoatrophy affecting HIV-infected patients was first identified in 1998.¹ The characteristic changes include subcutaneous fat loss from the face, limbs and buttocks. Although initially ascribed to protease inhibitor treatment,¹ subsequent clinical studies implicated the use of thymidine nucleoside reverse-transcriptase inhibitors (NRTIs), particularly stavudine and zidovudine, as a dominant risk factor.^{2 3} This article presents a unique case of severe bilateral enophthalmos in combination with

lagophthalmos and facial lipoatrophy in a HIV-positive man who had been taking highly active antiretroviral therapy (HAART) for longer than two decades.

CASE PRESENTATION

A 45-year-old man presented with extreme posterior recession of his eyes (figure 1). He had not been able to fully close his eyes for 2 years and suffered from dry eye symptoms despite the use of cyclosporine ophthalmic drops, frequent lubrication with artificial tears and punctal plug

Figure 1 (A) Frontal photograph demonstrating bilateral enophthalmos. (B) After placement of a bilateral orbital floor implant, the enophthalmos is much improved. AAADF Lateral photograph (C) before and (D) after placement of the orbital floor implant.

Figure 2 Axial T1 MRI demonstrating bilateral orbital fat atrophy.

placement. Because his eyelids would not close, he taped them shut while sleeping. He had been diagnosed with HIV in 1987 and had taken zidovudine from 1987 to 1995 and stavudine from 1996 to 2009. Additional medical history included inflammatory bowel disease, hypertension and dyslipidemia. He had undergone coronary angioplasty in 2005. Facial lipoatrophy had been treated with repeated sculptra (poly-L-lactic acid) injections over many years.

INVESTIGATIONS

The patient's best-corrected visual acuity was 20/20 in each eye. Most significant was extreme enophthalmos in both eyes. The patient's Hertel measurement (distance from the lateral orbital rim to the anterior corneal surface) was 14 mm bilaterally. Upper lid margin to pupil light reflex distance in primary gaze (MRD1) was 2 mm and lower lid MRD2 was 7 mm. He had bilateral lagophthalmos as well as superficial punctate keratopathy of the inferior one third of his corneas. An orbital MRI showed marked orbital fat atrophy (figure 2).

TREATMENT

Since more conservative measures had failed to control the patient's dry eye symptoms, surgical intervention was needed to correct his orbital anatomy. Bilateral orbital floor

implants (Medpor enophthalmos implant) were placed through a transconjunctival approach to decrease relative orbital volume.

OUTCOME AND FOLLOW-UP

The placement of orbital floor implants resulted in a reduction of enophthalmos (figure 1) and resolution of his lagophthalmos. Postoperative Hertel measurement was 17 mm and MRD1 and MRD2 were 1 mm and 5 mm respectively in both eyes. The patient still uses cyclosporine drops but was able to decrease the frequency of artificial tears to once daily and no longer needs to tape his eyelids closed at night. The improved lid closure has persisted for 6 months.

DISCUSSION

HIV-associated lipoatrophy has been strongly associated with use of the thymidine NRTIs stavudine and zidovudine, with more severe lipoatrophy correlated with cumulative drug exposure.³ Our patient had taken zidovudine for 8 years and stavudine for 13 years. Although the pathogenesis of lipoatrophy is not completely understood, it has been attributed to mitochondrial toxicity induced by the NRTIs through their interference with mitochondrial DNA polymerases. Peripheral fat samples taken from

NRTI-treated patients have shown significant adipocyte mitochondrial DNA depletion, adipose tissue macrophage infiltration and elevated proinflammatory cytokine levels compared with samples from control subjects and patients not taking thymidine NRTIs.³ Although there has been a significant reduction in lipoatrophy incidence with decreasing use of stavudine and zidovudine over the last decade,³ the persistent nature of established lipoatrophy, with only minimal recovery after switching or removing NRTI drugs,⁴ has ensured that the syndrome remains highly prevalent.

Lipoatrophy can be stigmatising and has been associated with depression.⁵ Moreover, it is independently associated with metabolic disorders, including dyslipidemia,⁶ insulin resistance⁷ and increased risk of cardiovascular disease.⁸ These co-occurring metabolic abnormalities may have contributed to our patient requiring coronary angioplasty at age 40.

Facial lipoatrophy, which includes fat loss from the nasolabial regions, the temples and the eye sockets, can have especially severe psychological effects. The emaciated facial appearance can make patients seem unwell despite good HIV control and lead to poor body image and social withdrawal. Merchante *et al*⁹ described a case of bilateral enophthalmos from orbital fat atrophy in a patient who had taken zidovudine for 3 years and then stavudine for 4 years. To our knowledge, our case is the first reported of lagophthalmos HIV-associated lipoatrophy as well as the use of bilateral orbital floor implantation to treat the rare associated enophthalmos. We hypothesise that the lagophthalmos seen in this patient may be secondary to a decrease in the mechanics of eyelid closure in an enophthalmic globe as well as possible mitochondrial orbicularis dystrophy, not unlike that reported for HAART-associated ptosis.¹⁰

Given that HIV-associated facial lipoatrophy is not readily reversible and can have profound psychological and physical ramifications, it is important to optimise procedures to improve patients' function and cosmetic appearance.

Learning points

- ▶ NRTIs, particularly stavudine and zidovudine, can cause permanently disfiguring lipoatrophy.
- ▶ Facial lipoatrophy is especially psychologically devastating.
- ▶ Orbital floor implants can improve the mechanics of eyelid closure.

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Competing interests None.

Patient consent Obtained.

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