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Case Report

A Rare Cause of Gastrointestinal Bleeding: Heyde Syndrome

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Abstract

Calcific aortic stenosis can be associated with gastrointestinal bleeding mainly from angiodysplasias which refer to Heyde syndrome. This association is considered as a form of acquiredVon Willebrand syndrome.Aortic valve replacement allows cessation of gastrointestinal bleeding and the need for blood transfusions in these patients. We describe three cases with medical history of aortic stenosisand they presented gastrointestinal bleeding related to angiodysplasias of the stomach and colon. In one case, aortic valve replacement leads to a stable hemoglobin with no further episodes of gastrointestinal bleeding.

Keywords: Aortic stenosis, gastrointestinal bleeding, Heyde syndrome, acquired Von Willebrand syndrome.

BACKGROUND

Sixty-two years ago, Dr. E. C. Heyde was the first to describe the association of gastrointestinal(GI) bleeding and calcific aortic stenosis (AS) [1]. The angiodysplasia represents the most source of GI bleeding that is recognized by focal or diffused venous and /or capillary lesions presenting as bright red ectatic vessels or pulsatile red protrusions, with surrounding venous dilatation or patchy erythema with or without oozing [2, 3]. Heyde syndrome has been estimated to affect nearly 20% of patients with severe AS [4]. Here, we report our experience with three cases of Heyde syndrome.

CASE PRESENTATION

Case 1

A 50 year-old-female with a history of multiple GI bleedings with severe AS, presented for worsening dyspnea, fatigue, and hematemesis associated with melanotic stools. On physical exam, she was hemodynamically stable with a marked ejection systolic murmur in the aortic area. Labs showed hemoglobin of 9 g/dl, platelets, and international normalized ratio were normal. Esogastroduodenoscopy (EGD) showed Gastric angiodysplasia of the fundus that coagulated with Argon plasma coagulation (APC). Echocardiogram showed rheumatic severe aortic stenosis with a valve area of 0.3 cm^2/m^2 and a peak gradient of 101 mmHg and conserved ejection fraction of 70%. The angiocoronography was normal. The patient was addressed for the assessment ofaortic valve replacement (AVR).

Case 2

A 66-year-old male, with a medical history of severe aortic stenosis, was admitted to our facility for hematochezia. He was hemodynamically stable with 6.9 g/dl of hemoglobin. After blood transfusions, the patient underwent colonoscopy that identified multiple lesions of angiodysplasia of the right colon that were treated with APC (Fig 1). The patient is undergoinga workup for AVR.

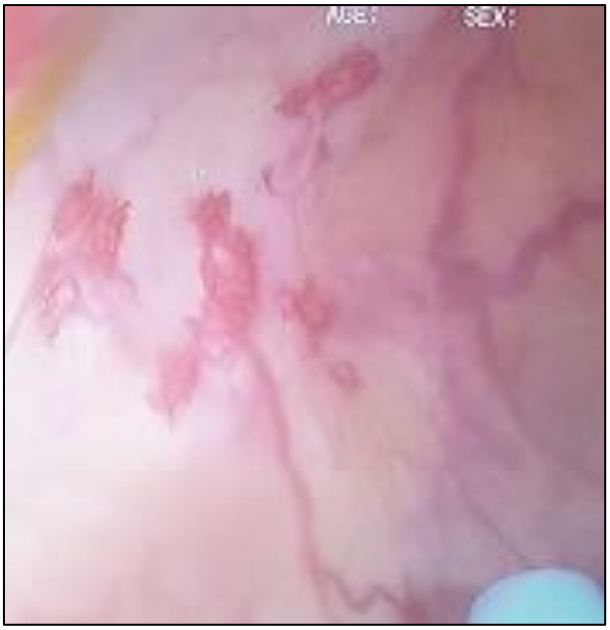

Fig 1: Endoscopy view showed colonic angiodysplasia

Case 3

A 65-year-old female with no medical history was admitted to our department for severe anemia and hematemesis. Her hemoglobin was at 6 g/dl. EGD was performed, after packed red cells transfusion, showed antral angiodysplasia that cauterized with APC (Fig 2). Six mounts later the patient was readmitted for the same symptoms and another EGD revealed angiodysplasia which was treated for the second time with APC. An echocardiography was carried out that identified a severe AS. The patient has benefited from AVR and she kept a stable hemoglobin at 12 g/dl during the whole follow-up and she was not requiring any further blood transfusions.

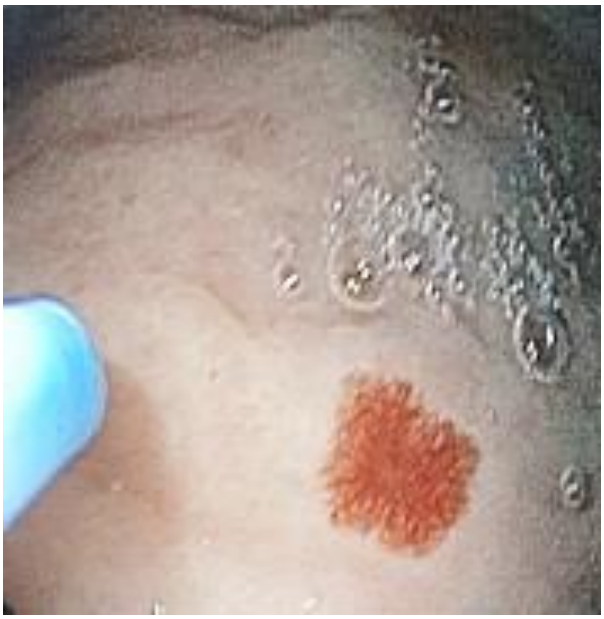

Fig 2: Endoscopy view showed gastric angiodysplasia

DISCUSSION

In 1958, Heyde EC. Reported 10 cases of calcific AS with GI bleeding [1]. Later numerousreports and studies search to explain this association. The source of bleeding was related to GI angiodysplasia [5] and the most commonlocalization wasthe right colon [2]. In an earlier report, the association between GI bleeding and AS was established for 15 out of 16 patients who underwent AVR withan effective cure of GI bleeding [6] and was confirmed by ThompsonJ. and colleagues for 45 patients [2]. Heyde syndrome was identified as a form of type IIA Von Willebrand (VWF) disease or an acquiredVon Willebrand syndrome (AVWS)defined as a result of dysfunction or degradation of VWF function that occurs in many

clinical situations such as malignant hemopathies, and aortic valve stenosis, and in patients with aortic and mitral prosthesis dysfunction [7]. VWF is a glycoprotein synthesized in endothelial cells and megakaryocytes and has a well-characterized role in primary and secondary hemostasisas a mediator of platelet adhesionto the endothelium following vascular injury and as a carrier for coagulation Factor VIII [8]. The pathogenesis of Heyde syndrome involvesa modification of high-molecular-weight VWF multimers in the area of high turbulence flow through a stenotic aortic valveknown as the shear stress effect, the VWF multimers become opened and extended, and exposea specific site (A2 domaine) to cleavage by a plasmatic protease: ADAMTS13 (ADisintegrin And Metalloproteinase with Thrombospondin type 1 motif, member 13) which return VWF smaller in size and less hemostatically competent than itsoriginmultimers [5]. The mechanismunderlyingthe formation of angiodysplasia during Heyde syndrome is debated, some authors suggest that the prevalence increases with the age, and severe aortic stenosisseems to decrease gastrointestinal perfusion which leads to hypoxia-induced vasodilation and the origin of angiodysplasia [9] through the increase of VEGFR2 (vascular endothelial growth factor 2) activity [10], others mentioned that a normal VWF controls angiogenesis by inhibiting VEGFR2 signaling [8]. Laboratory assessment of AVW Srequires the VWF multimers analysis, the level of VWF Antigen and activity, and the Factor VIII Activity [1]. The severity of abnormalities of VWF seems to be correlated to the severity of AS, and then the risk of bleeding [4]. The GI bleeding is generally controlled byelectrocautery with APC and medical treatment like octreotide but they have a temporary effect and bleeding relapse in at least one-third of patients, so the best management of GI bleeding in documented Heyde syndrome is AVR, which leads to significant improvement in VWF multimeters after surgery, and cessation of GI bleeding in nearly 80% of patients [2, 4, 6]. In one of our cases, the AVR allows stable hemoglobin with no further episodes of GI bleeding or need for blood transfusions.

CONCLUSION

Heyde syndrome is a rare cause of GI bleeding that gastroenterologists need to be aware of this disorder. Once the diagnosis is made, AVR should be considered which allows in most cases cessation of bleeding and normalization of VWF multimers.

Disclosure: No Conflict of Interest.

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