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SHORT COMMUNICATION

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Cicatrization of cytomegalovirus retinitis following introduction of highly active anti-retroviral therapy: uveitis as a possible indicator of good ocular prognosis

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Abstract ● Purpose: To quantify the inflammatory reaction that can be seen in HIV-infected patients with cytomegalovirus (CMV) retinitis after the introduction of an HIV protease inhibitor and correlate it with ocular findings and systemic HIV parameters. ● Methods: Report of a patient with CMV retinitis systematically followed by slit-lamp examination, funduscopy, fundus photographs and laser flare photometry before and after introduction of an HIV protease inhibitor. ● Results: Manifest granulomatous panuveitis developed 2 months after the introduction of the protease inhibitor indinavir (CD4 rise from 2 to 64 CD4/mm^3) and coincided with cicatrization of the CMV retinitis in the absence of efficient anti-CMV therapy. ● Conclusion: Occurrence of uveitis in patients with CMV retinitis following the introduction of HIV protease inhibitors may be a factor indicating a good ocular prognosis, possibly pointing to the presence of the anti-CMV repertoire in the reconstituting CD4 cell population.

Introduction

Highly active anti-retroviral therapy (HAART) refers to the new combination treatment of HIV infection with two HIV reverse transcriptase inhibitors and an HIV protease inhibitor. This new approach has proven itself to be an extremely potent anti-HIV therapy that usually leads to a significant rise in CD4 lymphocytes and a dramatic drop of the viral load as well as a spectacular improvement in the patient's general condition [2, 5]. HIV protease inhibitors contribute essentially to the efficacy of HAART [2, 5]. It is, however, still unclear to what extent the immune system is restored and thus whether anti-cytomegalovirus (CMV) therapy could be discontinued in patients with CMV retinitis. It has been suggested that despite a substantial increase in CD4 cells, the restitution of the T-cell population may be incomplete with omissions in the CD4 cell repertoire [1]. The influence of HAART on the course of CMV retinitis probably depends on whether the anti-CMV repertoire is preserved or lost. We report here a case of retinitis where post-HAART resolution of the retinitis in the absence of anti-CMV treatment coincided with the occurrence of severe panuveitis.

Case report

A 35-year-old patient had lost his left eye because of retinal detachment secondary to CMV retinitis. He was treated for a CMV retinitis of the right eye by intravenous ganciclovir maintenance therapy 5 mg/kg once a day on 5/7 days per week until his infected central catheter had to be removed. From this time on, the patient refused all further intravenous therapy. His CD4 count was 4 cells/mm^3 and the viral load was 28 000 RNA copies/mm^3. Indinavir (2.4 g day) was added to his anti-HIV treatment regimen consisting of azidothymidine and lamivudine. One month after discontinuation of anti-CMV therapy, CMV retinitis

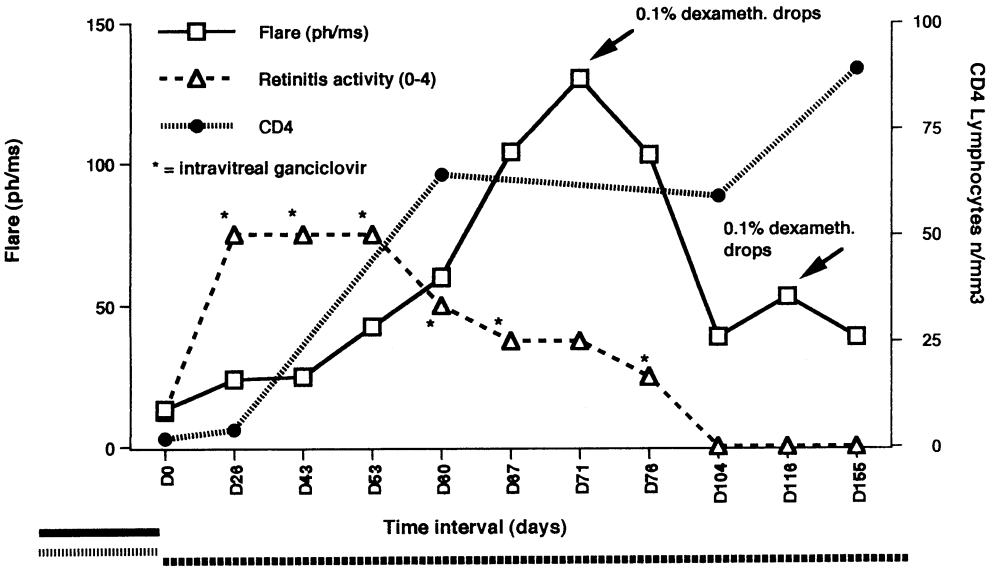

Fig. 1 Paradoxical inflammatory reaction in resolving CMV retinitis following treatment including the HIV protease inhibitor indinavir (lines under figure: *solid* intravenous ganciclovir; *light interrupted* dual reverse transcriptase inhibitor therapy; *heavy interrupted* HAART, combination of two HIV reverse transcriptase inhibitors and an HIV protease inhibitor)

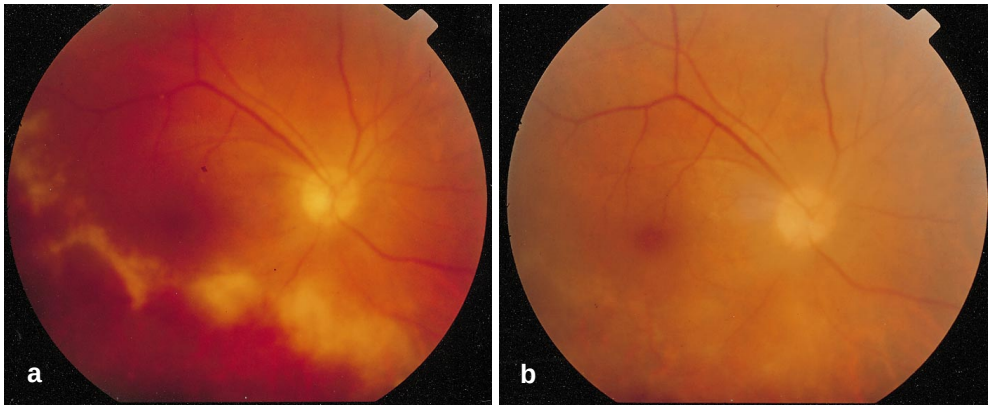

Fig. 2 a, b Resolution of CMV retinitis following the introduction of protease inhibitor therapy. **b** CMV retinitis recurrence 1 month after discontinuation of maintenance ganciclovir therapy. **b** Resolution of CMV retinitis 2 months later (3 months after introduction of the HIV protease inhibitor indinavir) without any anti-CMV therapy. The fundus is still slightly cloudy because of residual vitritis

reactivated, accompanied by a slight increase of laser flare photometry values from 13.5 to 24 photons per millisecond (ph/ms; normal values 4–6 ph/ms). The only anti-CMV therapy accepted by the patient was intravitreal injections of ganciclovir given every 7–10 days once reactivation of CMV retinitis was detected (six injections in total, Fig. 1). One month later (2 months after the introduction of indinavir) a sharp rise in laser flare photometry values from 24 to 130 ph/ms occurred in association with panuveitis including synechiae formation, Koeppe nodules, small mutton-fat keratitic precipitates and vitritis. At this time the CD4 level had increased from 4 to 64 cells /mm^3 and the viral load had decreased from 28 000 to 1600 copies/mm^3. Uveitis responded to hourly topical 0.1% dexamethasone drops and mydriasis with a decrease of flare from 130 to 37 ph/ms within 4 weeks and partial clearing of vitritis. CMV retinitis activity decreased during the same period, and cicatrization was observed within another month (3 months after the introduction of indinavir therapy) without any meaningful anti-CMV therapy. After 14 months' follow-up the patient remained free of CMV retinitis without any specific anti-CMV therapy; CD4 counts stabilized around 60 cells/mm^3. Flare photometry values stabilized around 20 ph/ms without any topical or systemic anti-inflammatory treatment.

Discussion

Pronounced inflammatory reactions, in excess of background inflammation, in patients with CMV retinitis following the initiation of HAART are known to ophthalmologists taking care of AIDS patients. Using laser flare photometry we were able to precisely follow the level of inflammation in such a patient, showing a slight increase of flare at the time of recurrence of CMV retinitis, a finding that is well known and has been described before [3]. The noteworthy finding here was, however, the marked flare-up of inflammation, 2 months after the introduction of the HIV protease inhibitor indinavir, that coincided

with the resolution of CMV retinitis. Because efficacious anti-CMV therapy was refused by the patient, resolution of the retinitis here can be attributed exclusively to the restoration of the immune function brought about by HIV protease inhibitor therapy that was added to the ongoing anti-reverse transcriptase therapy. The pronounced inflammatory reaction may reflect the presence of CMV specific CD4 cells fighting CMV infection in the retina. Recently, regression of AIDS-related Kaposi's sarcoma following HAART has been reported [4]. In that report also, resolution of lesions was attributed exclusively to the restoration of immune function.

In conclusion, inflammatory flare-up, seen after introduction of protease inhibitor therapy in HIV patients with CMV retinitis was an indicator of good ocular prognosis in our case. Attention should be paid to this phenomenon in future cases. Close, laser flare photometry-assisted follow-up of CMV retinitis at the time of introduction of protease inhibitors might be useful in monitoring the ocular impact of HAART and might assist therapeutic decisions.

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