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LETTER TO THE EDITOR

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Diagnosis of cytomegalovirus retinitis after heart transplantation

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Sir: Cytomegalovirus (CMV) disease is a well-known complication in the immunocompromised host. However, isolated CMV retinitis is most frequently encountered in AIDS patients. In this population, treatment is usually based on a diagnostic funduscopy and invasive procedures are omitted if ever possible.

With regard to solid-organ transplant recipients, many centers rely on CMV antigenemia in order to start preemptive ganciclovir therapy. Unless tissue invasion by CMV can be readily documented, this sensitive and quantitative technique serves as a confirmation of suspected CMV disease. Isolated retinitis is rather exceptional in transplant recipients, the most frequent localisation of CMV disease being in the lungs and gastrointestinal tract. This letter details the diagnostic difficulties we encountered dealing with CMV retinitis in a heart transplant recipient.

A 45-year-old male patient underwent heart transplantation for ischemic cardiomyopathy in June 1998. He was CMV-antibody positive and *Toxoplasma gondii*-antibody negative. The donor was negative for CMV and *Toxoplasma gondii* antibodies. The patient underwent induction therapy with antithymocyte globulin and triple immunosuppressive treatment with cyclosporine, mycophenolate mophetil and corticosteroids thereafter. No CMV prophylaxis was administered. In accordance with our preemptive protocol, CMV antigenemia and PCR on serum were followed weekly during the first 2 months. Four weeks after transplantation, both were found positive (9 positive leukocytes per 200.000 counted). At that time, no therapeutic changes were made. After 6 months, no episodes of rejection or serious infections had occurred. In November 1998, the recipient complained of blurred vision and floaters in the left eye. Funduscopy confirmed the diagnosis of necrotizing retinitis. Because of the elevated pressure in the infected eye (40 mm Hg), acetazolamide and mannitol were administered intravenously. Anti-CMV (intravenous ganciclovir 10 mg/kg per d, CMV specific hyperimmune globulin 2 ml/kg per d) and antitoxoplasma treatment (intravenous clindamycine 800 mg/d followed by sulfadiazine 3 g/d and pyrimethamine 25 mg/d) were initiated. To avoid an anterior chamber puncture under general anaesthesia, a test for CMV antigenemia (demonstration of tegument phosphoprotein pp65 using monoclonal antibodies) was performed and found to be negative. After the first dose of hyperimmune globulin, anaphylaxis ensued, characterised by fever, chills and hypotension. The patient was treated with a bolus of methylprednisolone (125 mg) and intravenous colloids and recovered. *Toxoplasma gondii* and CMV IgM (ELISA) were negative. Because of persisting diagnostic uncertainty, anterior chamber punction was eventually performed 4 days after admission. PCR on aqueous humour was positive for CMV and negative for *Toxoplasma gondii.* CMV antigenemia was repeated at that time and remained negative. Pyrimethamine and sulfadiazine were discontinued. After 2 weeks of intravenous therapy, treatment was switched to high dose oral ganciclovir (3 × 1000 mg) with good clinical result. PCR, antigenemia, and IgM assays performed weekly during more than one month remained negative. There was a non significant rise of the CMV IgG titer (100 before the transplantation, 200 one month after the diagnosis of CMV retinitis).

This case-report adds to the evidence that, similar to observations in AIDS patients, CMV retinitis in solid-organ transplant recipients does not necessarily implicate systemic activation of the virus in peripheral leukocytes with concomitant positive CMV-PCR or antigenemia. Pannuti et al. found a positive antigenemia in only 8 out of 24 AIDS patients (33.3%) with CMV retinitis and out of these, only 3 had an antigenemia of more than 10 positive leukocytes per 300.000 counted [2]. In the control group (AIDS patients without present or past retinitis), none of the 24 patients was positive. These findings illustrate the low sensitivity of CMV antigenemia in AIDS patients with isolated retinitis. In contrast, Hansen et al. found a higher sensitivity of CMV-PCR on serum for the diagnosis of CMV chorioretinitis in HIV seropositive patients: CMV-PCR was positive in 11 out of 19 patients who subsequently developed CMV retinitis, while CMV-PCR became positive at the onset of clinical retinitis in 3 other patients [1].

No comparative data have been published for solid-organ transplant recipients with CMV retinitis. Although it is arguable that the clinical diagnosis of retinitis is sufficient to initiate empirical treatment, the possible toxic side effects of the therapy, as was illustrated in our case, do not favour this approach. Moreover, the possibility of other ocular infections caused by *Toxoplasma gondii*, Varicella Zoster and

Herpes Simplex viruses, has to be ruled out. While CMV antigenemia is generally considered to be a reliable and highly sensitive assay in cases of systemic CMV disease, this appears not to be the case in isolated CMV retinitis occurring in both transplant recipients and AIDS patients. Several authors suggested that differences in viral load may be relevant in this respect, and this could influence the diagnostic accuracy of CMV antigenemia and PCR assays in cases of infection of larger visceral organs [3, 4].

Until a reliable less invasive test becomes available, we strongly advise diagnostic anterior chamber puncture and PCR assay on aqueous humour in transplant recipients with the clinical tentative diagnosis of necrotizing chorioretinitis.

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