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Trancatheter Aortic Valve Implantation in the Treatment of Heyde's Syndrome: A Case Report

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Abstract **Case Report**

Calcified aortic stenosis is the most common valvulopathy of the elderly. Its association with angiodysplasia and digestive bleeding is known as Heyde syndrome. This clinical case highlights the importance of the diagnosis of this syndrome whose complications can be fatal. The cessation of gastrointestinal bleeding is often remarkable after aortic valve replacement. Transcatheter aortic valve implantation (TAVI) can represents a good alternative to surgical valve replacement, especially in patients with high surgical risk. We report a case of 62-year-old patient, admitted for management of global cardiac decompensation on a tight aortic stenosis, confirmed by transthoracic echocardiography as well as a few episodes of syncope. He had a history of repeated lower digestive hemorrhages that required several transfusions. The evolution was marked by the appearance of heavy rectal bleeding on cecum angiodysplasia lesions confirmed by colonoscopy. The association of digestive bleeding and aortic stenosis raised the diagnosis of Heyde syndrome. An assay of von Willebrand factor (vWF) antigen, vWF binding collagen activity and their ratio confirmed a qualitative deficiency of vWF type 2A. The proposed treatment was TAVI because of the high surgical risk and the patient's refusal of the surgery. The evolution at 1 month post TAVI was marked by the improvement of hemostatic parameters related to the vWF and the disappearance of cardiac symptomatology. The cessation of gastrointestinal bleeding in Heyde's syndrome is conditioned by percutaneous aortic valve replacement in the high-risk surgical subject with a good clinical and biological evolution.

Keywords: Heyde syndrome, von Willebrand disease, aortic stenosis, TAVI, case report.

INTRODUCTION

Patients with aortic valve stenosis present with gastrointestinal bleeding during Heyde syndrome. It is defined by the combination of aortic vavlve stenosis, bleeding GI angiodysplastic lesions and acquired von Willebrand factor type 2A deficiency. The treatment of Heyde's syndrome consists of surgical replacement of the aortic valve. In our case, we performed trancatheter aortic valve implantation (TAVI) to study the effect of this procedure on vWF as well as on Heyde syndrome.

CASE PRESENTATION

The patient was 62 years old and was admitted to the cardiology department for repeated short and rapidly resolved dyspnea and fainting episodes. He was known to have ischemic heart disease with moderate left ventricular dysfunction and several episodes of global heart failure. He was treated with a combination of furosemide, bisoprolol, converting enzyme inhibitors, statins and aspirin. He has been hypertensive for 4 years and is a poorly controlled chronic smoker with 40 pack-years of tobacco.

The history of his disease goes back to 1 year with the aggravation of a dyspnea stage II becoming stage IV of the NYHA associated with syncopes and bilateral and not painful edemas of the lower limbs. The interrogation notes the occurrence of several episodes of lower digestive haemorrhage having required repeated transfusions and then put on martial therapy, which were not documented.

Clinical examination revealed an asthenic patient, pale with discolored conjunctiva, crepitating rales reaching midfield, edema of the lower limbs reaching the roots of the thighs, turgidity of the jugular veins and a sloping dullness of the flanks. On cardiac

auscultation, the presence of an aortic narrowing murmur was noted. The biological workup showed an anaemic microcytic hypochromic anemia with a hemoglobin of 7.2 g/dl and a ferritin level of 20 ng/ml.

Colonoscopy revealed angiodysplasia lesions in the cecum associated with internal hemorrhoids. The esogastroduodenal fibroscopy showed a non-ulcerated gastric stromal tumor without red signs.

Transthoracic echocardiography showed global hypokinetic heart disease in the dilated stage with an ejection fraction of 30%. Valvulopathy was noted as a tight calcified aortic stenosis with an aortic surface area of 0.9cm2, a mean gradient of 68.31mmHg and a peak transvalvular velocity of 6.07m/s.

The evolution during hospitalization was marked by the occurrence of an episode of heavy rectal bleeding, without hemodynamic instability, which required the discontinuation of aspirin and the transfusion of 4 red blood cells. In terms of cardiac decompensation, the patient was completely depleted on furosemide and spirinolactone.

In view of the presence of recurrent digestive bleeding, angiodysplasia and aortic stenosis, the diagnosis of Heyde syndrome was raised. We performed the antigenic determination of Won Willebrand factor (vWF:Ag) by immunoturbidimetry which came back normal at 3.59ui/ml (normal value > 0.5 ui/ml). The functional study of vWF was performed by measuring the collagen binding activity of von Willebrand factor (vWF:CB) which returned to 2.15ui/ml (normal value > 0.5 ui/ml). The ratio of these two values was calculated and returned to 0.59 (vWF:CB/vWF:Ag, normal value> 0.7), which confirmed the deficiency of high molecular weight multimers corresponding to a deficiency in von Willebrand factor type 2A.

Given the high surgical risk with a Euroscore 2 to 9 (mortality risk of 12.85%) and the patient's refusal of surgery, transfemoral TAVI was performed. Double anti-platelet aggregation was prescribed after the procedure. At 1 month post TAVI, there was a significant improvement in biological parameters. Thus, the vWF:Ag level was 3.81ui/ml, the vWF:CB was 3.2ui/ml and the vWF:CB/vWF:Ag ratio was 0.83. The blood count showed a stable hemoglobin level of 12g/dl. Dyspnea, syncope, and GI bleeding disappeared.

DISCUSSION

In 1958 Edward Heyde sent a letter for the new england journal of medicine, here an abbreviated version to the editor: ¨During the past 10 years I have seen at least 10 patients with calcifying aortic stenosis and massive gastrointestinal bleeding for which we have been unable to discover any cause. They were almost always elderly and most of them had classic signs of aortic stenosis. I would appreciate it if you printed this letter¨ [1]. And it is from this that Heyde syndrome emerged. It is defined by the combination of hemorrhagic angiodyplastic lesions resulting in GI bleeding, aortic narrowing, and an acquired qualitative deficiency of vWF type 2A [2].

Aortic valve stenosis as well as other degenerative diseases in elderly subjects may promote GI bleeding through complex mechanisms. First, aortic stenosis is thought to cause bleeding by reducing gastrointestinal perfusion and causing hypoxia-induced blood vessel dilation. Second, it has been suggested that in patients with aortic stenosis, gastrointestinal bleeding would be promoted by an acquired Von Willebrand syndrome type 2A caused by shear through the aortic stenosis [3].

In the physiological state, high molecular weight vWF multimers cross a healthy aortic valve and remain intact in their spiral forms. In the event of bleeding, vWF in its multimeric form adheres to the subendothelial lesion and to platelets, thus initiating the blood clot formation process. In Heyde's syndrome, there is a despiralization of the high molecular weight vWF multimers due to shear forces across the aortic stenosis. The A2 domain site of vWF is then exposed to a protease called ADAMTS 13, which will cleave the despiralized multimers and transform them into an inactive form, unable to adhere to the subendothelial wall and to platelets [4].

Deficiency of the high molecular weight molecule of vWF is diagnosed by agarose gel electrophoresis, which is the reference test. This test remains expensive and unavailable in our facility. There are other markers capable of identifying type 2A VWD. First, the vWF antigen (vWF:Ag) assay is usually normal (no quantitative deficiency). Then, the assay of the collagen binding activity of vWF (vWF:CB). Then the vWF:CB/vWF:Ag ratio, whose value is less than 0.7, confirms the deficiency in high molecular weight multilayers [5].

In a study conducted by Mayoclinic published in 1987, 91 patients presented with calcified aortic stenosis associated with recurrent lower GI bleeding. Their age range was 38 to 80 years. They were divided into 3 groups and followed for a period of 8 to 12 years. The first group consisted of 40 patients who had not received any treatment, all of whom continued to bleed and had recurrent transfusions. The 2nd group consisting of 37 patients who had benefited from digestive surgery, 95% continued to bleed. Conversely, the 3rd group consisting of 16 patients who had undergone surgical aortic valve replacement, only 2 patients continued to bleed, 1 of whom presented with gingivorrhagia following therapeutic elevation of prothrombin levels. King et al concluded that in patients with unexplained gastrointestinal bleeding and

concomitant aortic valve stenosis, AVR offered a likely cure. This shows that AVR is an effective treatment not only for severe aortic stenosis but also for bleeding due to intestinal angiodysplasia [6].

TAVI represents a good alternative in patients at high surgical risk. The 1st cohort done in this sense was published in 2013 by Godino *et al*., It was conducted on 400 patients who all underwent TAVI, 7 of whom had the diagnostic criteria for Heyde syndrome. The surgical risk was high in all 7 patients. The TAVI procedure was performed by a transfemoral approach in 6 patients and transaxillary in 1 patient. Only one case of procedural failure occurred because of the inability to cross the iliofemoral artery. At discharge, dual antiplatelet therapy was prescribed for 6 months in 4 patients. Whereas in 3 patients with atrial fibrillation, single antiplatelet therapy, in addition to anticoagulant therapy, was recommended for 6 months. The follow-up interval was 22 months, 6 patients with TAVI had no recurrence of gastrointestinal bleeding, 1 patient with failed TAVI had recurrent bleeding requiring iterative transfusions. It is noted that after TAVI, recurrence of GI bleeding was abolished in all successfully treated patients [6].

Marggraf *et al*., [7] studied the improvement of hemostatic parameters in relation to vWF in a small group of patients with Heyde syndrome who underwent TAVI. High molecular weight multimers increased after the procedure.

CONCLUSION

In the absence of guidelines and according to expert consensus, aortic valve replacement is the recommended first-line treatment for Heyde syndrome. The TAVI procedure improves hemostatic parameters in acquired type 2A VWD and stops GI bleeding in patients at high surgical risk.

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