

Atherosclerosis and Inflammation

1.1 Platelet Activation and Cognitive Impairment in Elderly Patients with Metabolic Syndrome

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Introduction. Metabolic syndrome is associated with increased risk for developing cognitive impairment in the elderly population. We have recently described the potential involvement of CD40 ligand (CD40L) in the pathophysiology of Alzheimer's disease. CD40L also exists in a soluble(s) form which is mainly released from activated platelets thus representing an index of platelet activation.

Aim. To evaluate the relationship between platelet activation and cognitive impairment in patients with metabolic syndrome (NCEP – ATP II criteria).

Methods. We studied 80 patients (74±6 year, 49 F) with metabolic syndrome but without evidence of cerebrovascular disease and/or overt dementia. Cognitive functions have been explored by MMSE, TMTA and TMTB. The scores of psychometric tests have been then transformed to generate a composite z score. Sixty healthy subjects (72±4 year, 32 F) without evidence of dementia or cardiovascular disease, were studied. Circulating levels of sCD40L and P-selectin were studied as indexes of platelet activation. Furthermore, we analyzed circulating levels of 8-iso-prostaglandin(PG) F2alpha, a well accepted index of lipid peroxidation and a potential determinant of platelet activation.

Results. Patients with metabolic syndrome exhibited worse cognitive performance (z score: 0.58±0.32 vs -0.39±0.28, p<0.0001) and increased circulating levels of sCD40L (+35%, p<0.005), P-selectin (+34%, p<0.002) and 8-iso-PGF2alpha (+43%, p<0.0001). When patient population was distinguished into tertile of sCD40L, we observed worse cognitive performance in patients with higher sCD40L levels (p<0.001). In the whole patients population circulating levels of sCD40L were directly correlated with cognitive impairment (r= -0.445, p<0.007). A significant relationship between plasma sCD40L levels and plasma total 8-iso-PGF2alpha concentration was also found in the whole patient population (r=0.502, p<0.001).

Conclusions. Our data suggest that enhanced sCD40L release, likely related to oxidative stress-mediated platelet activation, might represent a key determinant of cognitive impairment in elderly patients with metabolic syndrome.