LETTERS TO THE EDITOR

CD8+ T lymphocytes in cytomegalovirus retinitis in a patient with AIDS

EDITOR,—Cytomegalovirus (CMV) retinitis has become one of the most common manifestations of the virus and a common cause of visual loss in patients with AIDS because the disease is usually progressive without treatment.[1] However, there are a few reports of spontaneous regression[2] of the retinitis or resolution with zidovudine[3–5] which has no anti-CMV activity in vitro, although reasons for the regression were not fully investigated.

We encountered a case of CMV retinitis with spontaneous regression in a patient with AIDS. In this case, the number of circulating CD8+ T lymphocyte cells (CD8 count) but not CD4 count had increased along with the resolution of the retinitis.

CASE REPORT

A 47-year-old HIV seropositive man was referred to our hospital because of AIDS diagnosed by recurrence of the bacterial pneumonia on 3 December 1991. The retina showed no abnormality at that time. IgG antibody against CMV in the serum was positive. CD4 and CD8 counts were 17 × 10^6/l and 242 × 10^6/l, respectively. *Pneumocystis carinii* pneumonia (PCP) developed on 20 December and was treated with pentamidine for 3 weeks. After improvement of PCP, zidovudine 400 mg/day was started on 25 January 1992. The general condition of the patient improved thereafter. However, CD4 and CD8 counts on 3 February were still low (CD4 30 × 10^6/l, CD8 235 × 10^6/l). The ophthalmic examination on 10 February showed a small and faint exudative lesion in the left eye (Fig 1A). The lesion developed into a retinal necrosis which was multiple granular satellite lesions which was compatible with the start of CMV retinitis on 2 March (Fig 1B). Although the CD4 count was still low (44 × 10^6/l), the CD8 count increased to 581 × 10^6/l on 23 March. In association with the increase in the CD8 count, the retinal lesion began to improve at that time and markedly reduced without any anti-CMV therapy by 30 March (Fig 1C). The patient's condition was well during the ensuing 8 months. On 2 November when the CD8 count again was depressed at 149 × 10^6/l (CD4 count 8 × 10^6/l), the typical lesion of CMV retinitis reappeared in the same area as the previous necrotic lesion in the left eye (Fig 1D). The lesion showed a good clinical response initially after treatment with ganciclovir, but it had progressed by 8 February 1993 (Fig 1E); the CD4 and CD8 counts did not increase thereafter (CD4 5 × 10^6/l, CD8 163 × 10^6/l). The lesion had increased by 19 July 1993 (Fig 1F) in spite of the treatment.

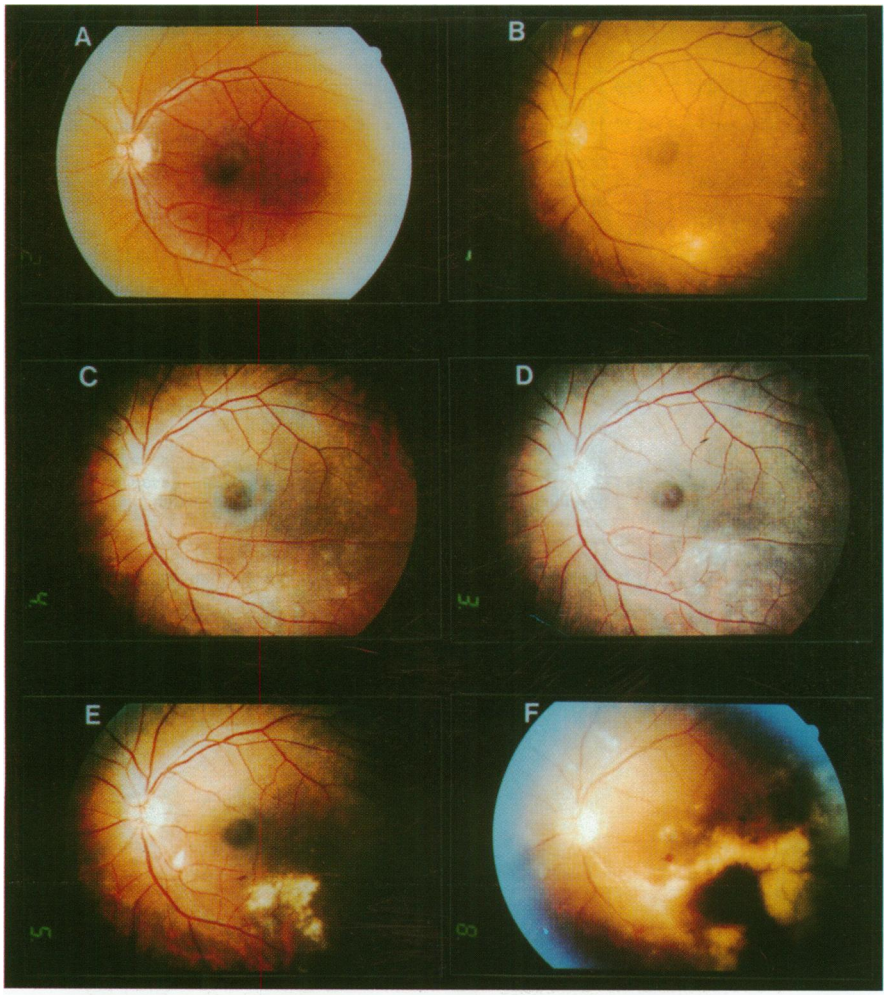

Figure 1 Spontaneous regression of CMV retinitis in association with the increase of CD8 count. For details see text.

COMMENT

The CD4 count has mainly been considered, so far, with regard to immunological status and has been used as a predictor of opportunistic infections in patients with AIDS.[6] To prevent the visual loss caused by CMV retinitis and to maintain a better quality of life, early detection of the disease is important. Kuppermann *et al* clearly showed in a prospective and cross sectional study that AIDS patients with CD4 counts below 50 × 10^6/l had an increased risk of CMV retinitis.[7] Lowder *et al* further demonstrated that patients with low CD8 counts as well as low CD4 counts are at high risk for CMV retinitis.[8] It was suggested that a CD8 count below 500 × 10^6/l give the same risk as a CD4 count below 50 × 10^6/l for the occurrence of CMV retinitis. Our case of spontaneous regression of the retinitis along with an increase in the CD8 count over 500 × 10^6/l but a relatively stable low CD4 count, strongly supported Lowder and colleagues' observation. Consequently, close and periodic observations of the ocular fundus for the early detection of CMV retinitis are recommended in AIDS patients with a CD8 count below 500 × 10^6/l after CD4 depletion. After starting periodic ophthalmic examinations (once a month) in those patients whose CD8 count is below 500 × 10^6/l, the number of patients with visual loss caused by advanced CMV retinitis are dramatically decreasing in our hospital (unpublished data). Thus, monitoring of CD8 count as well as CD4 count may prove valuable as a predictor of CMV diseases in severely immunocompromised hosts.

SHINICHI OKA
Department of Infectious Diseases, Institute of Medical Science, University of Tokyo

YOICHI NAGATA
YUJIRO FUJINO
Department of Ophthalmology, University of Tokyo School of Medicine

AKIRA YASUOKA
NATSUO TACHIKAWA
KAORU SHIMADA
SATOSHI KIMURA
AIKICHI IWAMOTO
Department of Infectious Diseases, Institute of Medical Science, University of Tokyo

MANABU MOCHIZUKI
Department of Ophthalmology, Kurume University School of Medicine

Correspondence to: Dr Shinichi Oka, Department of Infectious Diseases, Institute of Medical Science, University of Tokyo, 4-6-1, Shirokanedai, Minato-ku, Tokyo 108, Japan.
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1 Bowen EF, Wilson P, Atkins M, Madge S, Griffiths PD, Johnson MA, *et al.* Natural history of untreated cytomegalovirus retinitis. *Lancet* 1995;**346**:1671–3.
2 Muller-Jensen K, Fischer JT, Meyer HJ. Transient spontaneous regression of cytomegalovirus retinitis in AIDS. *Ophthalmologica* 1991;**203**: 154–6.

3 D'amico DJ, Skolnik PR, Kosloff BR, Pinkston P, Hirsch MS, Schooley RT. Resolution of cytomegalovirus retinitis with zidovudine therapy. *Arch Ophthalmol* 1988;**106**:1168–9.
4 Guyer DR, Jabs DA, Brant AM, Beschorner WE, Green WR. Regression of cytomegalovirus retinitis with zidovudine. A clinicopathological correlation. *Arch Ophthalmol* 1989;**107**:868–74.
5 Carter JE, Shuster AR. Zidovudine and cytomegalovirus retinitis. *Ann Ophthalmol* 1992;**24**: 186–9.
6 Masur H, Ognibene FP, Yarchoan R, Shelhamer JH, Baird F, Travis W, *et al.* CD4 counts as predictors of opportunistic pneumonias in human immunodeficiency virus (HIV) infection. *Ann Intern Med* 1989;**111**: 223–31.
7 Kuppermann BD, Petty JG, Richman DD, Mathews WC, Fullerton SC, Rickman LS, *et al.* Correlation between CD4+ counts and prevalence of cytomegalovirus retinitis and human immunodeficiency virus-related noninfectious retinal vasculopathy in patients with acquired immunodeficiency syndrome. *Am J Ophthalmol* 1993;**115**:575–82.
8 Lowder CY, Butler CP, Dodds EM, Secic M, Recillas-Gispert C. CD8+ T lymphocytes and cytomegalovirus retinitis in patients with the acquired immunodeficiency syndrome. *Am J Ophthalmol* 1995;**120**:283–90.

Bilateral cytomegalovirus retinitis in a patient with systemic lupus erythematosus

EDITOR,—Cytomegalovirus (CMV) retinitis is common in patients with AIDS. In other immunocompromised hosts this devastating eye condition is much rarer despite the frequent systemic CMV infections in these patients.

We report a patient with systemic lupus erythematosus (SLE) presenting with bilateral CMV retinitis and retinal detachment. Remarkably, active SLE or manifest systemic CMV infection were absent. Our patient responded well to reduction of the immunosuppressive therapy, ganciclovir therapy, and surgery. We conclude that clinicians should be aware of the possibility of CMV retinitis in rheumatological patients on mild immunosuppression.

CASE REPORT

A 27-year-old woman presented in March 1993 with decreased vision, floaters, and photopsia of the left eye for a few days. From the age of 5 she has suffered from SLE with chronic immune complex mediated nephritis. In September 1992 a severe exacerbation of SLE complicated by nephritis, pericarditis, and cardiac failure was treated with nine intravenous pulse doses of 1000 mg methylprednisolone and 100 mg azathioprine daily. In 1977, both eyes had suffered from severe SLE retinopathy with widespread vasculopathy resulting in poor vision of the right eye.

On presentation in March 1993 visual acuities were 1/60 in the right eye and 6/9 in the left eye. No signs of inflammation in the anterior segment or vitreous were present in either eye. Fundus examination showed right optic nerve pallor, severe bilateral venous frosted branch sheathing (Fig 1), and large areas of white necrotic retina with haemorrhages in the right nasal periphery and left upper retina (Figs 1 and 2). The peripheral retina of the left eye was detached (Fig 2) and showed several atrophic breaks. Physical examination and laboratory investigations (anti-ds DNA and complement factors C3, C4, and C1q) indicated that SLE was in remission. Leucocyte and lymphocyte counts were normal.

Her medication at this time consisted of oral prednisone 20 mg and azathioprine 50 mg daily. The azathioprine was stopped, the prednisone slowly tapered, and treatment with foscarnet 200 mg/kg daily was started. The next day the left retinal detachment was treated with vitrectomy, scleral buckling, cryotherapy, and silicone oil tamponade and a prophylactic scleral buckling procedure was performed on the right eye. Analysis of the left vitreous revealed intraocular production of anti-CMV antibodies (Goldmann–Witmer coefficient 4.0) and a polymerase chain reaction (PCR) positive for CMV. PCR reactions for herpes simplex virus, varicella zoster virus, Epstein–Barr virus, and *Toxoplasma gondii* and tests for local antibody production against these agents were all negative. Because of impaired kidney function the foscarnet was stopped and intravenous ganciclovir was started and maintained for 6 weeks until the retinitis had been inactive for 3 weeks. Visual acuity of the left eye remained 6/9 after removal of the silicone oil. No antiviral maintenance therapy was given and in the next 3 years of regular follow up visits no recurrence of retinitis has occurred nor has her general health changed. She remained on 10 mg prednisone a day.

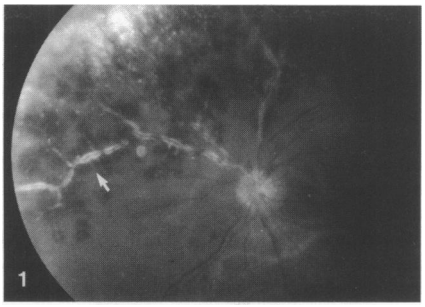

Figure 1 Left eye demonstrates extensive sheathing of retinal venules (frosted branch vasculitis, indicated by arrow) in the posterior pole and classic CMV retinitis in the upper peripheral retina.

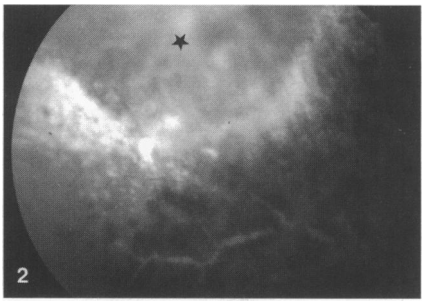

Figure 2 Upper peripheral retina of left eye demonstrates a large area of typical CMV retinitis with retinal detachment (indicated by asterisk).

COMMENT

The diagnosis of CMV retinitis was established in our patient by its typical aspect and associated frosted branch vasculitis,[1] and the demonstration of CMV by PCR and intraocular anti-CMV antibodies. Remarkably, at the time of CMV retinitis, the SLE in this patient was inactive and her immunosuppressive medication was mild, with normal leucocyte and lymphocyte counts. Furthermore, she lacked other signs of systemic CMV infection. This clinical picture is different from the severe systemic CMV infections, often with a fatal course, that are common in immunosuppressed SLE and other rheumatic patients and transplant recipients,[2–9] particularly in those treated with azathioprine or cyclophosphamide.[9] In fact, such patients only rarely show concurrent CMV retinitis.[2 6–9]

Our patient's presentation with bilateral severe CMV retinitis, without systemic signs, more resembled CMV infections as seen in patients with AIDS.[10] AIDS in our patient could not be excluded as she refused an HIV test. However, the lack of recurrent CMV retinitis or other opportunistic infections and her survival in the 3 years of follow up make it unlikely that she has AIDS.

No clear clinical guidelines are established for treating patients on immunosuppressive therapy who develop isolated CMV retinitis. A reduction in immunosuppressive medication may be sufficient in some cases (C Pavesio, personal communication). Others, like our patient, may also need a course of ganciclovir and surgical therapy. In our opinion, maintenance ganciclovir therapy, as is given to AIDS patients,[10] is not necessary in this patient group.[9]

We conclude that severe CMV retinitis without systemic symptoms may develop in patients with quiescent SLE on mild immunosuppression and that clinicians should be aware of visual symptoms in these patients.

R O SCHLINGEMANN
Department of Ophthalmology, Academic Medical Center, University of Amsterdam

P WERTHEIM-VAN DILLEN
Department of Medical Microbiology, Academic Medical Center, University of Amsterdam

A KIJLSTRA
The Netherlands Ophthalmic Research Institute

P J M BOS
Department of Ophthalmology, Academic Medical Center, University of Amsterdam

C MEENKEN
Department of Ophthalmology, Academic Medical Center, University of Amsterdam

E J FERON
Rotterdam Eye Hospital, Rotterdam, the Netherlands

Correspondence to: Dr R O Schlingemann, Department of Clinical Ophthalmology, Moorfields Eye Hospital, City Road, London EC1V 2PD.
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1 Rabb MF, Jampol LM, Fish RH, Campo RV, Sobol WM, Becker NM. Retinal periphlebitis in patients with acquired immunodeficiency syndrome with cytomegalovirus retinitis mimics acute frosted retinal periphlebitis. *Arch Ophthalmol* 1992;**110**:1257–60.
2 Bowness P, Davies KA, Norsworthy PJ, Athanassiou P, Taylor-Wiedeman J, Borysiewicz LK, *et al.* Hereditary C1q deficiency and systemic lupus erythematosus. *QJM* 1994;**87**:455–64.
3 Bulpitt KJ, Brahn E. Systemic lupus erythematosus and concurrent cytomegalovirus vasculitis: diagnosis by antemortem skin biopsy. *J Rheumatol* 1989;**16**:677–80.
4 Bresser P, Toben FM, van Son WJ, Anema J, Beukhof JR. Current developments in the diagnosis and therapy of cytomegalovirus infections. *Ned Tijdschr Geneeskd* 1989;**133**:455–7.
5 Iwasaki T, Satodate R, Masuda T, Kurata T, Hondo R. An immunofluorescent study of generalized infection of human cytomegalovirus in a patient with systemic lupus erythematosus. *Acta Pathol Jpn* 1984;**34**:869–74.
6 Egbert PR, Pollard RB, Gallagher JG, Merigan TC. Cytomegalovirus retinitis in immunosuppressed hosts. II. Ocular manifestations. *Ann Intern Med* 1980;**93**:664–70.
7 Scott WJ, Giangiacomo J, Hodges KE. Accelerated cytomegalovirus retinitis secondary to immunosuppressive therapy. [Letter] *Arch Ophthalmol* 1986;**104**:1117–24
8 Winkler A, Finan MJ, Pressly T, Roberts R. Cytomegalovirus retinitis in rheumatic disease: a case report. *Arthritis Rheum* 1987;**30**:106–8.