An Extensive Search for GI Bleed: A Case Report on Heyde Syndrome and Subsequent Aorto-Atrial fistula (AAF)

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INTRODUCTION

Heyde Syndrome is a rare condition characterized by a classical triad of Aortic Stenosis, Angiodysplasia of the Gastrointestinal tract often manifesting as Gastrointestinal bleeding and acquired Von Willebrand factor deficiency[1,2]. Although described by Edward Heyde in 1958, the exact pathophysiology and prevalence are still not clear. This condition is thought to be underreported due to a lack of clinical suspicion and the absence of diagnostic modalities in countries with less equipped health infrastructures. It is more commonly diagnosed at ages over 65 years. Although definite protocols for the management of Heyde Syndrome have not been defined, it has been observed that correction of Aortic Stenosis, with medical and endoscopic interventions for angiodysplasias provides a favorable result[3].

CASE PRESENTATION

76 years male with a past medical history of Gastrointestinal Bleed, Anemia, Prostate Cancer status post prostatectomy and radiation treatment, Cutaneous T – Cell Lymphoma, Multiple Seborrheic Keratosis, Diastolic Heart Failure with LVEF: 55-60%, Aortic Valve Stenosis status post-BiPAP Prosthetic Valve Replacement, Coronary artery disease, carotid artery stenosis, hyperlipidemia, Type 2 Diabetes Mellitus, GERD, Hypothyroidism, Peripheral Arterial Occlusive Disorder was admitted with a complaint of dark colored stool for over a week. On investigation, Hemoglobin was below the normal range and a blood transfusion was done. He also had a history of multiple transfusions in the past. The patient gives no history of fever, chills, nausea, vomiting, diarrhea, chest pain, shortness of breath, or abdominal pain. The patient is married, a former smoker, an alcohol consumer and has no history of smokeless tobacco, vaping and recreational drug use. He has a known allergic reaction to penicillin. He was under several outpatient medications such as Alprazolam, Vitamin C, Aspirin, Carvedilol, Empaglifazon - Metformin, Ferrous Gluconate, Folic Acid, Levothyroxine, Losartan, Melatonin, Multivitamin Tablets, Nitroglycerine Sublingual, Pantoprazole and Rosuvastatin. A general physical examination revealed pallor and hypertension. Cardiovascular examination revealed crescendo- decrescendo murmur. Multiple seborrheic keratoses were present in the chest and back.

METHODS

UGI endoscopy revealed multiple angiodysplastic lesions on the second part of the duodenum and jejunum. Coagulation for bleeding prevention using Argon Plasma was done. Enteroscopy revealed single bleeding angiodysplstic lesion in the third portion of the duodenum. A colonoscopy revealed multiple diverticulosis and polyps, however, angiodysplasia was not visible. Nuclear Medicine examination of Gastrointestinal Blood Loss was done and no scintigraph evidence of active bleeding was detected. CECT Abdomen and Pelvis were obtained which shows no active bleeding, no free or loculated collection and metastasis was detected. Transthoracic Echocardiography showed a prosthetic pericardial valve in situ with an Ejection fraction: of 55-60 %. The rest of the findings were unremarkable. Lab investigation revealed low hemoglobin

(7.5 gm/dl), Low Hematocrit (24.5%), low MCH, MCHC and high RDW. Haptoglobin and Ferritin were also found to be decreased. Peripheral Blood flow cytometry was normal. The fecal Occult Blood Test was positive. Von Willebrand Factor analysis revealed an absence of the highest molecular weight multimers suggestive of acquired deficiency (Type 1)

On a recent transesophageal echocardiogram, the patient was found to have developed a fistula between the aorta and the left atrium, and there was also the presence of moderate paravalvular leak with hemolytic anemia and symptoms of dyspnea on exertion.

OUTCOME AND FOLLOW-UP

After a discussion in the structural heart meeting, a decision was subsequently made to proceed with percutaneous closure of the aortic paravalvular leak/fistula arising from the aortic root and left atrium. Successful percutaneous closure of the fistulous tract from the aortic root to the left atrium was achieved. In post-procedure echocardiography, successful aorto-atrial fistula closure was noted with no residual flow into the left atrium and a significant reduction of the associated paravalvular leak.

DISCUSSION

Although described in the 1950s by Dr, Edward Heyde, as the combination of calcific aortic stenosis and iron deficiency anemia resulting from gastrointestinal bleeding. Heyde syndrome now refers to a triad of aortic stenosis, acquired coagulopathy (von Willebrand syndrome type 2A, abbreviated here vWS-2A) and anemia due to bleeding from intestinal angiodysplasia or an idiopathic site[4]. The definitive pathophysiology of Heyde Syndrome has yet to be agreed upon. Currently, the most widely accepted one is the acquired deficiency of von Willebrand factor due to high shearing stress due to the flow of blood through the narrowed valve as in conditions such as aortic Stenosis[5]. The high shearing force leads to a significant conformational change in the high- molecular-weight (HMW) von Willebrand factors (vWF) which enables the A2 domain of vWF to be degraded by ADAMST13, a well-known plasma protease. The resulting HMW vWF multimers are less effective in coagulation and are cleared away easily which leads to the development of acquired Von Willebrand factor deficiency.[5,6] Even though the pathophysiology of the development of Acquired VWF deficiency (AVWS) is well laid out, a study of case reports has found that almost 65 % of the cases didn't develop AVWS. Thus, other modalities of pathophysiology should be explored[1].

Angiodysplasia in the Gastrointestinal tract as described in the original triad should also be taken into consideration as a potential source of bleeding in adjunction to the acquired VWF deficiency. The available literature on Heyde syndrome suggests that the site most common for the development of angiodysplasia was the small intestine with jejunum in particular whereas the site most common for development of isolated angiodysplasias is caecum. This may hint towards different pathogenesis of angiodysplasia in Heyde syndrome and also highlights the importance of examining the jejunum and small intestine.[1] AVWS may potentially be a factor in the development of angiodysplasias.[7]

In an elderly patient with established aortic stenosis, if there is development of iron deficiency anemia, Heyde syndrome should be kept in consideration[4]. One of the challenges of diagnosing a case such as Heyde syndrome is establishing the connection between arteriovenous malformation (AVM) and aortic stenoses. The evidence that aortic stenosis is the root cause of coagulopathy is much stronger than the evidence for a causal association with angiodysplasia[8]. However, one study demonstrates that AS is substantially more common in individuals with concurrent AVMs and that the stenoses are more severe, which may have an impact on how both AVMs and AS are managed. Since there may be changes in how patients with a recognized Heyde syndrome are managed, current studies likely underestimate the true prevalence of the Heyde syndrome[9].

Our patient had a history of recurrent GI bleeds requiring blood transfusions. Similar findings have been reported from other studies indicating Heyde disease as having a high risk of bleeding and subsequent mortality requiring urgent interventions.[10]Patients with Heyde syndrome who are treated by intestinal resection generally continue to bleed from other sites, while AVR usually cures clotting disorder and anemia. Although

aortic valve replacement is the mainstay of treatment in Heyde syndrome, newer interventions such as TAVI (Transcatheter Aortic Valve Implantation) have been found to durably reduce the events of Gastrointestinal bleeds in Heyde syndrome[11]. As the recurrence rate was significant during follow-up, a possible association with residual PVL (Paravalvular Leakage) requires further investigation to improve treatment options and outcomes in patients with HS[12]. Episodes of severe bleeding may necessitate blood transfusions and emergency bowel resections.

In our case, aorto-atrial fistula was noted on TTE with a paravalvular leak from the previous repair of aortic stenosis. Aorto-atrial fistulas are infrequent but have the potential to be life-threatening by creating excessive burden on the heart's volume. They occur when an abnormal connection develops between the structures of the aorta and the cardiac atria. The diagnosis of AAFs is frequently delayed due to the non-specific nature of the symptoms presented, and the sensitivity of trans-thoracic echocardiography (TTE) is only around 50%.[13] The aorto-atrial fistula usually is caused as a sequela of endocarditis, congenital causes and rarely as a complication of cardiac surgery[13]. In recent years, there has been an increasing utilization of percutaneous closure for Atrial-Arterial Fistulae (AAF). Although there are no dedicated devices designed exclusively for transcatheter closure of fistulas, devices that are primarily intended for closing atrial septal defects, have shown its effectiveness for this application. The overall success rates for the treatment are at least 70%, albeit with a mortality rate of approximately 15%[14].

CONCLUSION

Heyde syndrome is a relatively underdiagnosed and less understood medical condition. The diagnosis is challenging and its potentially fatal episodes of gastrointestinal bleeding make this diagnosing this condition a priority in elderly with aortic stenosis with a high degree of suspicion. Further studies are needed to inquire into the pathophysiology to improve the outcome and prognosis.

AUTHOR CONTRIBUTIONS

Swotantra Gautam: Writing – original draft; writing – review and editing. Aakash Neupane: Writing – review and editing. Ghaith Maksoud: Writing – review and editing. Robert Ryad: Supervision; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

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ETHICS STATEMENT

All methods were performed in accordance with the relevant guidelines and regulations. Written informed consent was obtained from the patient.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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