Canakinumab: can it untie the Gordian knot of cardiovascular disease in patients with familial Mediterranean fever?

Dimitrios Ioannis Patoulias

Familial Mediterranean fever (FMF) is a monogenic autoinflammatory disease, characterized by inflammatory attacks of fever and polyserositis [1]. Missense mutations in the MEFV gene triggering abnormal activation of the pyrin inflammasome and the subsequent excessive production of interleukin-1β (IL-1β) constitute the major underlying pathophysiological mechanism [2].

Patients with FMF are at high cardiovascular risk, which adds a significant burden to their quality of life, complicating at the same time their therapeutic management [3]. In their cross-sectional study with a prospective 3-year follow-up period, Yilmaz et al. observed that patients with FMF and secondary amyloidosis had increased risk of cardiovascular events, highly associated with elevated levels of asymmetric dimethyl arginine (ADMA), decreased flow-mediated dilatation (FMD) and an excessive inflammatory state [3].

Cakar et al. observed that patients with FMF during disease attacks had higher pulse wave velocity (PWV) and lower branchial and aortic augmentation indexes, both surrogate markers of arterial stiffness [4], when compared with asymptomatic patients and healthy controls [5]. Impaired arterial stiffness, as represented by PWV, correlated significantly with the main inflammatory markers, including serum C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white blood cells count (WBC), fibrinogen and neutrophil/lymphocyte ratio. In another cross-sectional study, Acay et al. observed that atherogenic index (triglycerides/high-density lipoprotein-cholesterol) was significantly higher in patients with FMF compared to healthy controls [6]. The authors concluded that the atherogenic index may be an indicator of accelerated atherosclerosis in those patients, an observation that needs to be further elucidated in large-scale prospective studies.

A recently published study by Basar et al. shed light on the association between MEFV gene mutations and early coronary artery disease (CHD) [7]. More specifically, the researchers observed that MEFV gene mutations were significantly more frequent in patients with early CHD, when compared with those suffering from CHD in the presence of well-established risk factors or healthy controls. Interestingly, there were twice as many patients with early CHD and at least one MEFV gene mutation, compared with the two other study groups [7].

Puricel et al. conducted a retrospective clinical study, involving all patients admitted with acute coronary syndrome (ACS) aged less than 30...
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Canakinumab is a monoclonal antibody against IL-1β, which plays a crucial role in terms of decrease in cardiovascular morbidity and mortality in FMF (95% CI: 0.66–0.85, p < 0.0001), and 31% reduction in both cardiovascular (HRadj = 0.69; 95% CI: 0.56–0.85, p = 0.0004) and all-cause mortality (HRadj = 0.69; 0.58–0.81, p < 0.0001), while those patients featuring greater inflammatory activity with hsCRP levels higher than 2 mg/l did not benefit from canakinumab treatment at a statistically significant level [15].

Conflict of interest

The author declares no conflict of interest.

References

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