The impact of Human Cytomegalovirus on atherosclerotic plaque instability and its implications for risk stratification

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Objective:

Human cytomegalovirus (HCMV) is associated with atherosclerosis and destabilization of atherosclerotic plaques. In some patients, HCMV promotes Natural Killer (NK) cells increased expression of NKG2C receptor with augmented production of cytokines.

This study aims to investigate the involvement of HCMV in reconfiguration of NK cells and potential impact of this NK cell subset in the pathogenic mechanisms underlying plaque instability.

Methods:

A total of 64 patients were enrolled in a follow-up protocol for carotid artery stenosis. Based on morphologic characteristics, the degree of stenosis, and the common carotid artery intima-media thickness, patients were classified into low-risk group (LRG) and high-risk group (HRG). High-risk patients underwent carotid endarterectomy according to the European Society for Vascular Surgery (ESVS) guidelines.

Carotid plaques and pre-operative peripheral blood samples were obtained from all patients to be processed. Flow cytometric analysis was performed on blood samples instead flow cytometric and immunohistochemical analysis was performed on carotid plaques. HCMV serological status was determined using the chemiluminescent immunoassay LIAISON CMV IgG and IgM (SiaSorin, Saluggia, Italy).

Results:

Among the 64 patients, 38 patients were included in the HRG instead, 26 were low-risk patients. In the HRG, 12 patients were symptomatic instead 26 were asymptomatic. Among all patients, 6 were HCMV seronegative (3 in the LRG vs 3 in the HRG) instead 58 were seropositive (23 in the LRG vs 35 in the HRG).

HCMV-associated NK cell subset reconfiguration is increased in peripheral blood of high-risk patients compared to low-risk patients (% $CD56^{+}Fc\ RI^{-}$ NK cells 41.1± 17.8% versus 26.7 ± 15.5%; P=

0.0036). NK cells from High-Risk HCMV positive patients have enhanced CD16-mediated effector functions compared to Low-Risk patients and increased CD16-mediated IFN-𝛄 release (% $CD56^{+}$ IFN- $^{+}$ 39.9 ± 21.9% versus 17.9 ± 16.2%; P= 0.0185).

Conclusion:

In conclusion, our data show the potential role of detecting HCMV and specific subsets of memory-like NK cells as markers to identify high-risk patients who could suffer from plaque destabilization and subsequent negative outcomes.