

# Cytomegalovirus retinitis in human immunodeficiency virus negative patients

*Retinite por citomegalovírus em pacientes HIV negativos*

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## SUMMARY

**Purpose:** Cytomegalovirus (CMV) retinitis is a widely recognized complication of advanced disease due to human immunodeficiency virus (HIV) infection. It can also occur in patients with other causes of immunosuppression. We describe three cases of CMV retinitis in immunosuppressed HIV negative patients.

**Methods:** Case report of CMV retinitis in three patients with immunosuppression related to glomerulonephritis, leukemia associated to bone marrow transplantation and renal transplantation.

**Results:** CMV retinitis was unilateral and the macula was involved in all patients. The first patient developed CMV retinitis lesion in one eye that healed after discontinuation of the immunosuppressive therapy and a rhegmatogenous retinal detachment successfully repaired by surgical treatment with vitrectomy, silicone oil injection and endolaser. The second patient received a ganciclovir implant and died in two weeks. The third patient had the diagnosis of chorioretinitis due to toxoplasmosis in one eye and posteriorly developed suggestive CMV retinitis lesion in the fellow eye that healed with the suspension of the immunosuppressive drugs.

**Discussion:** Although CMV retinitis has been less frequent in HIV negative patients than in AIDS, it is necessary to be aware of this complication in patients under chemotherapy, following organ transplantation or with malignancies. The retinitis may present remission on reduction of systemic immunosuppression or by using local therapy.

**Key-words:** Retinitis; Cytomegalovirus; Human immunodeficiency virus; Immune suppression.

## INTRODUCTION

Cytomegalovirus (CMV) retinitis is the most important opportunistic ocular infection that affects patients with acquired immunodeficiency syndrome (AIDS)<sup>1,2</sup> and is less frequent in immunodeficiencies secondary to leukemia, lymphoma and therapy with immunosuppressive drugs<sup>2-7</sup>. The prognosis of CMV retinitis in the HIV negative population may be better because of the different natural course of the underlying disease and the improvement of the specific anti-viral therapy<sup>8</sup>.

We report three cases of CMV retinitis in HIV negative patients with immunodeficiency secondary to radiation or chemotherapy for glomerulonephritis, leukemia associated to bone marrow transplantation and renal transplantation.

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## CASE REPORTS

### Case 1

A 57 year-old white man with glomerulonephritis, that had been treated with azathioprine (50 mg/day), was examined in February 96 with progressive blurred vision in the OD for two months. The visual acuity in the OD was 5/400 and in the OS was 20/20. The OD showed 1+ vitreous cells and a necrotizing retinitis suggestive of CMV that had extensive hemorrhages among exudation areas began in the temporal superior arcade with extension to macular and nasal superior regions. A toxoplasmosis scar was seen in the retina of the OS.

Laboratory tests showed a CD4 of 108 cells/mm<sup>3</sup> and a CD8 of 245 cells/mm<sup>3</sup>. Toxoplasmosis serology was positive for IgG and negative for IgM. Toxoplasmosis was excluded because of the characteristics of the lesions. Laboratory tests for HIV-1 and HIV-2 were negative.

The azathioprine was suspended and the retinitis healed progressively while the treatment of the glomerulonephritis was changed for ciclosporine (250 mg/day). Four months later, the retinitis was inactive, but a retinal detachment was noticed and successfully treated with vitrectomy, silicone oil injection and endophotocoagulation. The retina was attached in the end of the surgery but the visual acuity reminded the same.

### Case 2

A 15 year-old white boy with leukemia that was submitted to body radiation and bone marrow transplantation one year before was seen because of visual loss in the OD for two months due to CMV retinitis. Laboratory tests for HIV-1 and HIV-2 were negative. Ganciclovir therapy had to be discontinued because of severe leukopenia. Visual acuity was 20/60 in the OD and 20/20 in the OS. Fundus examination disclosed an active CMV retinitis in the temporal inferior arcade, and the patient was treated with ganciclovir implant (Vitrasert®). Two weeks later visual acuity was 20/30 in the OD. The patient died in two months due to disseminated bacterial infection.

### Case 3

A 44 year-old white man that was submitted to a renal transplantation 10 months before, was seen because of decreased vision in the OS. The patient had been under hemodialysis for two years and was receiving azathioprine (50mg/day), prednisone (20 mg/day), ciclosporine (250mg/day), sulfamethoxazole (800mg/day) and trimethoprim (160mg/day).

The ophthalmological examination disclosed a visual acuity of 20/20 in the OD and 20/200 in the OS. The OD was normal. The OS presented an exudative lesion in the nasal superior region and a 3+ vitreous haze. Toxoplasmosis serology was positive for IgG and negative for IgM. After 45

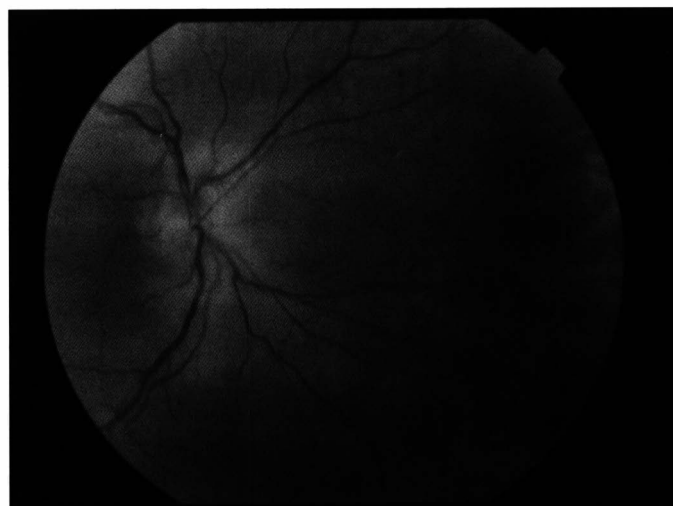


Fig. 1 - Fundus picture the right eye showing the margin of the active CMV lesion.

days with the use the specific therapeutic for toxoplasmosis the visual acuity improved to 20/30. One week later the patient developed a decreased visual acuity from 20/20 to 20/40 in the OD, related to an extensive hemorrhagic and necrotizing lesion with vasculitis in the nasal region considered suggestive of CMV retinitis (Figures 1 and 2). All medication was discontinued and the lesions healed in 6 weeks.

## DISCUSSION

CMV retinitis can affect 20-40 % of AIDS patients<sup>1</sup> and is also a recognised but rare complication of the immunosuppression related to chemotherapy, malignancies or organ transplantation<sup>2, 9</sup>. As the use of immunosuppressive agents

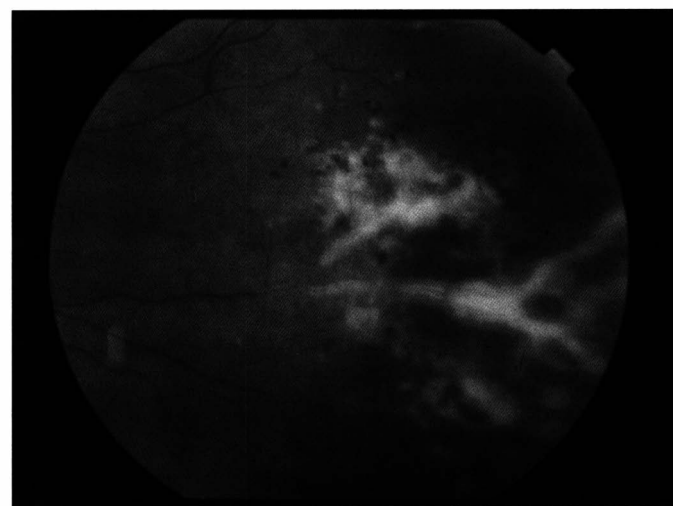


Fig. 2 - Fundus picture of the right eye showing the nasal CMV retinitis and vasculitis.

increases in the treatment of several diseases, the incidence of CMV retinitis may raise<sup>3</sup>.

The HIV negative patients included in our evaluation were using immunosuppression therapy for a long time and it was considered the main predisposing factor to develop an opportunistic infection. In these cases CD4 and CD8 could be valuable tests to determinate the evolution of the CMV retinitis.

The most commonly implicated drugs used in patients who have developed CMV retinitis have been azathioprine, cyclophosphamide and corticosteroids<sup>5,6</sup>. CMV retinitis may be unilateral or bilateral and the severity is usually lower than that occurring in patients with AIDS<sup>4</sup>.

Although systemic therapy with antiviral drugs has been implicated in the improvement of the CMV retinitis in HIV negative patients, in our cases the retinitis healed with the discontinuation of systemic immunosuppression or use of local therapy. In order to avoid worsening of the systemic disease a therapeutic alternative must be introduced while the ocular infection is been controled.

We believe that the institutions that use immunosuppression therapy, should evaluated the occurrence of CMV retinitis into these situations and perform extensive studies in order to make an early diagnosis and treatment of the ocular infectious complications.

## RESUMO

**Objetivo:** Retinite causada por citomegalovírus (CMV) é uma complicação amplamente reconhecida da doença avançada devido a infecção pelo vírus da imunodeficiência (HIV), podendo também ocorrer por outras causas de imunossupressão. Descrevemos três casos de retinite por CMV em pacientes imunossuprimidos sem infecção pelo HIV.

**Métodos:** Apresentamos as características clínicas da retinite pelo CMV em três pacientes com imunossupressão relacionada a glomerulonefrite, leucemia associada a transplante de medula óssea e transplante renal.

**Resultados:** A retinite por CMV era unilateral e a mácula esteve envolvida em todos os casos. O primeiro paciente

desenvolveu retinite pelo CMV em um olho que cicatrizou após a descontinuação da terapia imunossupressora e um deslocamento de retina regmatogênico foi submetido com êxito a um tratamento cirúrgico com vitrectomia, injeção de óleo de silicone e endolaser. O segundo paciente recebeu o implante de ganciclovir e faleceu duas semanas depois. O terceiro paciente teve o diagnóstico de coriorretinite por toxoplasmose em um olho e posteriormente desenvolveu lesão sugestiva de retinite por CMV no olho contralateral que cicatrizou com a suspensão das drogas imunossupressoras.

**Conclusão:** Apesar da retinite por CMV ser menos freqüente em pacientes HIV negativos do que em pacientes com AIDS, deve-se estar ciente da possibilidade dessa complicação em imunodeficiências relacionadas à quimioterapia, transplante de órgãos ou doenças malignas. A retinite pode apresentar remissão pela redução da imunossupressão sistêmica ou com o uso de terapia local.

**Palavras-chave:** Retinite; Citomegalovírus; Vírus da imunodeficiência humana; Imunossupressão.

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