

### Cytomegalovirus retinitis in an AIDS patient without severe depletion in CD4 cell count

EDITOR.—Ophthalmic involvement in patients with AIDS occurs in more than 90% of cases at postmortem examination.<sup>1</sup> It is characterised both by infectious manifestations (HIV retinitis, cytomegalovirus retinitis, *Pneumocystis carinii* choroiditis, fungal choroiditis, toxoplasmosis) and by non-infectious manifestations (eyelid Kaposi's sarcoma, retinal microvasculopathy, keratoconjunctivitis sicca<sup>2</sup>). Cytomegalovirus (CMV) retinitis is the most common severe ocular complication occurring as a late manifestation with severe CD4 lymphocyte depletion.

We report the case of a 32-year-old man, with a high CD4 lymphocyte count, who developed a unilateral retinitis. Clinical examination and the investigations performed were positive for a CMV infection.

#### CASE REPORT

A 32-year-old man was referred to us with sudden visual loss of the left eye in October 1994. In May 1993, AIDS was diagnosed after he suffered pulmonary *Mycobacterium tuberculosis*. Current therapy consisted of zidovudine 750 mg daily and trimethoprim 480 mg with sulphamethoxazole 2400 mg orally per week. He was not asplenic and had not received any other antiretroviral therapy.

On examination, the visual acuity was 6/5 in the right eye and light perception in the left eye. Slit-lamp biomicroscopy examination was normal. Intraocular pressure was 10 mm Hg in both eyes. There were 1+ cells in the anterior vitreous with mild posterior vitritis. Left fundus examination revealed a necrotic macular lesion and dot macular haemorrhages (Fig 1). The right fundus was normal. Both general and neurological examination were normal.

Investigations showed an erythrocyte sedimentation rate of 10 mm/h (normal range 1–12), a white blood count of  $8 \times 10^9/l$  (normal range  $4–11 \times 10^9/l$ ) with a normal differential count. CD4 lymphocyte count was  $355 \times 10^6/l$  (normal range  $600–1950 \times 10^6/l$ ), CD8 lymphocyte count was  $967 \times 10^6/l$  (normal range  $300–1100 \times 10^6/l$ ), Agp24 was positive and  $\beta 2$  microglobulin 5.15 mg/l (normal range 0.75–1.75 mg/l). On the basis of the clinical appearance of the left fundus a CMV retinitis was suspected. We administered foscarnet intravenously (60 mg/kg every 8 hours for 3 weeks) followed by a maintenance dose (90 mg/kg/day). In view of the CD4 lymphocyte count an anterior chamber tap was performed. Results were positive for local production of anti-CMV immunoglobulins; Goldmann-Witmer coefficient was 4.12 for CMV, 2.02 for herpes simplex virus, and not calculable for varicella zoster virus. Early CMV antigen was detected in the urine. After 5 weeks of treatment resolution of the active retinitis in the left eye had occurred (Fig 2).

The patient decided to discontinue the therapy. After 1 month a reactivation of macular infection was noted (Fig 3). CD4 lymphocyte count was  $259 \times 10^6/l$ , CD8 lymphocyte count was  $818 \times 10^6/l$ , Agp24 was positive and  $\beta 2$  microglobulin 3.88 mg/l. We again administered foscarnet intravenously (60 mg/kg every 8 hours for 3 weeks) on admission. After 5 weeks of treatment resolution of the CMV retinitis was observed; maintenance foscarnet therapy was continued.



Figure 1 (October 1994) Fundus photograph of the left eye: macular retinal necrosis surrounded by white areas of active infection. Dot haemorrhages.



Figure 2 (November 1994) Fundus photograph of the left eye: macular retinal scar. Folds of internal limiting membrane.

#### COMMENT

Ocular manifestations of a CMV infection occur more often after a congenital infection (retinitis, optic atrophy, anophthalmia) or as the result of an acquired immunocompromised state (chemotherapy, malignancies, AIDS<sup>3,4</sup>). To date, only two cases of CMV retinitis,<sup>5,6</sup> a case of bilateral CMV acute retinal necrosis,<sup>7</sup> and a case of bilateral CMV papillitis<sup>8</sup> have been reported in immunocompetent individuals.

The most common ocular complication of AIDS is CMV retinitis (12–46%),<sup>4</sup> becoming a major cause of morbidity and the leading cause of impaired vision or blindness among these patients. The ocular condition appears as a unilateral or bilateral retinitis composed of scattered yellow-white areas of retinal necrosis with intraretinal haemorrhages, vasculitis, and soft exudates. These lesions often follow a perivascular distribution. Non-

granulomatous keratic precipitates and a mild vitreous inflammation may be present.<sup>4</sup>

CMV retinitis is a late complication of AIDS, associated with severe CD4 lymphocyte depletion; some clinical studies have suggested a temporal sequence in the development of opportunistic infections and malignancies accounting for the decrease of the CD4 lymphocyte count. It has been shown that CMV retinitis occurs when a low CD4 lymphocyte count is reached ( $100 \times 10^6/l$ ); the highest risk occurs below a level of  $50 \text{ CD4 lymphocytes} \times 10^6/l$ .<sup>9</sup> This observation suggests that CD4 lymphocyte count may be of predictive value for the development of some opportunistic infections, but the qualitative function of these cells is also of great importance. Effectively, our patient developed CMV retinitis with a CD4 level of  $355 \times 10^6/l$  and recurrence of the disease at  $259 \text{ CD4} \times 10^6/l$ .



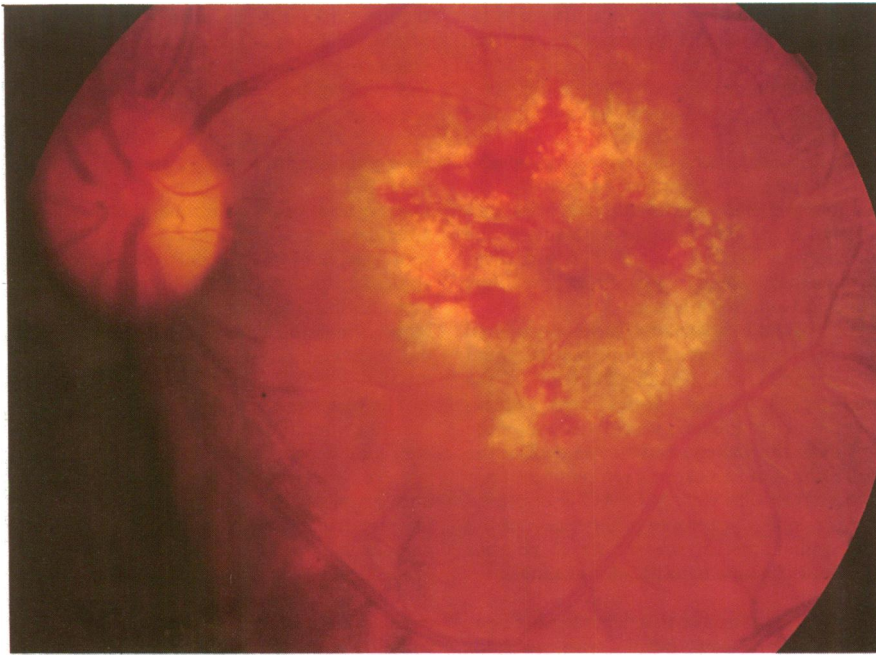


Figure 3 (January 1995) Fundus photograph of the left eye: active macular retinal retinitis and haemorrhages.

Some authors have demonstrated that AIDS lymphocytes have a decreased blast transformation in vitro to mitogens and to some antigens. Moreover, AIDS mononuclear cells seem to be unable to mount a cytotoxic lymphocyte response against CMV infected cells.<sup>10</sup> Some aspects of the HIV pathogenesis appear to be characterised by a profound defect in cell mediated immunity. This is due to a decrease in the number of the helper/inducer lymphocytes and an alteration in their function and ability to mount an efficient cytotoxic response, promoting the

development of CMV ocular manifestations in patients having a subnormal CD4 lymphocyte count.

This case suggests that criteria for routine screening in AIDS patients may change and that an elevated CD4 lymphocyte count is not incompatible with CMV retinitis.

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