To the editor:

Vascular complications after splenectomy for hematologic disorders

In a recent issue of Blood, Crary and Buchanan published the most perceptive and comprehensive review to date of thrombotic vascular complications arising with functional or surgical asplenia in patients with hematologic, and especially hemolytic, disorders. Their overview of the literature presents a great deal of food for thought regarding the apparent role of splenic function in protecting against thromboembolic disease, including venous thrombosis, pulmonary thromboembolism, and even arteriosclerosis and pulmonary hypertension. As the authors describe, these risks are reported even in subjects without hematologic disease who undergo splenectomy, but chronic hemolytic disease may compound this risk. I would like to point out 2 important additional pathophysiologic links.

The authors discuss the paradox that the incidence of arteriosclerotic events is lower in hereditary spherocytosis patients with intact spleens compared with their hematologically unaffected first degree relatives, and this low risk of arteriosclerosis is shared with patients with sickle cell disease. Crary and Buchanan propose a protective effect of hemolysis, mediated possibly by the lower serum cholesterol level seen in several forms of anemia. Importantly, clearance of hemoglobin-haptoglobin or heme-hemopexin complexes by CD163- and CD91-expressing reticuloendothelial macrophages triggers induction of hemeoxygenase-1 (HO-1), an enzyme that performs the first committed step in heme catabolism. Besides producing carbon monoxide, a metabolic product of HO-1, this enzyme is also involved in the production of carbon monoxide, biliverdin, and bilirubin. Supporting this idea, HO-1 gene transfer experiments in mice protect against the development of arteriosclerosis in mice. In patients with chronic hemolysis, I agree with Crary and Buchanan that loss of splenic function shifts the predominant site of hemolysis from extravascular to intravascular. More specifically, Westerman and colleagues have observed that plasma hemoglobin and microparticle levels are higher in splenectomized thalassemia patients than those with intact splenic function. Although in a nonrandomized study such as this, splenectomy might simply be a marker of patients who underwent splenectomy due to more severe disease, the findings are fully consistent with a delay in hemolysis, but with a proposed shift of site of hemolysis to intravascular, causing plasma hemoglobin levels to rise. The significance of this shift lies in the pathologic effect of plasma hemoglobin, which is documented to scavenge nitric oxide. This decreased nitric oxide bioavailability promotes a generalized vasculopathy phenotype of vasoconstriction, smooth muscle proliferation, and activation of adhesiveness of platelets and endothelial cells, with particular affinity to the pulmonary vasculature. Furthermore, microparticles are believed to be prothrombotic.

I would like to commend Drs Crary and Buchanan for their valuable contribution to the literature on vascular disease and splenic function. Blood readers should also be aware of the emerging biology of heme-induced HO-1 vasculoprotection and of splenectomy-associated shifts of hemolysis promoting a state of relative nitric oxide deficiency. It is likely that these proposed mechanisms are only part of a multifactorial pathobiology linking asplenia and vasculopathy.

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References

To the editor:

Restoration of the human stem cell niche after stem cell transplantation

Recently, Dominici et al very elegantly demonstrated restoration of the osteoblastic hematopoietic stem cell (HSC) niche after lethal marrow radioablation in mice. Based on their data, the authors propose a model in which radiation induced an increase in stromal cell–derived factor 1α (SDF-1α), causing the attraction of CXCR4-positive megakaryocytes that survived radiation. A concomitant
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