CORRESPONDENCE

White Blood Count Components as Risk Predictors for Coronary Heart Disease: The Role of Eosinophils

To the Editor:

We read with great interest the paper by Madjid and Fatemi[1] about the components of the complete blood count as indicators of inflammation and risk predictors of coronary heart disease. Although all subtypes of the white blood count have been associated with an increased risk of coronary heart disease, the role of eosinophils has been underestimated. The authors[1] correctly refer to genetic analysis of the inflammatory role of eosinophils, because a single nucleotide polymorphism at 12q24, in *SH2B3*, was found to have a significant association with myocardial infarction (MI).

Eosinophils play an important role in inflammation, and their existence denotes hypersensitivity inflammation. Hypersensitivity inflammation can induce acute MI, and the Kounis hypersensitivity acute coronary syndrome is well described.[2] In patients who had vasospastic angina pectoris, eosinophil counts were significantly increased and could predict the severity of the disease. After these patients underwent medical therapy and attained relief from chest symptoms, their eosinophil counts decreased significantly, to the same level as those of the control group.[3] Clinical reports have shown that the absolute number of eosinophils and the eosinophil-to-leukocyte ratio are significantly elevated in patients who have coronary artery disease.[4] Coronary vasospasm associated with eosinophilia responds poorly to conventional vasodilator therapy, and although the risk of recurrent coronary events is high, most patients respond to therapy that suppresses eosinophilia, such as corticosteroids.[5] Eosinophils are pleiotropic multifunctional leukocytes involved in the initiation and propagation of inflammatory responses, and they express H_4 histamine receptors on their surface. These receptors facilitate eosinophil chemotaxis toward mast cells, which are a source of inflammatory soluble mediators. These mediators can induce the coronary hypersensitivity associated with Kounis syndrome that manifests itself as vasospastic angina, acute MI, or both.[2] Soluble mediators secreted by mast cells and eosinophils also modulate reciprocal interactions between these 2 cells in the so-called "allergic effector unit." Major basic cationic protein released from eosinophils can activate mast cells.[6] This activation elicits exocytosis and new eicosanoid and cytokine production, both of which are prominent responses after FcεRI-dependent activation of mast cells.

Mediators similar to those found in Kounis syndrome are found in cases with nonallergic causes, which suggests that this is a more general problem. A common pathway between allergic and nonallergic coronary syndromes seems to exist.[2]

Eosinophil count has emerged as a novel biomarker of risk stratification in patients who have coronary artery disease. This reality is essential for elucidating the cause of inflammation.

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Discovery of Biomarkers for Chronic Graft-versus-Host Disease

To the Editor:

We read the article by Dogan and colleagues[1] regarding the cardiac effects of chronic graft-versus-host disease (cGVHD) in patients who had undergone allogeneic stem cell transplantation. Chronic GVHD is a severe complication after allogeneic bone marrow transplantation, which is an immunotherapeutic option in several hematologic diseases.

Although the pathogenesis of cGVHD remains unclear, it is solidly linked to graft-versus-leukemia (GVL) reactions; the balance between GVHD and the benefi-

cial GVL-effect anticancer capacity of donor immune cells is crucial to the outcome of transplantation. Several variables have been observed clinically, such as the type of disease, the conditioning regimen, and relevant polymorphisms of the genes that might contribute to interpatient variability in alloimmune responses.

Investigators in Spain have found that the cytotoxic T-lymphocyte antigen 4 (CTLA-4) CT60 AA genotype is associated with an increased risk of relapse and a higher transplant-related mortality rate.[2] In addition, investigators have proposed that the major histocompatibility complex class I chain-related protein A (MICA) is a genetic marker of cGVHD: MICA is a molecule of particular interest because of its participation in non-T-cell receptor-mediated immune function. In particular, Boukouaci and colleagues[3] have found that the presence of MICA-129 values increases the risk of cGVHD in an allele dose-dependent manner. Unfortunately, it is unclear how to use these genetic markers as candidate biomarkers for cGVHD in the clinical setting.

We agree that high-sensitivity C-reactive protein (hs-CRP) is a useful biomarker in patients in whom cGVHD develops after bone marrow transplantation.[4] Other investigators have studied the tissue damage caused by the conditioning regimen, infections, and allogeneic immune reactions accompanying the initial elevation of hs-CRP levels during the course of allogeneic hematopoietic stem cell transplantation.[5] These findings indicate the possible association of hs-CRP values with the substantial increase in tissue damage that leads to GVHD.[5] However, results of a recent study[6] show that cGVHD has no impact on cardiovascular risk and that hs-CRP (which is usually considered to be an important biomarker that predicts the risk of cardiovascular events) does not correlate with profiles of high cardiovascular risk. Hence, does hs-CRP exert a direct cardiac effect through an increase in left ventricular mass, or is it a surrogate biomarker only for cGVHD patients? Future efforts in biomarker discovery and consequent validation are needed for an understanding of the pathogenesis of cGVHD.

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