sCD163 increase in HIV/CMV coinfected subjects included in ICONA Cohort

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Background

Accumulating evidence suggest that inflammatory cytokines produced by monocytes/macrophages play a role in the vascular disease and cognitive decline. In HIV patients, herpes virus coinfection has been proposed as a key factor in sustaining immune activation, even in presence of HIV plasma viral control. In our previous study on the ICONA cohort we showed that in HIV patients (pts), CMV infection is an independent risk factor for non AIDS events/deaths (fig. 1).

Aims

• To study the differences in plasma markers of myeloid immune activation, related to cardio-cerebro vascular diseases in HIV monoinfected and HIV/CMV coinfected pts,
• To correlate CMV IgG levels in HIV/CMV+ with soluble activation markers.

Study population

Screening of all the ICONA patients with an available CMV serology at enrolment (or within 6 months) and a plasma sample after ≥1 year of successful ART (defined as an undetectable HIV viral load and CD4+ count more than 200/μl).

Among these patients 2 different groups have been constituted: CMV-infected and CMV-uninfected patients. CMV chronic infection was defined on CMV IgG presence.

We selected HIV CMV+ and CMV- patients with a plasma sample after 1 year or more of successful therapy, matched for sex, age, CD4 nadir, HBV and HCV (see table 1).

Exclusion criteria

Previous or current CMV organ diseases, organ transplantation, use of immunosuppressive or immunomodulating drugs in the last year, cancer or treatment for cancer in the previous 5 years, insulin dependent diabetes mellitus, glomerular filtration rate < 39 ml/min, severe liver disease, endocrine disorders, autoimmune disease.

Materials and methods

Immunological Assays

Plasma levels in duplicate of:
• IL-6 and TNFα (pg/ml) eBiOScience, sCD163 and sCD14 (ng/ml) R&D Systems

CMV ELISA Quantitation Kit: GenWay Biotech used to retest all samples and in the CMV positive populations to quantify Ab levels in duplicate.

Statistical analysis

Mann-Whitney Test, Spearman correlation analysis (Prima 6.0 software)

Results

A total of 69 subjects were recruited, 46 HIV monoinfected (CMV-) and 23 HIV/CMV (CMV+) coinfected.

A higher median of sCD163 level (927.7 vs. 497.8 ng/ml, p=0.018) was found in CMV+ compared to CMV- group (fig. 2A). TNFα, sCD14 were also elevated but did not reach a significant difference in comparison to HIV/CMV- subjects (fig. 3).

In HIV/CMV+ subjects a significant correlation was shown between anti-CMV IgG levels and sCD163 (r=0.29, p=0.04) and CD4+ cells levels (r=0.40, p=0.006) (fig 2B). Moreover in CMV+ subjects sCD163 levels were related to the duration of HIV infection (r=0.29, p=0.04). In the CMV positive group comparing CMV IgG levels with CD4 count, at the time of sampling, we found a significant negative correlation (r=0.39, p=0.0006).

Conclusions

CMV chronic infection appears to be linked to an increase in sCD163, a marker of myeloid activation, in HIV infected subjects under successful ART with controlled biological (age and sex) and HIV related (HIV suppression, CD4 nadir and CD4 recovery) factors. The persistent activation of monocytes and macrophages that has been implicated in the accelerated development of vascular and neurological disease in general population, may explain the increased risk of non AIDS events found in HIV/CMV coinfected subjects.