Recurrent Bleeding Gastrointestinal Angioectasias and Acquired von Willebrand Deficiency (Heyde's Syndrome) Developing in the Setting of Mild Hypertrophic Obstructive Cardiomyopathy

Ravi Moghe, DO[1]; Andrew Volio, DO[1]; Musa Abu-Jubara, DO[1]; Levi Atinda, DO[1]; Zeryab Khan, DO[1]; Kristin Lescalleet, DO[1]; Robert Palma, DO[1]

[1] OhioHealth Doctor's Hospital, Columbus, OH

ABSTRACT

Heyde Syndrome is classically described as a triad of gastrointestinal (GI) arteriovenous malformations, aortic stenosis (AS), and acquired von Willebrand syndrome (aVWS). Reportedly under-diagnosed, the syndrome is frequently missed even in the presence of classically associated moderate-to-severe AS. Adding difficulty is the increasing recognition of alternative forms of structural heart disease, including hypertrophic obstructive cardiomyopathy (HOCM), having the ability to produce the syndrome.

We present a case of 68-year-old woman with mild HOCM that resulted in 5 years of melanotic episodes before the discovery of bleeding duodenal angioectasias. In the setting of known "HOCM morphology" without obstruction, bleeding episodes began to develop shortly after annual surveillance echo demonstrated a progression to a mildly increased left ventricular outflow tract (LVOT) gradient. Cardiac magnetic resonance imaging (MRI) confirmed mild primary HOCM and confirmed mild flow acceleration across the LVOT. Within a year, GI bleeding would ensue, beginning a prolonged clinical course with multiple hospitalizations for melena and symptomatic anemia. Demonstration of bleeding angioectasias during esophageal duodenoscopy (EGD) on multiple occasions prompted von Willebrand Factor analysis. The patient was found to have acquired Von Willebrand Factor deficiency, suggesting the diagnosis of Heyde syndrome. She was subsequently referred for evaluation and treatment of her HOCM with septal ablation.

This case highlights the ability of mild states of structural heart disease to produce Heyde Syndrome. Diagnostic suspicion must remain high and von Willebrand factor analysis considered in the combined presence of bleeding angioectasias and any state of structural heart disease.

Kristin Lescalleet
OhioHealth Doctor's Hospital
Email: Kristin.Lescalleet@ohiohealth.com
Phone: 804-513-7806

INTRODUCTION

Heyde Syndrome is a multisystem disorder classically described as a triad of aortic stenosis, acquired Von Willebrand Syndrome, and arteriovenous (AV) malformations of the GI tract. First described by Dr. Edward Heyde in New England Journal of Medicine in 1958, that at least ten patients with calcific aortic stenosis also suffered from massive GI bleeding (1). The association of these pathologies has not been without controversy (2)(3)and with more recent evidence shows increasing acceptance of a distinct, causally-related, diagnostic entity (4). Discovery of the link between aortic stenosis and acquired Von Willebrand Factor deficiency has provided a mechanistic rationale for the development of a coagulopathy secondary to valvular heart disease (5), namely that shear force and hemodynamic turbulence are capable of degrading the hemostatic protein. Perhaps solidifying the hypothesis, studies have shown that aortic valve replacement almost invariably reverses acquired Von Willebrand deficiency and subsequent episodes of GI bleeding in cases associated with aortic stenosis (6)(7). At present, it is the recognition that other forms of structural heart disease, including hypertrophic cardiomyopathy (HOCM), may also produce Heyde Syndrome (8) and that treatment can reverse the disease in these cases as well (9). Regardless of structural etiology, most reported cases of Heyde Syndrome are found in the presence of severe underlying disease. Reported here is a case of mild HOCM provoking Heyde Syndrome shortly after the lesion became of modest hemodynamic significance, a less described occurrence.

Case Report

68-year-old female with mild hypertrophic obstructive cardiomyopathy presented with a history of 5 years of GI bleeding episodes before the discovery of bleeding duodenal angioectasias. Initially diagnosed with "HOCM morphology" without evidence of dynamic obstruction on stress echocardiogram, bleeding episodes began to develop shortly after routine annual surveillance echo demonstrated a progression to mildly increased left ventricular outflow tract (LVOT) gradient. Cardiac magnetic resonance imaging (MRI) (Figure 1) not only confirmed mild primary HOCM without secondary cause of hypertrophy, but also demonstrated mild flow acceleration across the LVOT, consistent with the hypothesized hemodynamic turbulence and sheer-stress believed to be the mechanism behind acquired Von Willebrand deficiency. Within a year, GI bleeding would ensue, beginning a prolonged clinical course with multiple hospitalizations for symptomatic anemia requiring transfusions. The eventual discovery of angioectasias (Figure 2) prompted Von Willebrand Factor analysis which found evidence of acquired deficiency and confirmed the diagnosis of Heyde Syndrome. The patient was subsequently referred for evaluation and definitive treatment of her HOCM with septal ablation, an intervention with which case series have demonstrated the potential for reversal of Von Willebrand Factor deficiency and bleeding episodes.

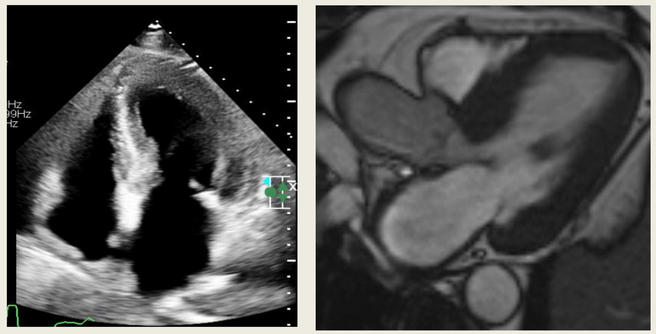

Figure 1. Echocardiography (on left) and cardiac MRI (on right) showing intraventricular wall hypertrophy.

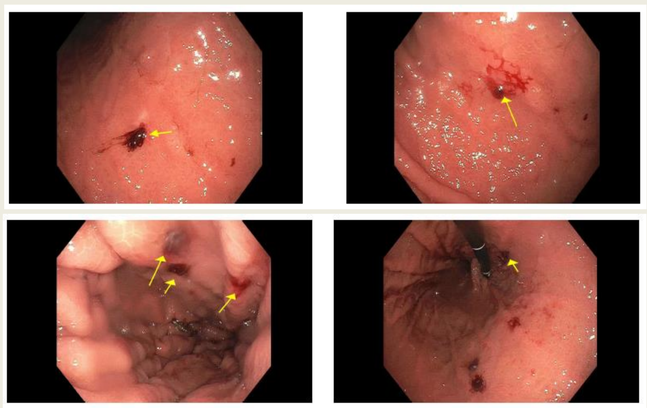

Figure 2. Duodenal bulb and gastric body angioectasia.

DISCUSSION

Despite the known association of acquired Von Willebrand disease with multiple cardiac and non-cardiac pathologies, Heyde syndrome is likely underdiagnosed, even in the presence of classically associated severe aortic stenosis. The patient described in the report suffered from multiple years of recurrent GI bleeding episodes requiring transfusion and endoscopy before a unifying diagnosis was made. Thus, diagnostic suspicion must remain high in the presence of structural heart disease associated with GI bleed and, as this case demonstrates, perhaps even in association with mild structural disease. More cases require identification to confirm this and reported outcomes, especially when intervention is performed, may strengthen the indication for valvular/septal intervention for patients with persistent bleeding GI angioectasia that do not otherwise meet traditional structural or symptom-based criteria.

CONCLUSIONS

Heyde Syndrome, although classically associated with aortic stenosis, can occur with other cardiac and non-cardiac pathologies, perhaps even mild in nature, and should be evaluated in patients with recurrent GI bleeding from angioectasias. In patients with syndromic, multisystem pathology, a unifying diagnosis not only helps guide short term intervention, but can also help patients receive appropriate therapy which can lead to long term improvement. After being diagnosed with Heyde Syndrome secondary to HOCM, our patient was referred for evaluation for definitive treatment of her HOCM.

REFERENCES

1. Heyde, EC. Gastrointestinal Bleeding in Aortic Stenosis. *N Engl J Med. 1958; 259:196 DOI: 10.1056/NEJM195807242590416*
2. Gostout, CJ. Angiodysplasia and aortic valve disease: let's close the book on this association. *Gastrointest Endosc*. 1995 Nov; 42(5):491-3. DOI: 10.1016/s0016-5107(95)70058-7
3. Cevik C, Islam E, Attaya H, Nugent H. Heyde's syndrome: A critical review of the literature. *J Heart Valve Dis.* 2011 Jul; 20(4):366-75
4. Loscalzo J. From Clinical Observation to Mechanism — Heyde's Syndrome. *N Engl J Med*. 2012 Nov; 367:1954-1956. DOI: 10.1056/NEJMc1215053
5. Warkentin TE, Morgan DG, Moore JC. Aortic stenosis and bleeding gastrointestinal angiodysplasia: is acquired von Willebrand's disease the link? *The Lancet*. 1992 Jul; 340(8810):35-7. DOI: 10.1016/0140-6736(92)92434-h
6. King M, Pluth JR, Guiliani ER. The Association of Unexplained Gastrointestinal Bleeding with Calcific Aortic Stenosis. *Ann Thorac Surg*. 1987 Nov; 44(5):514-16. DOI: 10.1016/S0003-4975(10)62112-1
7. Vincentelli A, Susen S, Le Tourneau T, et al. Acquired von Willebrand Syndrome in Aortic Stenosis. *N Engl J Med*. 2003 Jul; 349:343-349. DOI: 10.1056/NEJMoa022831
8. Blackshear JL. Heyde Syndrome: Aortic Stenosis and Beyond. *Clin Geriatr Med. 2019 Aug;* 35(3):369-379. DOI: 10.1016/j.cger.2019.03.007
9. Blackshear JL, Schaff HV, Ommen SR, Chen D, Nichols WL. Hypertrophic obstructive cardiomyopathy, bleeding history, and acquired von Willebrand syndrome: response to septal myectomy. *Mayo Clin Proc*. 2011 Mar; 86(3):219-24. DOI: 10.4065/mcp.2010.0309