Resolution of acquired von Willebrand Syndrome secondary to hypertrophic obstructive cardiomyopathy following septal myectomy

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Abstract

We report the case of a 69–year–old Caucasian male patient with hypertrophic obstructive cardiomyopathy, severe gastrointestinal bleeding, and acquired von Willebrand Syndrome. The patient had previously been known to have hypertension, hyperlipidemia, and a family history of early atherosclerosis. Pre–operative blood tests showed normal von Willebrand factor activity with a decrease in high molecular weight multimers. Septal myectomy was performed in treatment of his hypertrophic disease. Follow–up blood tests indicated normal von Willebrand factor activity and high molecular weight multimer levels. Gastrointestinal bleeding has not recurred following surgery. In conclusion, septal myectomy resolves von Willebrand syndrome secondary to hypertrophic obstructive cardiomyopathy, in this case. As von Willebrand factor multimer testing can be used for the diagnosis of acquired von Willebrand syndrome, it should be considered in patients who have gastrointestinal bleeding coinciding with hypertrophic obstructive cardiomyopathy.

Background

Von Willebrand Syndrome (vWS) is defined as a deficiency of the blood protein von Willebrand factor (vWF) that can result in excessive bleeding. It can be inherited and, in rare cases, acquired vWS can develop later in life secondary to many conditions such as autoimmune and congenital and acquired cardiac diseases.[1-3] While there is no cure for inherited vWS there are several treatment options that help supplement vWF. In acquired cardiac cases, repair of jet lesions will result in normalization of vWF.[4-7] In patients who have been investigated for severe bleeding and who have been found to have vWS, it would not be unreasonable to screen for cardiac lesions with echocardiography.

In 1958, Dr. Heyde first described an association between gastrointestinal (GI) bleeding and aortic stenosis.[8] Heyde's syndrome, as it is now known, has been linked to the development of acquired vWS. High shear stress, brought on by aortic stenosis, was subsequently shown to cause the proteolysis of high molecular weight multimers (HMWM) of vWF.[4] This deficiency in HMWM causes acquired vWS and leads to the GI bleeding as described in Heyde's Syndome. Recently, it has been indicated that hypertrophic obstructive cardiomyopathy (HOCM) can also lead to a decrease in vWF through an analogous mechanism to aortic stenosis in Heyde's syndrome.[4-7] Here, we describe a patient diagnosed with HOCM and acquired vWS who had a decrease of HMWM.

Case

A 69–year–old man was seen in the Toronto General Hospital (TGH) cardiac clinic with New York Heart Association and Canadian Cardiovascular Society class III symptoms of shortness of breath and angina. Beginning in 2009, the patient was found to be anemic and, over the next four years was transfused a total of 119 units of blood. The year prior to cardiac referral, he was found to have bleeding small bowel angiodysplasia as the cause of his blood loss following upper and lower endoscopy. This was definitively treated with endoscopic sclerotherapy. In the process of the patient's GI bleeding investigations he was also diagnosed with HOCM and coronary artery disease. Over the intervening year, the patient's cardiac symptoms progressed precipitating a referral. The patient's coronary risk factors included hypertension, hyperlipidemia, and a family history of early atherosclerosis. His medications, at the time of assessment, consisted of acetylsalicylic acid, metoprolol, atorvastatin, and disopyramide. Prior to endoscopic treatment, 1-3 units of blood each week were necessary to maintain acceptable hemoglobin levels. At the time of presentation to TGH, a cardiac workup demonstrated significant left ventricular outflow tract obstruction associated with typical findings of HOCM. On review of this patient's echocardiogram, his basal septum measured 27 mm in maximal thickness (normal 8-12 mm). A left ventricular outflow obstruction gradient was measured at 53-63 mmHg, which increased to 86 mmHg with Valsalva maneuver. A left ventricular outflow track gradient of less than 20 mmHg is considered normal and should not increase with Valsalva maneuver. Posteriorly directed mitral regurgitation was also visualized. A coronary angiogram demonstrated significant two–vessel coronary disease. Based on his symptom status, the patient was considered for myectomy surgery. Pre–operative blood work indicated the patient had vWF well within normal range, finding the vWF antigen to be 120 units/mL and activity to be 107 units/mL. Multimer studies showed absent or markedly decreased HMWM without the increase in low molecular weight multimers that would indicate acquired vWS.

Over the course of the investigation, the patient was diagnosed with Heyde's syndrome. This is normally described in patients with severe aortic stenosis where, presumably, the shear stress of blood going through the aortic valve causes an acquired form of vWS with recurrent bleeding. In those patients, aortic valve replacement often leads to resolution of the vWS.

The patient was admitted to hospital for septal myectomy and aorto–coronary bypass grafting. During surgery, the myectomy was performed, spanning the mid portion of the right coronary artery cusp

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to the lateral border of the mitral valve annulus. The specimen was approximately 15 mm in thickness and carried nearly 40 mm into the ventricle. A wedge of ascending aorta approximately 1.5 cm in length was excised anteriorly. Following the myectomy, saphenous vein grafts were constructed to the diagonal and distal right coronary arteries.

Ten months after surgery, the patient had no symptoms of angina or shortness of breath. He had not experienced any bleeding since the surgery. A follow–up vWF profile, performed at nine months post–surgery, found vWF antigen was 144 units/mL with activity at 133 units/mL; both are within the normal range. The follow–up multimer test showed normal HMWM levels following surgery. Both HMWM, as well as intermediate weight multimers, were present at normal levels. This indicates normal vWF function and resolution of vWS.

Discussion

Septal myectomy for HOCM, resulting in resolution of left ventricular outflow tract obstruction, normalized the HMWM level in a patient with severe GI bleeding and acquired vWS. There is a documented link between HOCM and acquired vWS.[6,7] It has been previously determined that shear stress brought on by high velocity restrictive lesions such as aortic stenosis, ventricular septal defect, and patent ductus arteriosus can cause the proteolysis of HMWM.[4] High amounts of shear stress, brought on by HOCM, can cause the proteolysis of HMWM. The turbulence and flow restrictions caused by HOCM have also been shown to cause a reduction in HMWM.[6] This case supports the theory that HOCM causes the proteolysis of HMWM. The HMWM loss present prior to surgery normalized after cardiac repair. We propose the decreased shear stress after septal myectomy resolved the severe GI bleeding caused by acquired vWS secondary to HOCM. Therefore, patients diagnosed with HOCM who experience severe GI bleeding should be considered as possibly having acquired vWS and pre–operative vWF multimer testing may be of benefit. While there is other evidence of HOCM leading to acquired vWS[5,6] there is still a lack of knowledge regarding the correct protocol to follow. This case study hopes to further indicate proper procedures when presented with patients with HOCM and severe GI bleeding.

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