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A Case of Heyde Syndrome: Resolution Following Aortic Valve Replacement

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ABSTRACT

Heyde syndrome is a triad of aortic stenosis, acquired coagulopathy, and anemia due to bleeding from intestinal angiodysplasia. Here we describe a case of this syndrome. An 80-year-old woman with severe aortic stenosis was referred to our department for an aortic valve replacement. She suffered from recurrent iron-deficiency anemia and required transfusions every 2 weeks. Gastroscopy and colonoscopy were normal with the exception of angiodysplasia without bleeding in the cecum. After aortic valve replacement her anemia was resolved. She was discharged on postoperative day 22. No transfusions were needed after the procedure. To date, her hemoglobin has remained stable at >10 mg/dL.

INTRODUCTION

Heyde syndrome is the combination of aortic stenosis with gastrointestinal bleeding associated with acquired von Willebrand syndrome type 2A (vWS-2A) [Heyde 1958]. The source of bleeding in patients with this syndrome has been attributed to intestinal angiodysplasia, which is present in 2.6%-6.2% of patients with gastrointestinal bleeding [Love 1982; Foutch 1993; Massyn 2009]. Iron-deficiency anemia and aortic stenosis are common in the elderly, but the association between them is not generally recognized [Massyn 2009]. Therefore, the prevalence of Heyde syndrome is not clearly determined and many mild cases are likely to remain undiagnosed. While resolution of von Willebrand syndrome usually follows aortic valve replacement, the accurate diagnosis of Heyde syndrome is essential [Pate 2004]. Clinicians should be aware of acquired von Willebrand disease and gastrointestinal bleeding due to angiodysplasia in patients with aortic stenosis.

CASE REPORT

An 80-year-old woman was admitted to our hospital for severe fatigue on minimal exertion of two years' duration. Her hemoglobin was very low at 5.7 mg/dL and she required transfusions. Fecal occult blood tests were positive and an upper gastrointestinal endoscopy, capsule endoscopy and colonoscopy were performed. Non-hemorrhagic angiodysplasia in the cecum was the only finding (Figure 1). The hematological profile showed iron-deficiency anemia (MCV 82.7 fL, ferritin 9.9 µg/L) and normal bone marrow. In the year prior to admission the patient suffered from chronic symptomatic anemia and was started on ferrous sulfate supplements. She required red cell transfusions every two weeks. During follow-up for anemia, an echocardiography demonstrated severe aortic stenosis with an aortic valve area of 0.63 cm^2 and a mean pressure gradient of 62 mm Hg (peak of 140 mm Hg). Bioprosthetic aortic valve replacement (AVR) using a 19 mm Trifecta valve (St. Jude Medical Inc., St Paul, MN, USA) was performed. The patient required no blood transfusions postoperatively. On discharge her lab values showed Hb 10.6 mg/dL, MCV 95.1 fL and ferritin 356 µg/L. For 6 months post-surgery, her hemoglobin levels remained stable at > 10 mg/dL. A repeat colonoscopy 3 months after the procedure showed that the non-hemorrhagic angiodysplasia persisted (Figure 2).

DISCUSSION

Heyde syndrome was first described in 1958 by Edward C. Heyde as a combination of calcified aortic stenosis and

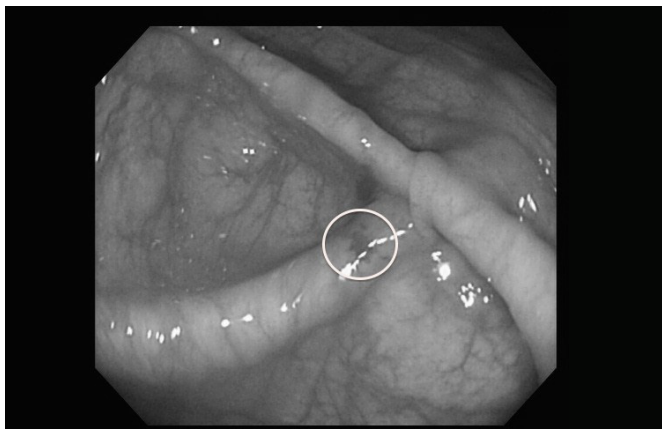

Figure 1. Angiodysplasia in the cecum identified during colonoscopy preoperatively.

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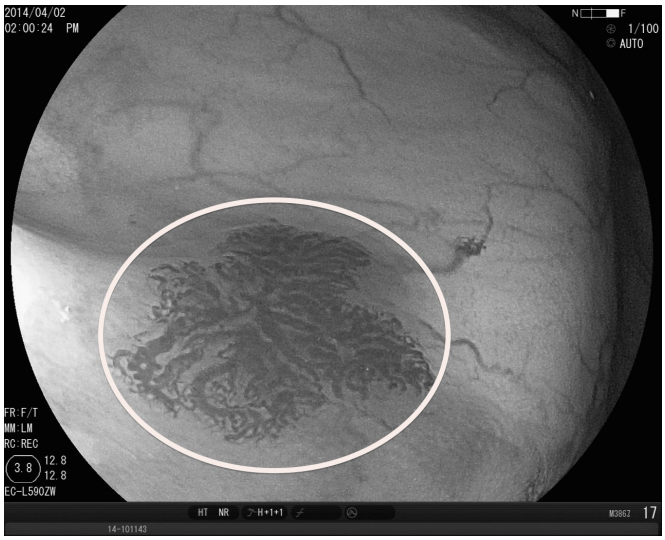

Figure 2. Angiodysplasia in the cecum identified during colonoscopy postoperatively.

gastrointestinal bleeding. Today this syndrome is recognized as a triad of severe aortic stenosis, angiodysplasia of the gastrointestinal tract, and acquired vWS-2A [Heyde 1958; Pate 2004]

Acquired vWS-2A in aortic stenosis arises from degradation of vWF multimers by shear stress across the diseased valve [Tsuji 2004]. The vWF multimers unfold from a coiled structure and become elongated filaments which are then cleaved by disintegrin and metalloproteinase with a thrombospondin type 1 motif 13 [Pareti 2000; Tsai 2003; Vincentelli 2003]. Degradation of the heaviest multimers of vWF, which are the most effective in platelet-mediated hemostasis, is the basis for the coagulopathy in Heyde syndrome [Vincentelli 2003]. Thus, patients with vWS-2A may be more likely to bleed from existing angiodysplasia [Pate 2004].

In a prospective study of colonoscopies in 1,938 patients, typical angiodysplasia was found in 3% of cases of which 80% were asymptomatic. The sites of highest prevalence of the lesions were the cecum (37%) and sigmoid colon (18%) [Hochter 1985]. Approximately 30%-40% of gastrointestinal bleeding from obscure sources was found to be linked to angiodysplasia, which is possibly the most common cause of lower gastrointestinal bleeding in the elderly [Pate 2004].

In elderly patients with established aortic stenosis, the development of iron-deficiency anemia should suggest the possibility of Heyde syndrome. Underlying gastrointestinal malignancy, celiac disease and nutritional deficiency should also be considered. The presence of angiodysplasia on colonoscopy and a failure to find any clear site of gastrointestinal bleeding led us to consider the possibility of Heyde syndrome. Localization of the culprit lesion in patients with angiodysplasia can be difficult as the bleeding source can be hidden and out of reach with conventional endoscopy [Thompson 2012].

The relationship between aortic valve stenosis and gastrointestinal angiodysplasia has yet to be established. Multiple theories have been proposed. Luckraz et al. hypothesized that hemodynamically relevant aortic valve stenosis is associated with reduced gastrointestinal perfusion; consequently, low-grade chronic hypoxia may stimulate reflex sympathetic vasodilation and smooth muscle relaxation progressing to true ectasia of the vessel walls [Luckraz 2003]. Some researchers have suggested that Heyde syndrome is the end result of senile degeneration of both aortic valvular and gastrointestinal mucosal tissue [Massyn 2009]. In our case, the angiodysplasia persisted after the procedure – a finding that likely supports the latter theory.

Patients with Heyde syndrome who are treated with intestinal resection generally continue to bleed from other sites, while AVR usually cures the clotting disorder and anemia [Pate 2004]. King et al. found that AVR was 93% successful in preventing recurrent bleeding compared to the 5% of patients who underwent gastrointestinal surgery, which led to the recommendation of AVR as a definitive treatment for this syndrome [King 1987]. Some authors have supported the use of AVR in the presence of iron-deficiency anemia, even if the aortic valve stenosis is clinically insignificant [Massyn 2009].

Elderly patients may be unfit for AVR or refuse surgery. Conservative management includes oral iron supplements, but regular transfusions may also be necessary. In patients with severe recurrent bleeding, endoscopy with laser therapy may be an option. Elderly patients often have co-morbidities requiring anticoagulants or antiplatelet agents, but these should be avoided, particularly in severe cases [Massyn 2009]. Transcatheter aortic valve implantation may be one treatment option for those patients with Heyde syndrome at high surgical risk [Gul 2012].

In a study of 50 consecutive patients with aortic stenosis, cutaneous or mucosal bleeding occurred in 21% of the patients, and hematological abnormalities, which are correlated with severity of stenosis, occurred in 67%-92% [Vincentelli 2003]. Iron deficiency anemia and aortic stenosis are common in the elderly, but the association with angiodysplasia and bleeding is not generally recognized. In this case post-surgical resolution of the anemia and a subsequent literature search led us to suspect Heyde syndrome. Postoperatively, there was no decrease in the heaviest vWF multimers; early correction of vWF multimers can be obtained in the first few hours after surgery [Vincentelli 2003].

Early diagnosis and appropriate treatment of Heyde syndrome require recognition and cooperation among the various specialties – family physicians, cardiologists, gastroenterologists, hematologists and surgeons. Heyde syndrome should be considered as a possibility in all patients presenting with iron-deficiency anemia and aortic stenosis.

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