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Cancer Science 2019: Antibodies titers against CMV putative predicts outcome in breast cancer patients - Leonel Alexander Rangel Reyna - Sonora Cancer Research Center (CICS)

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Clinically speaking is mainly unknown the association of antibodies against Cytomegalovirus (CMV) and the prognosis in cancer patients. We studied (n=25) samples of breast cancer patients in different stages to address the possible link between high load viral titers using ELISA and we correlated with several clinical parameters including but not limited to OS, ECOG and stage. One of the possible pathways that the chronic presence of CMV in breast cancer patients can affect the outcome as potentially this type of virus may distract the immune system specially when the treatment is based with the combination of immunogenic chemotherapy, treat locally and systemically, multi-peptide active antigen specific immunotherapy and immunomodulation of cytokines. With this in mind we make a retrospective analysis identifying breast cancer patients (n=25), measuring the titers against CMV antigens and its relation with the mentioned clinical parameters. We found statistical significance in patients with high viral titles and OS. However, there is no pattern at this point with this preliminary data in all the studied cases, which may have to be related with the tumor microenvironment, breast cancer subtype and previous lines of ablative chemotherapy received as all of them where studied in refractory status as mentioned previously. This data could be useful to include for all cancer patients not just limited to breast cancer to include the titers of several viruses other than CMV such as EBV, HTLV-1/2, HCV, HBV and potentially some microbiota for instance Fusobacterium nucleatum. If we validate this data we will propose to include some broad spectrum antiviral agents in patients with potential clinical benefit.

Untreated HIV infection is characterized by ongoing inflammation and immune activation. Despite suppressive antiretroviral therapy (ART), many HIV-infected individuals continue to have increased inflammation compared to uninfected controls. Soluble markers of inflammation, such as interleukin (IL)-6, soluble tumor necrosis factor (TNF)-alpha receptor I and II, soluble CD14 and soluble CD163 and cellular markers of immune activation, such as HLA-DR/CD38 co-expressing T cells remain elevated in these individuals and are associated with morbid AIDS and non-AIDS events, including death. The etiologies of these persistently elevated levels of inflammation and immune activation remain unclear, but are likely complex and variable across individuals. The direct effects of HIV, persistent HIV-related defects in the gut mucosal barrier with exposure to microbial products, reactivation of latent infections (eg, herpes viruses), chronic silent co-infections (eg, HCV) and persistent immune dysregulation are all potential drivers of ongoing inflammation and immune activation. With aging, host immune response is increasingly dominated by cytomegalovirus (CMV)-specific responses. This disproportionate CMV-specific response might contribute to immune senescence and might be associated with inflammation. The presence of CMV infection has been associated with a variety of aging-related diseases in both HIV-positive and negative populations. Among a large cohort of immunocompetent adults, higher anti-CMV immunoglobulin G (IgG) antibody levels were found to be associated with an increased incidence of ischemic heart disease and increased all-cause mortality. Similarly, one study on HIV-positive women found that higher anti-CMV IgG levels were associated with subclinical carotid artery disease, as diagnosed by carotid artery ultrasound in a subset of virologically suppressed participants. Another study found that CMV seropositivity was associated with a significantly increased risk for severe non-AIDS events, in particular cardiovascular and cerebrovascular diseases. It is not known whether these associations are causal in nature. Further, if there is a causal association between CMV and inflammatory conditions, it is not known whether this is due to a direct effect of CMV or if it is secondary to the inflammation associated with CMV-specific host immune responses. Further studies exploring the relationship between CMV and inflammatory conditions are needed, particularly among HIV-positive individuals.

In a previously reported case-control study within the AIDS Clinical Trials Group (ACTG) Longitudinal Linked Randomized Trials (ALLRT) cohort, soluble markers of inflammation (IL-6, sTNFR-I/II) and coagulation (D-dimer) measured 1 year after ART initiation were associated with subsequent non-AIDS events, but T-cell activation was not. In this current study, we utilize the same cohort and soluble inflammatory marker and T-cell activation data to determine whether the magnitude of CMV-specific antibody response might be associated with the occurrence of non-AIDS events.

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