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## Case Report

# Heyde's Syndrome – A Forgotten Association

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### ABSTRACT

Heyde's syndrome was originally described as the association of aortic stenosis (AS) and angiodysplastic gastrointestinal (GI) bleeding; epistaxis as a presentation was observed later. We present a case of the 80-year-old man admitted with recurrent episodes of epistaxis on a background of recurrent GI bleeds and AS. Examination showed telangiectasia on the nasal septum and endoscopic examination demonstrated small intestine angiodysplasia. The epistaxis was managed conservatively. This report hopes to emphasise the importance of further investigation for causes of nosebleed in patients with recurrent admissions.

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### Introduction

Heyde's syndrome, was named after Dr. Edward C. Heyde in 1958, following his report of a series of patients suggesting a rare relationship between calcific aortic stenosis (AS) and unexplained gastrointestinal (GI) bleeding due to angiodysplasia (Heyde 1958) [1]. This association is seen in approximately 3% of the population [2]. An interesting and rare additional complication of Heyde's syndrome, with only one reported case in English literature, is recurrent epistaxis [2]. In patients with recurrent epistaxis that fails to respond to conventional conservative therapy, this case hopes to show the importance of the consideration of a more complex aetiology. Thus, it is important to investigate for other underlying diagnoses, whereby addressing these may ameliorate the condition.

### Case Presentation

We present the case of an 80-year-old patient admitted on 15 separate occasions over a two-year period with epistaxis. Our patient has a background severe aortic stenosis (pressure gradient > 70mmHg), recurrent gastro-intestinal bleeding and COPD. No history of anticoagulation or antiplatelet therapy. On examination the nasal septum was slightly deviated to the right and the nasal mucosa displayed

multiple telangiectasia. Biochemically the patient's INR and APTT were normal as was the von Willebrand deficiency screen. Bleeding episodes were managed conservatively, with nasal packing and blood transfusions when clinically required.

During this same two-year period, our patient was separately and repeatedly admitted under the gastroenterology team with intestinal bleeding. Upper and lower GI endoscopies confirmed the presence of small intestinal angiodysplasia. These GI bleeds also resulted in multiple blood transfusions. As the bleeding source was usually in the small intestine, a number of double-balloon enteroscopies were occasionally successful in identifying bleeding points and haemostasis. However, despite commencing prophylactic tranexamic acid epistaxis and GI bleeding continued to be a frequent occurrence in our patient.

Due to multiple presentations to ENT and GI services a case review was performed to establish an underlying diagnosis. Taking into account the comorbidity of severe aortic stenosis (pressure gradient of >70mmHg), a literature search identified Heyde's syndrome as the most appropriate diagnosis. Due to his poor respiratory function (FEV1<1.5l), surgical intervention of aortic valve replacement is inappropriate. Therefore, he is being managed conservatively with blood transfusion when required.

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## Investigations

Routine biochemical investigations, including a clotting screen were normal, as was von Willebrand deficiency screen. Upper and lower GI endoscopies confirmed the presence of duodenal and small intestinal angiodysplasia.

## I Differential Diagnosis

Hereditary Hemorrhagic Telangiectasia (Osler-Weber-Rendu).

## II Treatment

Our patient was managed supportively with blood transfusions, Tranexamic acid (1g three times daily per oral) and nasal packing. Double balloon-enteroscopies and blood transfusion for GI bleeding.

## III Outcome and Follow-Up

The patient continues to have epistaxis and GI bleeds which require occasional intervention.

## Discussion

Heyde's syndrome appears to consist of bleeding from previously latent intestinal angiodysplasia as a result of an acquired haematological defect. This defect is an acquired type 2A von Willebrands disease – 'von Willebrands syndrome' (vWS) [3-5]. It is proposed that flow across a stenotic aortic valve induces conformational changes in vWF high Molecular Weight (HMW) multimers; this leads to the proteolysis of vWF by the protease ADAMTS 13 [6, 7]. Von Willebrand multimers are required to maintain haemostasis. Reduction, therefore, results in impairment of platelet-mediated haemostasis in angiodysplastic vessels, and thus the patient is predisposed to bleeding [8].

Initial investigation should explore other possibilities such as Hereditary Hemorrhagic Telangiectasis (HHT) and underlying malignancy. HHT can be differentiated clinically due to an earlier presentation and longer temporal nature of symptoms together with a history of other vascular malformations e.g., pulmonary and cerebral. The presence of intestinal angiodysplasia or a failure, after investigation, to find any clear site of gastrointestinal bleeding, in the presence of AS, should raise the suspicion of Heyde's syndrome. In a vWS-2A, routine screening tests for vWFS are usually normal. VWS-2A is characterized by absence of large vWF multimers seen on SDS-agarose electrophoresis- this is the gold standard [9].

Epistaxis patients, in the majority, are elderly, frailer and have multiple pathologies [10]. The pathogenetic mechanism of epistaxis in Heyde's syndrome could be the combination of von Willebrand disease type 2A and either congenital or acquired angiodysplasia in mucous membranes. In patients over 60-year-old, angiodysplasia is the second most common cause of lower GI bleeding accounting for 40% of cases [11]. Aortic stenosis is also common, occurring in 2% of patients aged over 65 years, 3% of those aged over 75 years, and in 4% of those aged over 85 years [12].

A review of the literature show treatment options for Heyde's syndrome range from medical treatment to an Aortic valve replacement (AVR) but must be tailored to the individual patients' preferences and comorbidities. Currently, the management of Heyde's syndrome often requires AVR that, usually, is employed in the management of severe AS [13]. AVR minimises the shear stress on the HMW multimers and can reverse the pathophysiological cause of angiodysplastic bleeding [13]. The conservative management of Heyde's syndrome in elderly patients, unfit for and/or refusing AVR, includes iron supplementation and regular blood transfusions as necessary [14]. It is important to avoid iron deficiency in patients with recurrent GI bleeding, as anaemia itself inhibits haemostasis, due to a reduced platelet sub-endothelium interaction and exacerbates the bleeding [6].

Recurrent epistaxis in association with aortic stenosis as an indication for valve replacement remains controversial among cardiothoracic surgeons. Consideration for AVR is usually focussed on cardiac symptoms alone. In cases where patients are unfit for valve replacement, the mainstay of treatment is regular blood transfusions. This provides symptomatic relief and can be used in conjunction with local treatment of the nose in the form of cautery and topical nasal sprays or creams [15].

However, despite surgical reticence, replacement of the stenosed aortic valve in Heyde's syndrome has been shown to be effective in stopping the recurrent bleeding episodes and resulting in haematologic recovery [13].

## Learning Points

- i. A High index of suspicion is required to diagnose Heyde's syndrome.
- ii. Heyde's syndrome is the association of GI bleeding, and/or epistaxis, and severe AS.
- iii. Heyde's syndrome can be managed successfully by cardiac valvular surgery.
- iv. Recurrent episodes of nosebleed warrants thorough investigation.

## Data Availability

Data is not available as it is a trial and is a health record.

## Conflicts of Interest

None.

## Funding

None.

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