CMV retinitis in HIV-positive patients in the pre-HAART era
Verbraak, F.D.

Citation for published version (APA):
Verbraak, F. D. (1999). CMV retinitis in HIV-positive patients in the pre-HAART era
OUTLINE OF THE THESIS
CMV is the most frequent viral opportunistic infection in HIV-positive patients. The annual incidence of CMV disease varied between 25 and 30% in the era preceding the introduction of Highly Active Anti-Retroviral Therapy (HAART). In the majority of patients (>90%) the eye is involved with a necrotizing retinitis. In treating these patients many questions arose, some of which we tried to answer: can we make our diagnosis more accurate, can we specify risk factors for developing CMV retinitis, can we make use of new polymerase chain reaction (PCR) based assays to analyse ocular derived CMV, and what is the influence of HAART on the determination of CMV viral load and the occurrence of CMV retinitis.

In the first chapter of the thesis an extensive review is presented of the clinical implications of CMV retinitis in the pre-HAART era. The pathogenesis, diagnosis, treatment, and prevention of the disease are discussed.

The diagnosis of CMV retinitis relies on the clinical findings and is most of the time straightforward for those experienced in judging these retinal infections. Problems in the diagnosis however do occur in the early stages of retinitis and in atypical presentations, where other pathogens could be involved. In the second chapter we present results of a combined serologic and PCR based analysis of aqueous humour samples in HIV-positive patients with necrotizing retinitis as an aid in the differential diagnosis.

Extra-ocular CMV disease is considered to be a risk factor for the subsequent development of CMV retinitis, but exact data were never reported. Our clinical impression was that retinitis is very frequent following extra-ocular CMV disease. In chapter 3 we present a retrospective analysis regarding the development of retinitis in HIV-positive patients with biopsy proven extra-ocular CMV disease.

The polymerase chain reaction based assays enabled the direct analysis of CMV recovered from intraocular fluid samples in HIV-positive patients with CMV retinitis. In chapter 4 results of CMV strain typing in ocular fluid samples and paired blood samples are reported, and in chapter 5 the observed frequency of glycoprotein B (gB) genotypes in ocular fluid samples is presented.

The presence of increasing levels of CMV viral load in blood of HIV-positive patients is considered to be a high risk factor for developing CMV disease. Quantification of the PCR assay to detect CMV DNA in blood has recently been introduced in the Academic Medical Centre.
At the same time Highly Active Anti Retroviral Therapy (HAART) became available. As a result of HAART, the CD4+ cell counts rise dramatically in most patients. The restoration of the immune system leads to a drop in the incidence of CMV retinitis and a better control of pre-existing CMV retinitis. We conducted a prospective follow-up study to evaluate the influence of HAART on CMV viral load, and the development of CMV retinitis in a group of HIV-positive patients at high risk for developing CMV retinitis. Results are presented in chapter 6.

The introduction of HAART has shown that restoration of the patient’s immune response is the best treatment of CMV retinitis. At the moment we are in a period of transition with many uncertainties regarding the management of HIV-positive patients, who previously were at high risk for developing CMV disease, or who have a pre-existing CMV retinitis. For this reason the following title of the thesis was chosen: “Cytomegalovirus retinitis in HIV-positive patients in the pre-HAART era”.

How long this period will be, and for what time HAART will remain as effective as it is now, nobody knows. Unfortunately the number of patients failing anti-retroviral therapy is growing, either because of development of resistance or as a result of the inability to tolerate the drug regime. With the subsequent loss of immunity, patients will again become prone to development of opportunistic infections like CMV retinitis.
In the first chapter of the thesis, an extensive review is presented of the clinical implications of CMV retinitis in the context of HIV/AIDS. The relationship between CMV retinitis and HIV infection is discussed, highlighting the importance of early diagnosis and treatment. The chapter also covers recent advancements in the field, including the role of antiretroviral therapy in preventing CMV reactivation.

Extraocular CMV disease is considered to be a risk factor for the subsequent development of CMV retinitis, but clinical data were never separately collected. It is well documented that retinitis is very frequent following extraocular CMV disease. In chapter 2, we present a comprehensive analysis regarding the development of retinitis in HIV-positive patients with necrotizing retinitis as an aid in the differential diagnosis.

The chapter also addresses the issue of the direct and indirect causes of CMV retinitis. Here, we discuss the importance of fluid samples in CMV diagnosis, the ability of CMV to be detected in extraocular fluid samples, and the development of specific methods for CMV PCR.

In chapter 3, the observed frequency of extraocular CMV disease in HIV-positive patients is discussed, introducing a novel technique for the diagnosis of CMV disease. Quantification of the PCR assay for CMV DNA in extraocular fluid samples is presented.