

Aortic Valve Replacement for the Management of Heyde Syndrome: A Case Report

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Heyde syndrome describes the triad of aortic stenosis, acquired coagulopathy, and anemia due to bleeding from intestinal angiodysplasia. An 87-year-old man with iron deficiency anemia due to melena was admitted to our hospital. On examination, a systolic murmur was heard and echocardiography confirmed the presence of aortic stenosis. Esophagogastroduodenoscopy and colonoscopy were unremarkable. Capsule endoscopy and double balloon endoscopy revealed angiodysplasia throughout the small intestine. Laboratory investigations were significant for reduced plasma levels of high molecular weight von Willebrand factor multimers. On the basis of these findings, the patient was diagnosed with Heyde syndrome. The patient required frequent blood transfusions because of the intestinal bleeding, and underwent bioprosthetic aortic valve replacement. Twenty months after the operation, the gastrointestinal bleeding resolved and the patient no longer required blood transfusions. This is the first case report to describe an improvement in bleeding from angiodysplasia, one year after aortic valve replacement. It demonstrates the effective treatment of Heyde syndrome with aortic valve replacement, and highlights the importance of considering this differential diagnosis when evaluating patients presenting with repeated episodes of gastrointestinal bleeding and a concurrent systolic murmur.

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Key words: acquired von Willebrand's syndrome, aortic stenosis, gastrointestinal bleeding, Heyde syndrome

Introduction

Heyde syndrome describes the triad of aortic stenosis (AS), acquired coagulopathy, and anemia due to bleeding from intestinal angiodysplasia¹. The coagulopathy is caused by a loss of high molecular weight multimers of von Willebrand factor (vWF)². Since AS is a common disease among older people, it is believed that the incidence of Heyde syndrome is increasing in proportion to population ageing and increasing numbers of people living with AS. Therefore, Heyde syndrome should be considered in patients presenting with AS and gastrointestinal (GI) bleeding. Herein, we report a case of Heyde syndrome that was diagnosed using capsule endoscopy,

double balloon endoscopy, and the analysis of vWF multimers.

Case Presentation

An 87-year-old man presented with a one-month history of melena and iron deficiency anemia. Since esophagogastroduodenoscopy and colonoscopy failed to reveal the source of the bleeding, small intestinal bleeding was suspected. The patient's melena continued despite bowel rest and blood transfusion, so he was transferred to our hospital for further investigation and management.

The patient's medical history was significant for diabetes mellitus, diagnosed when he was 70 years old. There

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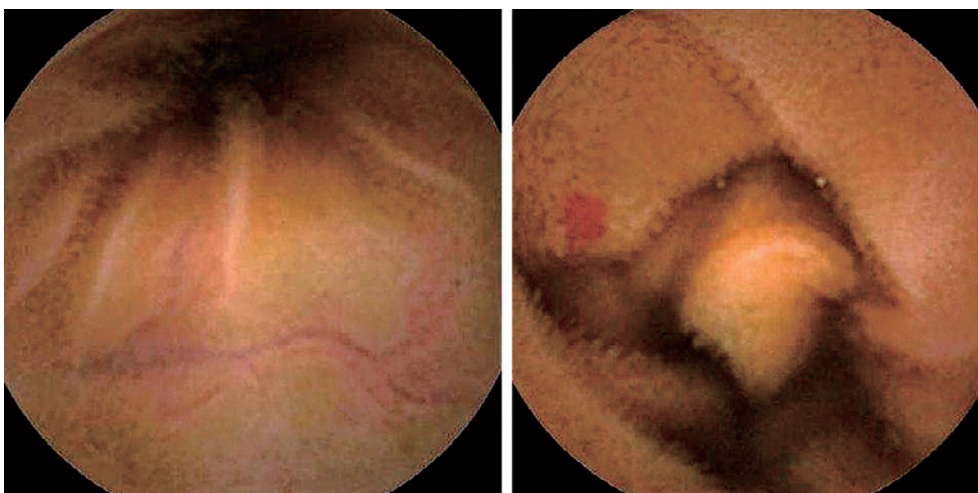


Fig. 1 Video capsule endoscopy showing multiple extending and meandering veins and angiodysplasia in the small intestine. No bleeding is evident.

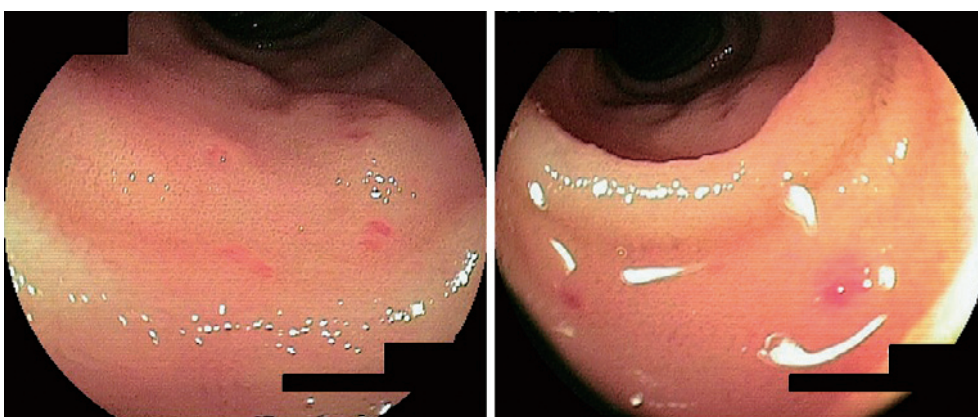


Fig. 2 Double balloon endoscopy showing multiple extending capillaries and spotty redness in the small intestine.

was no significant family history to note, he was a social drinker, and had smoked three cigarettes per day for 60 years. On initial presentation at our hospital, physical examination revealed conjunctival anemia and a Levine IV/VI systolic murmur. Laboratory investigations were significant for a microcytic anemia (hemoglobin 8.7 g/dL, hematocrit 25.3%), prolonged activated partial thromboplastin time (APTT) (35.1 seconds), mild renal dysfunction (creatinine 1.49 mg/dL), and low serum albumin (3.4 g/dL). Capsule endoscopy showed multiple angiodysplastic lesions in the ileum (Fig. 1). Oral and anal double balloon endoscopy also showed multiple angiodysplastic lesions; however, no active bleeding was noted (Fig. 2). As his melena continued, hemostatic forceps with soft coagulation and hypertonic saline-epinephrine injection were administered to prevent re-

bleeding. An echocardiogram was performed to further evaluate the systolic murmur. The echocardiogram showed a left ventricular ejection fraction of 77% and severe AS with an estimated 58.9 mmHg pressure gradient. Based on these findings, we suspected that the patient had Heyde syndrome, and performed gel electrophoresis of the peripheral blood to confirm the diagnosis. This revealed the loss of large multimers of vWF (Fig. 3A), and the patient was diagnosed with Heyde syndrome.

The patient's melena continued despite endoscopic treatment, and he required transfusions of red cell concentrates two to three times a week. The patient's clinical course after admission is shown in Figure 4. Bioprosthetic aortic valve replacement (AVR) was performed on the 33rd day after admission. After the operation, the patient's large vWF multimer index improved (Fig. 3B),

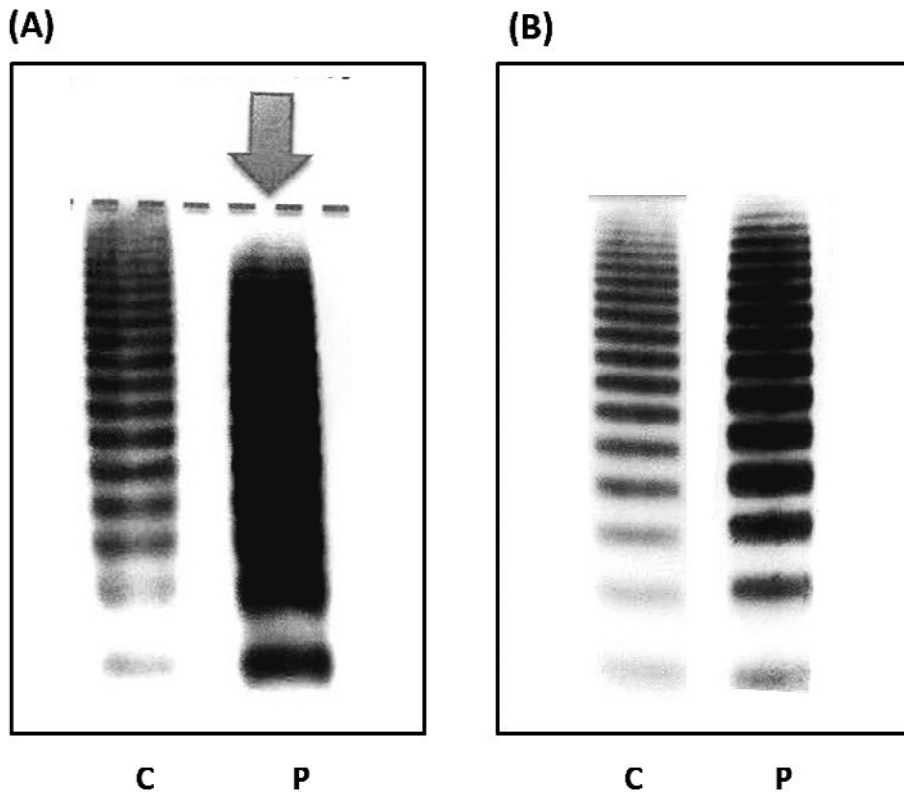


Fig. 3 Multimer analysis of von Willebrand factor (vWF) using gel electrophoresis. (A) Pre-operatively, large vWF multimers were absent. (B) Post-operatively, the levels of vWF multimers normalized. C: control, P: patient

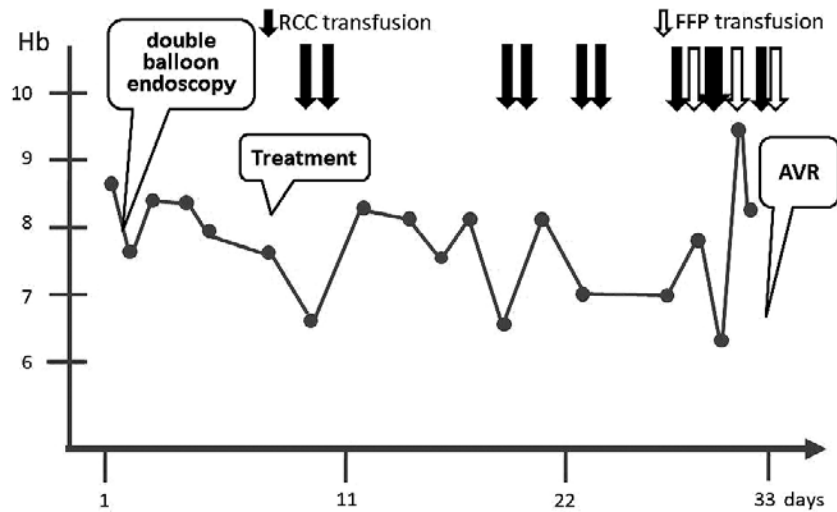


Fig. 4 Time course after admission. AVR: aortic valve replacement

and APTT normalized to 27.5 seconds. The frequency of melena and the need for blood transfusions also reduced, and he was discharged 51 days after admission. Follow-up consisted of monthly blood transfusions until one year and eight months post-operatively. Since then, the patient has had no further episodes of melena and has

not required any more transfusions. Follow-up capsule endoscopy showed almost complete resolution of ileal angiodysplasia (Fig. 5).

Discussion

Heyde³ first described the association between AS and GI



Fig. 5 Double balloon endoscopy showed the resolution of ileal angiodysplasia.

bleeding in 1958, and the combination of calcific AS and iron deficiency anemia due to GI bleeding was later called Heyde syndrome¹. In the same year, Goldman¹ reported that the incidence of GI bleeding in patients with AS was 3 times higher than initially predicted. Since then, there have been numerous case reports of Heyde syndrome in the medical literature worldwide⁴⁻¹⁴.

Recently, the definition of Heyde syndrome has been updated to include the combination of AS, intestinal angiodysplasia and acquired von Willebrand's syndrome. The pathogenesis of Heyde syndrome involves the transformation of high-molecular-weight vWF from the shear stress of blood flow through a stenotic aortic valve, and the exposure of sites on the A2 domains of the protein that can be cleaved by the plasma protease a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS13)². Consequently, destruction of high-molecular weight vWF is exacerbated and vWF multimers are reduced in size, resulting in the coagulopathy associated with Heyde syndrome. Vincetelli¹⁵ reported that decreased vWF collagen-binding activity and the loss of the largest multimers were present in 67-92% of patients with severe AS and correlated significantly with the severity of valve stenosis.

Unfortunately, there are no data on the prevalence of Heyde syndrome. Pate et al.⁴ retrospectively reviewed 3.8 million discharge summaries and found a significant association between AS and GI bleeding presumed to be due to angiodysplasia. In another retrospective case-note study of 3,623 patients with either aortic or mitral steno-

sis, GI bleeding was found to be significantly more common in the AS group¹⁶. Between 1968 and 2000, approximately 270 cases of acquired von Willebrand's syndrome were published, 12% of which were caused by a cardiovascular disorder¹⁷.

Heyde syndrome is diagnosed on the basis of the presence of AS and intestinal angiodysplasia, as well as gel electrophoresis confirming the presence of vWF¹. Red blood cell scintigraphy is useful in the evaluation of patients suspected to have GI bleeding caused by angiodysplasia¹⁴. The most effective treatment for Heyde syndrome is AVR, which usually improves the clotting disorder and anemia¹. Several case reports have described the treatment of Heyde syndrome using AVR^{10,11,13}. Thompson et al.¹⁸ reported that approximately 80% of cases of GI bleeding in patients with Heyde syndrome can be resolved by AVR. Alternative treatment options include colectomy for the treatment of colic angiodysplasia⁵, and endoscopic intervention^{10,13}. However, patients treated with intestinal resection or endoscopy generally continue to bleed from other sites, since angiodysplastic lesions tend to be found at multiple sites throughout the gastrointestinal tract⁸. In certain cases, patients can be managed conservatively⁶ or through interventional radiology^{9,12,19}. Notably, while desmopressin and factor VIII replacement are effective for the management of von Willebrand disease, patients with Heyde syndrome do not respond to these treatment options. Furthermore, patients often require blood transfusions.

In our case, the patient was successfully treated with a bioprosthetic AVR. Since patients with artificial aortic valves must be on lifelong anticoagulation, a biological valve may be a more suitable alternative in elderly patients. Gul et al.⁹ reported a case showing resolution of angiodysplasia two months after AVR; however, there are few reports about the duration of improvement of angiodysplasia after AVR. The mechanism of angiodysplasia involves chronic low-grade intermittent venous obstruction as a result of increased contractility at the level of the muscularis propria. Congestion of the capillaries and failure of the pre-capillary sphincters, results in the formation of small arterio-venous collaterals²⁰. Therefore, it is likely that complete resolution of angiodysplasia occurs over a long period of time. In this case, it is likely that the patient's bleeding resolved over a year after the AVR, and that the angiodysplasia gradually improved and eventually resolved at some time after the AVR.

In summary, Heyde syndrome is a rare disorder that is still not well known to gastroenterologists. To the best of

our knowledge, this is the first case report to describe an improvement in a patient's symptoms, namely bleeding from angiodysplasia, one year after AVR. With the incidence of AS rising in proportion to the increase in the aging population, it is expected that the incidence of Heyde syndrome will also increase. Therefore, clinicians should be mindful of Heyde syndrome as a potential differential diagnosis in patients with a systolic murmur and presenting with repeated episodes of GI bleeding.

Conflict of Interest: We have no conflict of interest.

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