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Case Report

Heyde Syndrome as Cause of New-onset Heart Failure in the Setting of Bioprosthetic Aortic Valve: A Case Report

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ABSTRACT

This report describes the case of a 70-year-old female with a history of bioprosthetic aortic valve replacement. She presented to the emergency department with significant shortness of breath and bilateral lower extremity edema, which was found to be secondary to new-onset acute symptomatic congestive heart failure in the setting of Heyde syndrome.

Keywords

Heyde syndrome; Aortic stenosis; Gastrointestinal bleeding; von Willebrand disorder; Clinical case report.

INTRODUCTION

Heyde syndrome is a constellation of multi-system disorders involving the classic triad of aortic stenosis, gastrointestinal bleeding, and acquired von Willebrand syndrome that is thought to be caused by cleavage of the A2 domain of large von Willebrand multimers by the ADAMTS13 enzyme in the high-shear environment of aortic stenosis into smaller fragments that subsequently interfere with the native inhibition of angiogenesis and delivery of clotting factor VIII throughout the body.[1-3] This syndrome appears to be significantly increasing in prevalence in the United States, with females of African-American descent continuing to be disproportionally affected.[4] Among all ethnic and gender groups, older adults are the most affected by this syndrome. This is likely because the causes of aortic stenosis (like atherosclerosis) and gastrointestinal bleeding (like angiodysplasia) become more prevalent and severe with age.[5] Heyde syndrome is usually diagnosed based on clinical signs such as aortic stenosis and gastrointestinal bleeding. The laboratory workup often includes a complete blood count with a platelet count and activated partial thromboplastin time. However, more sensitive tests like gel electrophoresis or platelet function assays are time-consuming and expensive and are usually used to rule out other conditions. Factor VIII levels may also be directly measured, though the presence of normal levels cannot rule out acquired von Willebrand syndrome. Heyde syndrome is usually managed by controlling gastrointestinal bleeding and considering aortic valve repair. Replacement of Von Willebrand factor, factor VIII, and octreotide therapy has not shown any benefit in these patients.[6]

CASE PRESENTATION

A 70-year-old female with a past medical history of bioprosthetic aortic valve replacement, coronary artery bypass graft, scleroderma, gastric antral vascular ectasia, iron deficiency anemia, hyperlipidemia, hypertension, prurigo nodularis, and gastroesophageal reflux disease. The patient's current medications included Losartan, Spironolactone, Atorvastatin, and Bumex. The patient presented to the emergency department with a six-day history of shortness of breath and leg swelling while awaiting intensive open-heart aortic valve enlargement at a quaternary care facility in three months. The patient's dyspnea was associated with such severe orthopnea that she was entirely unable to tolerate supine positioning. Symptoms typically associated with infectious or pulmonary etiology were notably absent, as was any evidence of acute bleeding. The physical exam upon admission was significant for mild respiratory distress, diffuse rales, grade III systolic ejection murmur loudest at the right upper sternal border, and grade IV pitting edema of bilateral lower extremities halfway up to tibial plateaus; the physical exam was otherwise unremarkable aside from the presence of multiple nodules on lower extremities consistent with a known history of prurigo nodularis. See Table 1 for the complete blood count and N-terminal pro–B-type natriuretic peptide (NT-proBNP) results. The patient was subsequently diagnosed with new-onset symptomatic acute congestive heart failure, and standard IV Lasix was begun. However, a transthoracic echocardiogram (Figures 1 and 2) unexpectedly dem-

onstrated only mild stenosis of the aortic valve with a preserved left ventricular ejection fraction of approximately 65% in the setting of diastolic dysfunction. Chest X-ray findings revealed a calcified aortic valve (Figure 3). Factor VIII activity level was inconclusive, as a von Willebrand factor inhibitor was detected on testing; platelet function analyzer testing was considered but not pursued due to a lack of impact on patient care. Regardless of etiology, the patient responded quite well to regular IV furosemide treatment and was able to be discharged home after only two days of inpatient treatment. The aortic valve was successfully repaired approximately one month later at a quaternary care facility.

Table 1. *Complete Blood Count and NT-BNP Results*

Complete Blood Count and NT-BNP Results	Results	Reference Range
White blood cells	7.4x10³ /µL	4.5-11.5x10³ /µL
Hemoglobin	8.7x10⁶ /µL	11.6-14.8 g/dL
Hematocrit	26.50%	36.0-48.0 %
Platelet count	315x10³ /µL	130-400x10³ /µL
Red blood cells	3.30x10⁶ /µL	3.50-5.50x10⁶ /µL
Mean corpuscular volume	80.1 fL	79.0-88.0 fL
Mean corpuscular hemoglobin concentration	32.8 g/dL	30.0-37.0 g/dL
Mean corpuscular hemoglobin	26.3 pg	24.4-34.0 pg
Red cell distribution width	17.7%	11.5-14.0%
Mean platelet volume	8.2 fL	7.5-11.5 fL
Relative neutrophils	65%	41-69%
Relative lymphocytes	16%	19-46%
Relative eosinophils	5%	0-5%
Relative monocytes	12%	4-12%
Relative basophils	1%	0-2%
Absolute neutrophil count	4.90x10³ /µL	1.80-7.50x10³ /µL
Absolute lymphocyte count	1.20x10³ /µL	1.10-3.80x10³ /µL
Absolute eosinophil count	0.40x10³ /µL	0-5%
Absolute monocyte count	0.90x10³ /µL	0.10-0.80x10³ /µL
Absolute basophil count	0.10x10³ /µL	0.00-0.20x10³ /µL
NT-BNP	2,050 pg/mL	<300 pg/mL

NT-BNP: N-terminal prohormone of brain natriuretic peptide

Figure 1. *Transthoracic Echocardiogram Demonstrating Mild Aortic Stenosis*

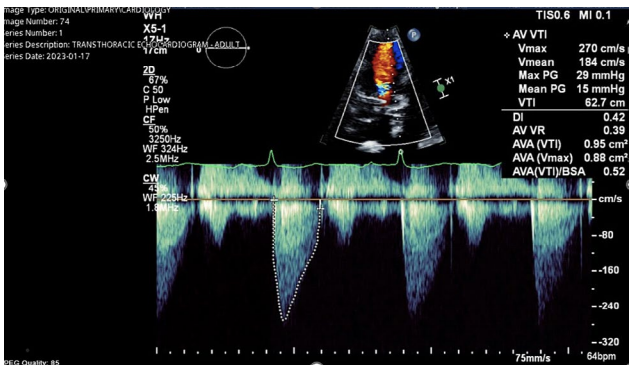


Figure 2. *Transthoracic Echocardiogram Demonstrating Mild Aortic Stenosis*

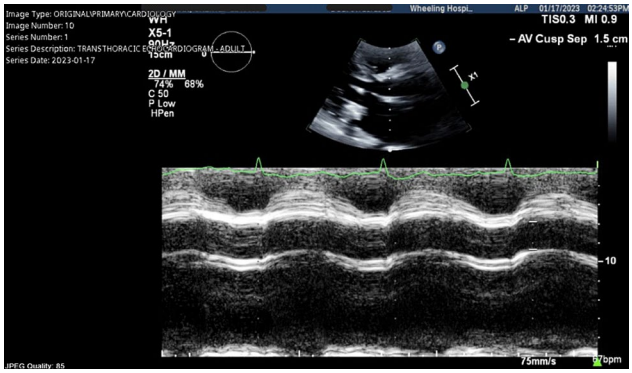
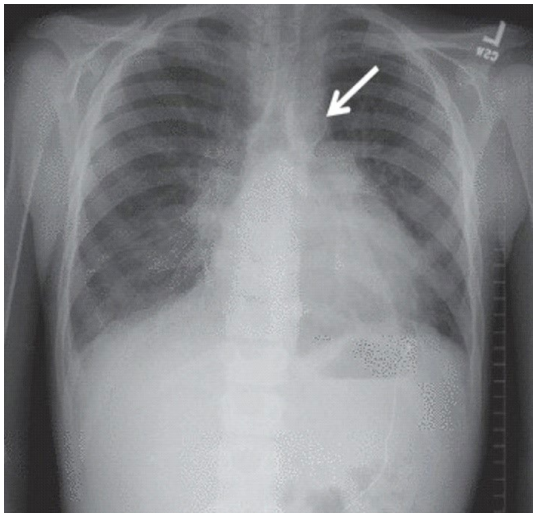


Figure 3. *Calcified Aortic Valve*



DISCUSSION

While this patient didn't show typical gastrointestinal bleeding seen in Heyde syndrome, her heart failure is likely linked to aortic stenosis, causing the shearing of large von Willebrand multimers, leading to demand ischemia. However, it is quite unusual to observe such a result with only mild aortic stenosis, with only one other case report in the literature describing this presentation thus far and severe aortic stenosis previously assumed to be a requirement of symptom development.[7-9] As more research confirms a connection between mild aortic stenosis and symptomatic Heyde syndrome, with an overall rise in Heyde syndrome cases in the general population, the demand for accurate diagnostics is growing.[4] Unfortunately, complete testing for acquired von Willebrand disorder can be costly and time-prohibitive in many community hospitals, as these laboratory tests are not commonly available outside of the university setting and are therefore often deferred in favor of the more readily available platelet function assay.[10] This patient was fortunate she did not require definitive testing as she was already awaiting aortic valve repair; the Heyde syndrome diagnosis merely

allowed her valve repair to be scheduled sooner than previously anticipated. Of further interest in this case is the fact that the aortic valve in question was a bioprosthetic one; it is unclear what role, if any, the bioprosthesis might have played in the development of Heyde syndrome in this patient—or if that is indeed the reason Heyde syndrome was able to develop in the setting of only mild aortic stenosis instead of the more typical severe aortic stenosis—as such cases do not appear to have been reported in the literature thus far.

CONCLUSION

This case emphasizes the need to consider Heyde syndrome as a potential cause in patients with anemia and any degree of aortic stenosis. This ensures timely arrangements for the appropriate treatment, such as aortic valve repair, to address symptomatic anemia and its associated effects.

In conclusion, Heyde syndrome is a rare condition that can lead to severe morbidity and mortality. It is essential to diagnose Heyde syndrome promptly in order to improve outcomes.

CONSENT

The authors have received written informed consent from the patient.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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