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КРИТИЧНА АОРТНА СТЕНОЗА, ПРОЯВЯВАЩА СЕ КАТО РЕЦИДИВИРАЩО РЕКТАЛНО КЪРВЕНЕ, ДОКЛАД НА СЛУЧАЙ И ПРЕГЛЕД НА ЛИТЕРАТУРАТА

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CRITICAL AORTIC STENOSIS PRESENTING AS RECURRENT BLEEDING PER RECTUM, A CASE REPORT AND REVIEW OF LITERATURE

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Резюме.

Въведение: Синдромът на Heyde е мултисистемно заболяване, характеризиращо се с триадата от аортна стеноза, придобита коагулопатия (синдром на von Willebrand тип 2A) и гастроинтестинална ангиодисплазия. Диагнозата на синдрома на Heyde при възрастни е предизвикателство поради високата честота на аортна стеноза и гастроинтестинална ангиодисплазия. Следователно клиничното подозрение е от съществено значение за диагностицирането. **Представяне на случай**: Представяме случай на мъж с повтарящи се хоспитализации и трансфузии за анемия след ректално кървене, който е бил диагностициран със синдром на Heyde. Пациентът е лекуван със смяна на аортна клапа и коронарен артериален байпас, включващ лява предна низходяща артерия. В хода на едногодишното му проследяване след подходяща терапия пациентът е безсимптомен. **Заключения**: Лечението на аортна стеноза при пациенти със синдром на Heyde води до разрешаване на анемията. Следователно решенията за лечение се основават на правилна идентификация.

Ключови думи: синдром на Heyde, аортна стеноза, ангиодисплазия, транскатетърно протезиране на аортна клапа, стомашно-чревно кървене

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Abstract.

Introduction: Heyde syndrome is a multisystem disorder characterized by the triad of aortic stenosis, acquired coagulopathy (von Willebrand syndrome type 2A) and gastrointestinal angiodysplasia. The diagnosis of Heyde syndrome in adults is challenging because of high frequency of aortic stenosis and gastrointestinal angiodysplasia. Clinical suspicion is therefore essential for diagnosis. **Case Presentation**: We present the case of a male with recurrent hospital admissions and transfusions for anemia post bleeding per rectum who was diagnosed to have Heyde's syndrome. The patient was managed with aortic valve replacement and coronary artery bypass surgery involving left anterior descending artery. He remained symptom free 1 year after appropriate therapy. **Conclusions**: The management of aortic stenosis in patients with Heyde syndrome results in resolution of anemia. Hence, treatment decisions are based on correct identification.

Key words: Heyde's syndrome, aortic stenosis, angiodysplasia, transcatheter aortic valve replacement, gastrointestinal bleed

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Introduction

Heyde syndrome consists of triad of aortic stenosis, gastrointestinal angiodysplasia, and acquired von Willebrand syndrome (AVWS) [1]. The exact prevalence of Hedye syndrome is unknown because gastrointestinal bleeding in the context of aortic stenosis are common in elderly [2]. Strong correlations between severe aortic stenosis and intestinal angiodysplasia causing bleeding per rectum in the elderly have been documented by multiple studies. Treatment for severe aortic stenosis may lead to the resolution of anemia [3].

Case Presentation

A 79-year-old male, presented with complaints of dyspnea on exertion (NYHA class II-III) since 8 months, which worsened over the last 2 months. He also had multiple episodes of per rectal bleeding. He was hospitalized and was found anemic. The patient had history of recurrent blood transfusions for multiple episodes of bleeding per rectum. He gave no history of smoking, alcohol or substance abuse. General physical examination revealed pallor, tachycardia and a low volume pulse. Cardiovascular examination revealed ejection systolic murmur with late peaking at the aortic area. Per abdomen examination was unremarkable. Transthoracic echocardiogram showed severe calcific aortic stenosis with an aortic valve orifice of 0.6 cm^2, peak gradient of 129 mm Hg and mean gradient of 69 mm Hg. Blood investigations revealed microcytic anemia with hemoglobin of 7.6 gm %, hematocrit of 32%, and platelet count of 2,30,000/μL. Also, we observed low levels of factor VIII and decreased von Willebrand factor activity. Test for fecal occult blood was positive. Colonoscopy showed angiodysplasia in the ascending and sigmoid colon (Figure 1) for which the patient underwent colonoscopy guided hemoclipping and adrenaline therapy. The diagnosis of Heyde syndrome was made. The patient underwent multiple blood transfusions to manage his anemia. Coronary angiogram revealed 75% stenosis in his left anterior descending artery and 90% stenosis in the diagonal branch of left anterior descending artery. The patient underwent aortic valve replacement (Figure 2) with 23 mm St Jude EPIC bioprosthesis along with coronary artery bypass surgery with sequential grafting of diagonal and left anterior descending artery using left internal mammary artery. He made a steady recovery in the postoperative period and was discharged on the 5th post-operative period. At 1 year follow up, the patient was asymptomatic, and hemoglobin levels were within normal limits.

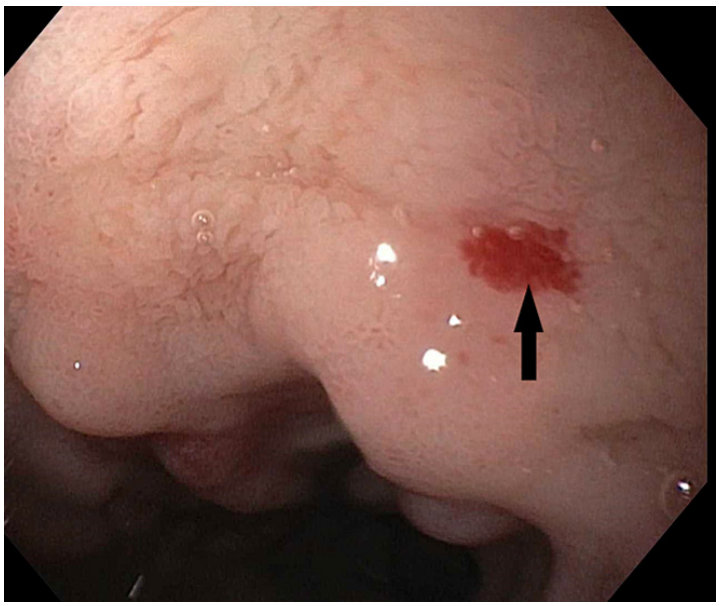

Fig. 1. Colonoscopic picture depicting angiodysplasia

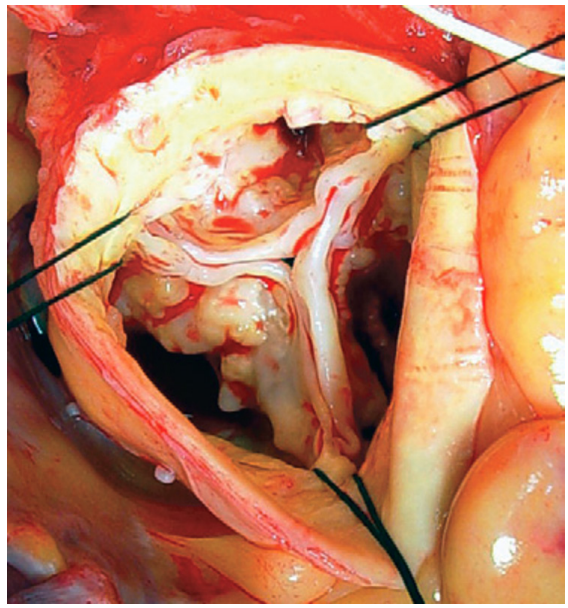

Fig. 2. Intra-operative image of aortic valve replacement

Discussion

Among older individuals, degenerative aortic stenosis is the most common valvular heart disease. ≈ 7.5% of individuals aged ≥ 75 years are found to have aortic stenosis [4]. A study of elderly individuals with moderate to severe aortic stenosis reported clinically significant gastrointestinal bleeding in ≈ 1% to 3% of patients [5]. Angiodysplasia is characterized by dilated, thin-walled tortuous vessels in the mucosa and sub-

mucosa of the gastrointestinal tract. It accounts for ≈ 1% to 6% of admissions to the hospital following gastrointestinal bleeding [6]. Heyde syndrome was first reported by Dr. Heyde in 1958 wherein he observed an increased tendency for gastrointestinal bleeding in elderly patients with signs of calcific aortic stenosis [7]. It is characterized by a triad of aortic stenosis, gastrointestinal bleeding and acquired von Willebrand syndrome. Warkentin and colleagues first described the role of acquired coagulopathy in the pathogenesis of Heyde syndrome in 1992 [8]. Heyde's syndrome (HS) is likely underreported because the prevalence of aortic stenosis (AS) increases with age [1]. Waldschimdt et al. showed that 1.8% of patients were diagnosed with Heyde syndrome after a review of 2500 patients who underwent TAVI for aortic stenosis over 9 years in Germany [9]. Saha et al. performed a systemic review of 74 articles to identify risk factors for Heyde's syndrome, which included older age, female sex, comorbid conditions such as hypertension, coronary artery disease, congestive heart failure, type 2 diabetes mellitus, atrial fibrillation, chronic kidney disease/end-stage renal disease, and severe/very severe aortic stenosis [10]. Blood passing through a stenotic aortic valve is subjected to severe shear stress, which is thought to be the etiology of acquired Von Willebrand syndrome. Von Willebrand factors (vWF) of high molecular weight (HMW) undergo a considerable conformational change as a result of this shear strain, exposing their A2 domain for digestion by plasma protease ADAMST13. The HMW vWF multimers are therefore smaller and less able to achieve hemostasis than the larger vWF multimers [11]. The development of angiodysplasia may also be directly influenced by smaller vWF molecules because vWF, in addition to its role in hemostasis, also contributes to the preservation of vascular integrity [12]. Other possible factors implicated in the pathogenesis of Heyde syndrome include mucosal ischemia, cholesterol embolization, acquired platelet dysfunction and inflammatory reactions [13]. Since aortic stenosis and colonic angiodysplasia are common in elderly adults, the association between the two is not often recognized, making the diagnosis of Heyde syndrome difficult to make. The estimated prevalence of both symptoms is as high as 40% [14]. A detailed history and physical examination with focus on multi-system examination is therefore crucial for the diagnosis of Heyde syndrome. This is especially important if the patient has ongoing gastrointestinal bleeding that has not been explained. Saha et al showed that the jejunum was the most commonly observed site for bleeding, with a slight female preponderance [10]. Another study indicated that the duodenum and right colon were the most common sites of angiodysplasia and bleeding [15]. Iron deficiency anemia results from prolonged blood loss through the gastrointestinal (GI) tract. It is imperative to rule out other potential causes of iron-deficiency anemia, such as nutritional deficiency, celiac disease, malabsorption syndromes, and malignancy. Endoscopic interventions are recommended to control the source of active bleeding, and visualize the angiodysplasia. Additionally, the clinician may look for history of diagnosis of aortic stenosis (AS) or any signs that suggest it including imaging tests, or echocardiograms. Diagnosis of acquired von Willebrand disease is made using vWF multimer assay. Platelet factor Assay (PFA) analyzes the ability of platelets to generate primary hemostasis. PFA is preferred over vWF assay in routine clinical practice because of quicker results [16]. First line management of Heyde syndrome is aortic valve replacement. Thompson et al. performed a retrospective assessment of patients treated at the Mayo Clinic between 1971 and 2007 for gastrointestinal bleeding and intestinal angiodysplasia who subsequently underwent aortic valve replacement for severe aortic valve stenosis. The authors observed that aortic valve replacement lowered the incidence of gastrointestinal bleeding in individuals with Heyde syndrome and was curative in about 80 percent of patients [15]. Goltstein et al. investigated the efficacy of aortic valve replacement in treating acquired von Willebrand syndrome and gastrointestinal hemorrhage. The study's findings revealed that aortic valve replacement is associated with rapid recovery of the bleeding diathesis in Heyde syndrome, and the cessation of gastrointestinal bleeding [17]. Transcatheter Aortic valve replacement (TAVI) can be considered in patients at a high risk for surgical AVR taking care to prevent para valvular leak which may reduce the benefits of the procedure [18]. Medical or endoscopic interventions for the bowel are often used as bridge therapies to valve replacement [19]. Following successful aortic valve replacement for Heyde syndrome, most patients receive dual antiplatelet agents. Multiple transfusions may help manage anemia, but offer only temporary relief. VWF or factor VIII replacement, octreotide and desmopressin commonly used in the management of hereditary von Willebrand disease, are ineffective for the treatment of Heyde syndrome [6]. For this reason, vWF replacement therapies are not generally recommended. The uniqueness of our case is that the patient was managed via transfusions multiple times for bleeding per rectum and the differential diagnosis of Heyde syndrome was not considered for several years. Once the diagnosis was made and valve replacement was completed, he remained symptom free at 1-year follow-up. The diagnosis of Heyde syndrome requires high index of clinical suspicion. Early diagnosis and prompt management improves outcomes and quality of life for the patient.

Conclusions

The differential diagnosis of Heyde syndrome must be considered in elderly individuals with significant aortic stenosis, gastrointestinal bleeding and anemia. Aortic valve replacement is found to be a definitive treatment option for aortic stenosis as well as anaemia in patients with Heyde syndrome.

Abbreviations:
AVWS: acquired von Willebrand syndrome
vWF: Von Willebrand factors
HMW: High molecular weight
TAVI: Transcatheter aortic valve implantation

No conflict of interest was declared

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