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Heyde's Syndrome – An Enigma

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Abstract

Heyde’s syndrome (HS) is described as the association between recurrent bleeding from angiodysplasia of the gastrointestinal tract and aortic stenosis. Aortic valve replacement has been reported to stop the bleeding. In unfit patients, the options available are interventional or conservative management. We hereby report an elderly obese patient with severe comorbidity with complicated HS involving a narrow aortic root. She underwent left ventricular outlet myomectomy and aortic root replacement to promote better forward flow and prevent restenosis and recurrence of symptoms. She was discharged home symptom-free despite being on coumadin anticoagulants.

Keywords: Aortic stenosis, Gastrointestinal bleeding, von willebrand, Angiodysplasia, Heyde’s syndrome, Cardiac surgery

Introduction

Heyde’s syndrome (HS) is a triad of aortic stenosis (AS), acquired coagulopathy (Von Willebrand syndrome -2A, (VWS-2A)) and anaemia due to bleeding from intestinal angiodysplasia. Replacement of the aortic valve has been reported to stop the bleeding. Recently, transcatheter aortic valve implantation (TAVI) or other conservative strategies have been recommended as treatments of choice for high-risk surgical patients. In addition, TAVI may not be technically suitable for a patient with a narrow aortic root, and haemostatic abnormalities may recur when a mismatch is found between the patient and prosthesis size.

Case presentation

A 66-year-old woman was admitted with chest discomfort and transient loss of consciousness. Her past medical history included anaemia, hypertension, type 2 diabetes and morbid obesity with a BMI of 42 and obstructive sleep apnoea. Blood investigations revealed a haemoglobin of 8.4 g/dl (12–15 g/dl), a platelet count of 169/mm3 (150–410/mm3) a troponin T of 16 ng/L (<14 ng/L) with normal vitamin B12 and folate levels, but iron levels were consistent with iron-deficiency anaemia with serum iron 44 mg/dL (37–145 mg/dL), Iron saturation 11.8% (15–45%) and serum ferritin 12.5 ng/mL (25–300 ng/mL), transferrin and iron binding capacity 474.98 mg/dL (250–435 mg/dL). Faecal occult blood was positive, and esophagastroduodenoscopy was normal. However, colonoscopy revealed multiple angiodysplasia in the splenic flexure and rectum. She underwent clipping and argon plasma coagulation at multiple sites (Fig. 1). AS was detected first time during this admission with transthoracic echocardiogram that showed severe AS, valve peak gradient of 96 and mean 63 mm Hg, Aortic valve area 0.8 cm², left ventricular outlet diameter 1.9 cms and left ventricular ejection fraction of 62% (Fig. 2). Her subsequent investigations including molecular

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genetic analysis for Von Willebrand factor (VWF) gene was negative. The Coomb's test was negative and the Gliadin antibody tests were performed were negative that excluded the diagnosis of haemolysis and celiac disease respectively. The underlying malignancy or other structural diseases of gastrointestinal tract were also excluded.

She was clinically diagnosed with HS with a narrow aortic root complicated by obesity. She continued to suffer from anaemia and required multiple transfusions to improve her haemoglobin. Considering her comorbidities with surgical EuroSCORE II of 16.8%, the initial choice of treatment was decided to be TAVI rather than surgical AVR.

Fig. 1. Endoscopic pictures showing angiodysplasia (yellow circle) in (a) and multiple argon coagulation treatment spots in (b).
(SAVR) during the multidisciplinary (MDT) meeting. However, in view of her calcified narrow aortic outlet in relation to a large body surface area, the decision was finally changed to Bentall procedure, as it will allow us to implant a larger biological valve to avoid turbulence, provide better forward flow and avoid a possible mismatch that can occur with surgical AVR. Patient underwent aortic outlet myomectomy and Bentall procedure with Medtronic freestyle 25 size porcine valve under cardiopulmonary bypass (see Fig. 3). The postoperative course was complicated by bleeding compounded by atrial fibrillation and hypoventilation, resulting in a few unsuccessful weaning trials. Tracheostomy was performed on the 11th postoperative day. She needed several days of high dependency and rehabilitation care. Her tracheostomy was decannulated on the 17th day and discharged home on the 23rd day with a haemoglobin of 10.6 g/dl. She did not show any more signs of intestinal bleeding during her hospital stay or follow-up for twenty months. She was treated with coumadin for 3 months and continued on aspirin.

Discussion

The evidence that AS is the root cause of coagulopathy in HS is compelling, with 5%–20% of these patients manifesting recurrent bleeding [1] with severity depending on the gradients across a stenotic AV [2]. VWS-2A arises from degradation of VWF multimers by shear stress across the AV, resulting in coagulopathy. These multimers are required to maintain haemostasis in high-flow conditions, such as in intestinal arteriovenous malformations in patients with AS [3]. The pathogenesis of angiodysplasia could be due to low-grade chronic

![Fig. 2. Preoperative Transthoracic Echocardiography showing severe calcified aortic valve in (a), a narrow LVOT gradient and AV area in (b) and narrow Increased AV gradient in (c).](image-url)
Fig. 3. Postoperative transthoracic Echocardiography showing Decline in postop LVOT gradient in (a) and decline in AV gradient in (b).
hypoxia that stimulates sympathetic vasodilation reflex progressing to fixed smooth muscle relaxation and true ectasia [4]. These could also be due to mucosal hypoxia caused by cholesterol emboli or by the altered pulse waveform secondary to AS. Most of them remain undiagnosed and are found as an incidental finding in 15%–25% of patients with repeated bleeding [5]. Unfortunately, Von Willebrand factor test could not be performed in our patient due to financial constraints and the diagnosis was made on clinical grounds. VWS-2A also occurs in other similar high-stress conditions such as left ventricular assist device implantation, hypertrophic obstructive cardiomyopathy, ventricular septal defect and patent ductus arteriosus.

Even though AV replacement eliminates the risk of bleeding [1], the procedure itself may cause serious bleeding complications. Other issues such as type of procedure (open vs interventional), prosthesis (mechanical vs biological) and perioperative anticoagulation are always debatable. More recently, TAVI has emerged as a feasible option with bioprosthetic valve [7] and postoperative low-dose aspirin. In the presence of prosthesis mismatch, GI bleeding has been found to recur because of the persistence of a pathophysiological mechanism. We opted for Bentall procedure, as it allowed us to place a larger valve with less gradient and better haemodynamics. Unlike surgery, endoscopic cauterisation alone was only temporarily successful and was associated with a high recurrence rate [6]. Our patient could even tolerate warfarin anticoagulation without bleeding recurrence following corrective surgery for three months. We opted 3 months of coumadin anticoagulation followed by aspirin as per recent guidelines [9]. However, we fully agree that the associated morbidity was not negligible, with significant postoperative complications and increased length of stay. Sleep-disordered breathing is highly prevalent in obese patients [8] with associated upper airway muscle weakness, vascular endothelial dysfunction, cardiac arrythmia, alveolar hypoventilation and sensitivity to anaesthetic medications leading to sudden cardiovascular death, myocardial infarction, stroke, worsening overall postoperative recovery and higher pacemaker use [10].

HS management requires a multidisciplinary approach. Treatment options include octreotide infusion, endoscopic interventions, colon surgery and AV replacement. Surgical excision of angiodyplasia is a high risk in the presence of AS, and studies have shown that bleeding recurrence remains with underlying AS pathophysiology [11]. If AVR cannot stop bleeding, subsequent anaesthesia for bowel resection would be less risky. In our patient, improvement in anaemia was possibly due to the resolution of angiodyplasia with improved cardiac output and recovery of VWF multimers. This case report suggests that more radical procedures offered to these high-risk complicated HS patients, such as Bentall procedure, can still be associated with favourable outcomes. However, a careful understanding of pathophysiology, preoperative optimisation including a multidisciplinary approach, endoscopic treatment, blood transfusion, perioperative echocardiography with appropriate postoperative ventilatory and rehabilitation strategy will be key to successful results.

To the best of our knowledge, this is the first patient who successfully underwent Bentall procedure in complicated HS with complete resolution of anaemia despite coumadin anticoagulation. Larger prospective studies are required to revise AVR guidelines to include anaemia and GI bleeding as criteria of the type, timing and type of surgery and anticoagulation regimen.

Author contribution

Fayaz Mohammed Khazi: Conception and design of Study. Fayaz Mohammed Khazi, Nayyer R Siddiqi, Yehia Mohamed Karaly, Obaid Aljassim, Zohair Y. Al-Halees: Literature review, Acquisition of data, Analysis and interpretation of data. Research investigation and analysis, Data collection, Drafting of manuscript, Revising and editing the manuscript critically for important intellectual contents, Data preparation and presentation.

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