ASK A SPECIALIST: ASK A PATHOLOGIST

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QUESTION

I am suspicious that my patient with aortic stenosis may have acquired von Willebrand syndrome. What laboratory tests should I order if I suspect this diagnosis?

ANSWER

The association between aortic stenosis and bleeding, particularly mucosal bleeding from gastrointestinal angiodysplasia, was described by Dr. Edward Heyde in 1958. Since that time, it has been determined that Heyde syndrome is associated with acquired type 2A von Willebrand syndrome (AvWS), characterized by a loss of large von Willebrand factor (vWF) multimers.

Although AvWS may also be seen in hematopoietic malignancies, hypothyroidism, and other conditions, the mechanism of this acquired deficiency in cardiovascular disorders such as aortic stenosis or left ventricular assist device patients is thought to be high shear forces which induce structural changes in vWF. These changes expose the cleavage site for ADAMTS13 protease, leading to degredation and loss of high molecular weight vWF multimers.

AvWS is common in patients with aortic stenosis and likely underdiagnosed; Vincentelli, et al, found abnormal platelet function assays and a reduction in high molecular weight vWF multimers in 92% of patients with severe aortic stenosis and 50% of patients with moderate aortic stenosis. Bleeding episodes, most commonly from skin or mucosal sites, occurred in 21% of patients with severe aortic stenosis within the 6 months prior to valve replacement surgery. Studies have found that AvWS due to aortic stenosis improves with surgical valve replacement.

Several laboratory tests are available to assist in the diagnosis of AvWS in patients with aortic stenosis:

Platelet function assays (PFA-100) generally show prolonged closure times in AvWS, however this test may also be abnormal in patients with platelet dysfunction from other causes and may be falsely prolonged in patients with significant anemia or thrombocytopenia.

The ristocetin cofactor activity and vWF antigen levels may be normal or even elevated in AvWS due to cardiovascular causes, as both are positive acute phase reactants. The interpretation of ristocetin cofactor activity and vWF antigen levels should include an assessment of ABO blood type, since baseline levels may be up to 30% lower in patients who are ABO blood type O. A decrease in the ratio of ristocetin cofactor to vWF antigen is consistent with the diagnosis of AvWS.

vWF multimer analysis, which is often performed by Western blot, will show the characteristic decrease in high molecular weight multimers.

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