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Impact of CMV infection on soluble markers of myeloid activation in HIV infected subjects

Serena Vita1, Miriam Lichtner2, Giulia Marchetti3, Claudia Mascia4, Ester Merlini3, Paola Cicconi3, Vincenzo Vullo4, Roberta Piolini5, Pierluigi Viale6, Alberto Costantini7, Cristina Mussini8, Antonella d'Arminio Monforte3 for the Icona Foundation Study

1Sapienza University of Rome, Cenci Bolognetti Foundation 2Sapienza University of Rome, Polo Pontino, Latina, Italy 3San Paolo Hospital, Milan, Italy; 4Sapienza University of Rome, Italy; 5Sacco Hospital, Milan, Italy; 6 University of Bologna, 7 University of Ancona, Clinical Immunology, Ancona; 8 Clinic of Infectious and Tropical Diseases, University of Modena and Reggio Emilia, Modena, Italy

BackgroundRecently, Cytomegalovirus has been linked to a variety of chronic diseases with an inflammatory component including cardiovascular disease (CVD), cancer, cognitive impairment. In HIV subjects premature aging and degenerative organ diseases are frequent events also during effective ART. CMV coinfection has been proposed as a key factor in sustaining immune activation. In our previous studies on the ICONA cohort we have shown that in HIV patients, CMV infection is an independent risk factor for non AIDS events/deaths. AimsTo evaluate the role of CMV chronic infection in sustaining increased levels of myeloid soluble markers, of immune activation and inflammatory cytokines in HIV infected subjects on virologically suppressive cART.MethodsWe performed a pilot study to screen all the ICONA patients with an available CMV serology at enrolment (or within 6 months) and a plasma sample after >1 year of successful cART (defined as an undetectable HIVviral load and CD4+ count more than 200/mc). Among these patients 2 different groups have been constituted: CMV-infected and CMV-uninfected patients.CMV chronic infection was defined on CMV IgG presence. Moreover they have been matched 2:1 for the following parameters: age, CD4 nadir, duration of HIV infection, hepatitis virus (HBV and HCV). We have excluded patients with: previous or current CMV organ diseases, organ transplantation, use of immunosuppressive or immunomodulant drugs in the last year, cancer or treatment for cancer in the previous 5 years, insulin dependent diabetes mellitus, glomerular filtration rate < 39ml/min, severe liver disease, endocrine disorders, autoimmune disease. Plasma sample at the sCD163, sCD14, IL-6, TNFa, were detected using ELISA tests (eBioscience and R&D Systems) on plasma samples selected following the above criteria.

Moreover all sample were retested for anti-CMV IgG (GenWay Biotech). Statistical analysis were performed using Mann-Withney Test and Spearman correlation analysis (Prima 6.0 software)Results46 HIV monoinfected and 23 HIV/CMV coinfected subjects were studied. A higher median level of sCD163 (927.7 vs. 497,8 ng/ml, p=0.018) and sCD14 (1.58 vs. 1.83 μ g/ml, p=0.06) were found in CMV+ compared to CMV- group. No differences in TNFa and IL-6 levels between groups were found. In HIV+CMV+ subjects, a significant correlation was shown between anti-CMV IgG levels and sCD63 (r=0.49, p=0.006), IL-6 (r=0.42, p=0.0041), TNFa (r=0.34, p=0.021). ConclusionsOur data show that CMV chronic infection appears to be related to an increase in soluble markers of myeloid activation in HIV infected subjects under successful ARV with similar biological (age and sex) and HIV related (HIV suppression, CD4 nadir and CD4 recovery) factors. This persistent activation of monocytes and macrophage that has been associated to cardiovascular and neurological damage in general population, may explain the increased risk of non AIDS events found in CMV/HIV coinfected subjects.