CLINICAL VIGNETTE

An Uncommon Case of Occult Gastrointestinal Bleeding

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Case Presentation

A 71-year-old male with a past medical history of coronary artery disease, hypertension, and severe aortic stenosis presents with shortness of breath, lightheadedness and three days of melena. He denies chest pain, abdominal pain, diarrhea, constipation, bright red blood per rectum, nausea or vomiting. He reports a remote history of peptic ulcer disease in his 20's. He takes aspirin 81 mg daily and no other nonsteroidal anti-inflammatory drugs. Other medications include allopurinol, metoprolol and rabeprazole. Social history includes remote alcohol abuse and a prior 60 pack-year smoking history, having quit 20 years ago.

Previous endoscopic procedures three years ago include a normal endoscopy for reflux and screening colonoscopy, with two polyps found.

On presentation, he is tachycardic with normal blood pressure. Exam is remarkable for conjunctival pallor and a systolic ejection murmur. Abdominal exam is unremarkable but digital rectal examination confirms melena. Hemoglobin is 6.7 g/dL, hematocrit 19.8% with mean corpuscular value of 84. Blood urea nitrogen is 25 mg/dL and the creatinine is 0.8 mg/dL.

Upper endoscopy showed mild antral gastritis and a 2 cm hiatal hernia. Colonoscopy was normal. A tagged red blood cell scan showed gastrointestinal bleeding in the small bowel, likely mid-jejunum. Single-balloon upper and lower enteroscopy did not identify a source of bleeding, however the marking tattoo could not be reached to ensure complete visualization of the small bowel. Intraoperative enteroscopy revealed two angiodysplasia which were successfully treated with cautery. The remainder of the small bowel proximal, distal to these lesions, was normal.

The patient's angiodysplastic bleeding in association with severe aortic stenosis, is described as Heyde's Syndrome. He underwent successful aortic valve replacement and has had no further gastrointestinal bleeding.

Discussion

The association of aortic valve stenosis and gastrointestinal angiodysplastic bleeding was originally described by E.C. Heyde in 1958.[1] It resurfaced again in 1986 with reports of association between aortic stenosis and submucosal angiodysplasia[2] as well as with a possible mechanism - the loss of high-molecular-weight multimers of von Willebrand factor in congenital and acquired aortic stenosis.[3,4] A year later, aortic valve replacement was associated with cessation of gastrointestinal bleeding in 14 patients.[5] In 1992, Warkentin, reported that acquired von Willebrand disease was the link between aortic stenosis and gastrointestinal angiodysplastic bleeding.[6]

Heyde's syndrome is associated with Type IIA von Willebrand disease, an acquired deficiency of the von Willebrand factor (vWF) multimers. It can be seen in up to 3% of patients with aortic stenosis. Von Willebrand factor is important in platelet-mediated hemostasis during high shear stress. Notably, high shear stress is present in angiodysplastic lesions and results in shear-stress dependent cleavage of vWF by plasma protease ADAMTS13 resulting in less effective hemostasis.[7]

A study by Vincentelli examined 50 consecutive patients with aortic stenosis.[8] Forty-two had severe aortic stenosis and of these, 21% had mucosal or dermal bleeding. The highest molecular weight multimers were decreased in 75% of those with moderate aortic stenosis and 79% with severe aortic stenosis. Abnormalities in platelet function under high shear stress, decreased collagen-binding activity related to wWF and loss of largest multimers were used to assess baseline function. Up to 92% of patients with severe aortic stenosis had at least one abnormalities, whereas only about 50% of those with moderate aortic stenosis had any abnormalities. The deficiency also correlated with severity of aortic stenosis assessed by transvalvular aortic gradient.[8]

The gold standard of treatment is aortic valve replacement. Vincetelli's study of 42 patient's aortic valve replacements, 31 received a biologic valve and 11 received a mechanical bileaflet prosthetic valve. Two patients were lost to follow-up, and 2 had issues with the valve (including 1 who developed epistaxis with restenosis). The remaining 38 had no further episodes of bleeding 6 months post-surgery.[8]

Transcatheter aortic valve implantation (TAVI) has also been used to treat Heyde's syndrome. In an Italian study of 400 consecutive patients with aortic stenosis, 37 patients had gastrointestinal bleeding of which 7 (1.7%) were found to have proven angiodysplasia by endoscopy or colonoscopy. Six patients had successful TAVI and the seventh patient had unsuccessful TAVI due to technical issues with the procedure. All 6 who underwent successful TAVI had no recurrence of gastrointestinal bleeding with a mean follow-up of 22 ± 15

months. The seventh had a severe transfusion dependent anemia requiring multiple hospitalizations.[9]

Angiodysplasia can be treated endoscopically and medically. Endoscopic therapy has included argon plasma coagulation (APC), clip placement, and other forms of electrocautery. Endoscopic therapy has proven to be effective, though recurrence rates are up to 36%. Medical therapy has included somatostatin analogs and antiangiogenics such as thalidomide. Hormonal therapy has not proven to be effective in limited studies.[10]

Heyde's syndrome is now a well-established association between aortic stenosis and angiodysplastic gastrointestinal bleeding. Additionally, the mechanism is now understood, and treatment options such as aortic valve replacement can resolve gastrointestinal bleeding.

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Submitted July 31, 2018