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CASE REPORT

Heyde's Syndrome: A Case Report

Síndrome de Heyde: un caso clínico

Alejandra González Esquerra[1]
Alexis Pérez Pérez[2]
Yendry Gattorno Aguila[3]
Marlon Durán Cárdenas[4]
Luis Alberto Rodríguez López[5]

[1] Cardiology Resident, Arnaldo Milián Castro Clinical-Surgical Hospital, Santa Clara, Villa Clara, Cuba. 2 Cardiology Service, Arnaldo Milián Castro Clinical-Surgical Hospital, Santa Clara, Villa Clara, Cuba. 3 Cardiology Service, Althaia Foundation, Manresa, Barcelona, Spain. 4 Internal Medicine Resident, Arnaldo Milián Castro Clinical-Surgical Hospital, Santa Clara, Villa Clara, Cuba. 5 Pre-Surgical Cardiology Service, "Ernesto Che Guevara" Cardiocenter Hospital, Santa Clara, Villa Clara, Cuba.

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Corresponding Author: Alejandra González Esquerra

ABSTRACT

Heyde's syndrome is the association between aortic valve stenosis and gastrointestinal bleeding due to intestinal angiodysplasia. The pathophysiological basis of this syndrome appears to be an acquired deficiency of von Willebrand factor, leading to bleeding from angiodysplastic arteriovenous malformations. Treatment options include localization and cauterization of the bleeding sites, although this therapeutic approach is associated with a high recurrence rate. Aortic valve replacement appears to offer the best long-term resolution of bleeding and should be considered in most cases.

Keywords: Gastrointestinal Bleeding; Severe Aortic Stenosis.

RESUMEN

El síndrome de Heyde es la asociación entre estenosis de la válvula aórtica y hemorragia gastrointestinal debida a angiodisplasia intestinal. La base fisiopatológica de este síndrome parece ser una deficiencia adquirida del factor de von Willebrand, que conduce a hemorragias por malformaciones arteriovenosas angiodisplásicas. Las opciones de tratamiento incluyen la localización y cauterización de los focos hemorrágicos, aunque este enfoque terapéutico se asocia a una alta tasa de recurrencia. La sustitución de la válvula aórtica parece ofrecer la mejor resolución a largo plazo de la hemorragia y debe considerarse en la mayoría de los casos.

Palabras clave: Hemorragia Gastrointestinal; Estenosis Aórtica Grave.

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INTRODUCTION

Heyde's syndrome was first described by internist Edward C. Heyde in Vancouver in 1958,(1) in a case series of ten patients with aortic stenosis and gastrointestinal bleeding of unknown cause. The link to intestinal angiodysplasia was later established by Galloway and colleagues through angiographic studies.(2) The prevalence of Heyde's syndrome in patients with aortic stenosis is unknown, although retrospective studies report a higher rate of idiopathic gastrointestinal bleeding in this population (2,6 %) compared to the control group (0,025 %).(1,2,3) In 2003, Vincentelli et al.(2) reported a high prevalence of the syndrome among patients scheduled for valve replacement (21,4 %) and demonstrated a direct relationship between stenosis severity—assessed via mean transaortic gradient—and degradation of high-molecular-weight von Willebrand factor multimers. They also confirmed early reversal of the hemostatic defect following surgery and its recurrence in cases of prosthetic valve mismatch, providing crucial evidence for a causal relationship. The first clinical guideline to acknowledge the syndrome—albeit without using the eponym—is the 2008 update of the 2006 American College of Cardiology/American Heart Association guidelines on valvular heart disease management. However, the document does not address its clinical relevance or establish management recommendations.

We present the case of a patient with severe aortic stenosis and gastrointestinal bleeding due to duodenal angiodysplasia, treated with sclerotherapy. This condition represents an uncommon cause of gastrointestinal bleeding in general surgery departments.

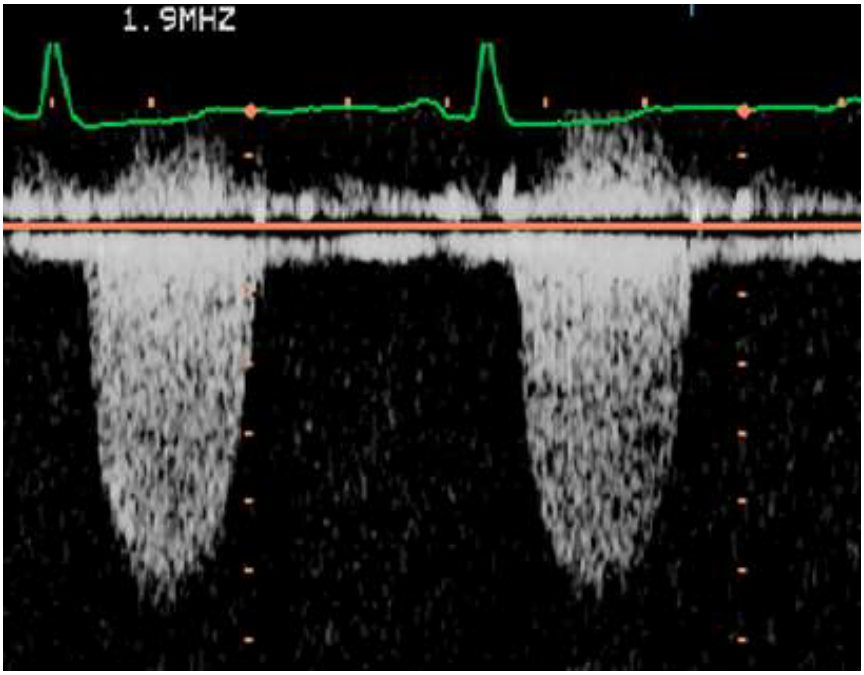
CASE REPORT

We present the case of an 81-year-old male patient of mixed skin tone from an urban setting, with a history of essential hypertension treated with Enalapril 20 mg every 12 hours, Amlodipine 10 mg (half tablet daily at 4 PM), and Hydrochlorothiazide 25 mg once daily. He also had a known diagnosis of severe aortic stenosis (see Image 1) for approximately five years and was admitted to the cardiology unit due to recurrent precordial chest pain with electrocardiographic signs of left ventricular overload. During his hospital stay, the patient developed symptomatic heart failure associated with anemia and dark, coffee-ground stools. A surgical consultation was requested, and the condition was interpreted as upper gastrointestinal bleeding of unknown etiology. At the time of the consultation, his hemoglobin level was 6,2 g/dL. After appropriate medical treatment and transfusion of packed red blood cells, the patient showed partial symptomatic improvement.

Figure 1

Angiodysplasia in the second portion of duodenum with sclerotherapy treatment

Figure 2



Despite the high risk associated with endoscopic procedures in a patient with severe aortic stenosis, the family opted to proceed with further studies. An initial upper gastrointestinal endoscopy revealed angiodysplastic changes in the second portion of the duodenum, which were treated with sclerotherapy. Colonoscopy showed nonspecific endothelial alterations.

Echocardiography showed a valve area of 0,52 cm^2, a peak transvalvular gradient of 98 mmHg, and a mean gradient of 51 mmHg, with preserved left ventricular systolic function. After clinical improvement and resolution of gastrointestinal bleeding, the patient was referred to the Cardiovascular Surgery Department at the Ernesto Che Guevara Cardiocenter Hospital for definitive treatment with aortic valve replacement.

DISCUSSION

Angiodysplasia is a chronic-degenerative condition of the intestinal mucosa related to the aging process and is one of the main causes of gastrointestinal bleeding in the elderly. Its association with aortic stenosis is well established.(1,2)Both conditions are linked to cardiovascular risk factors. Numerous studies suggest a higher occurrence of intestinal angiodysplasia in individuals with aortic stenosis, and vice versa.(3,4)The leading hypothesis behind this association is that both diseases are closely related to the physiological processes of aging.(5)

In 1992, Warkentin and colleagues (2) proposed an etiopathogenic mechanism whereby the acquired deficiency of high molecular weight multimers of von Willebrand factor (vWF)—specifically type IIA—due to qualitative class A defect resulting from fragmentation, impairs hemostasis under high shear stress conditions,(4)such as those found in angiodysplastic arteriovenous malformations. This mechanism appeared to be the link between the two components of the syndrome (figure 2). vWF is constitutively produced in endothelial cells—specifically within Weibel-Palade bodies—as well as in megakaryocytes and subendothelial connective tissue. It contributes to thrombus formation and mediates platelet adhesion at sites of vascular injury.(5)

The high shear stress caused by the stenotic aortic valve alters the structure of the vWF molecule, leading to proteolysis of its high molecular weight multimers by the enzyme ADAMTS13.(4)In summary, acquired von Willebrand disease type IIA due to aortic stenosis causes hemostatic defects that predispose to bleeding from previously subclinical intestinal angiodysplasia.(4)This was demonstrated in a prospective study by Veyradier et al.(6), who showed that the absence of large vWF multimers caused bleeding in angiodysplastic lesions of the gastrointestinal tract.

Further evidence came from Vincentelli et al.(7), who demonstrated that the severity of aortic stenosis is proportional to the extent of hemostatic alteration: the higher the transvalvular gradient, the lower the availability of high molecular weight multimers.

In their study, aortic valve replacement stopped the depletion of these multimers, with reversal observed in some patients as early as the first postoperative day.(5,7) In high surgical risk patients in whom no clear bleeding source can be identified, anemia management with periodic blood transfusions may offer some symptomatic relief.(4,6)

Aortic valve replacement appears to reduce the risk of gastrointestinal bleeding in patients with Heyde's syndrome, resolving bleeding in approximately 80 % of cases. Although bleeding recurrence rates do not differ significantly between biological and mechanical prostheses, the increased bleeding risk in patients on anticoagulation therapy favors the use of biological valves in most cases.(8)

Bleeding recurrence only occurs when the underlying pathophysiology is reestablished—either due to restenosis or patient-prosthesis mismatch (effective valve area/body surface area < 0,85 cm^2/m^2 on echocardiography), which can lead to persistently high postoperative gradients despite a normally functioning prosthesis.(6)

Godino et al.(9)reported an incidence of 1,7 % of Heyde's syndrome among 400 patients who underwent transcatheter aortic valve implantation (TAVI) at their institution, with complete resolution of gastrointestinal bleeding in all successfully treated patients.

Management of acute bleeding includes blood transfusion and emergency intestinal resection. However, segmental resection does not provide long-term benefit, as these patients often rebleed from different locations.

Bleeding ceases in nearly all patients who undergo aortic valve replacement (93 %), reinforcing the causal relationship between aortic stenosis and gastrointestinal bleeding.(10)

Heyde's Syndrome: Its Clinical Characterization in 10 Points

1. It was originally formulated by Edward Heyde in 1958 as the association between severe aortic stenosis and major gastrointestinal bleeding.
2. Its clinical-etiopathogenic definition and consolidation as a syndromic entity was a gradual and collaborative construction, with contributions from various disciplines.
3. The bleeding lesions are usually submucosal angiodysplasias, commonly located in the right colon, though they can occur anywhere along the digestive tract—from the cardia to the anal sphincter. The small intestine is often involved, and multifocal lesions are frequent.
4. Its presentation increases with age, due to the higher prevalence of aortic stenosis and angiodysplasias in elderly individuals.
5. It can manifest as overt bleeding, with visible angiodysplasias or no identifiable lesion (dark stools), or as chronic anemia with no external signs of bleeding (occult bleeding). It may also be accompanied by cutaneous or mucosal bleeding signs.
6. The bleeding trigger is a platelet dysfunction caused by a deficiency of high-molecular-weight von Willebrand factor (vWF) multimers, processed by the ADAMTS13 protease. This is due to a conformational alteration in vWF when it is elongated into a fibrillar shape, which exposes the cleavage site. The high shear stress caused by the aortic stenosis increases the breakdown of these multimers. The largest multimers are particularly necessary for effective hemostasis at sites of angiodysplasias.
7. Once its pathophysiology is understood, the syndrome is configured as the triad of aortic stenosis, gastrointestinal bleeding, and an acquired type 2A von Willebrand disease—and should be treated as such, including its therapeutic consequences.
9. Aortic valve replacement surgery usually resolves both the aortic stenosis and the bleeding in most cases. However, recurrence may occur if there is prosthesis–patient mismatch or a high residual gradient, a more frequent and risky condition in older patients with small aortic roots.
10. In principle, TAVI is preferable to surgical valve replacement due to its lower invasiveness in elderly patients, those with comorbidities, or those with anemia. However, its durability and effective prosthetic valve area must be considered.
11. The diagnostic process must include ruling out malignancy, as well as acquired vWF disease and aortic stenosis. Management usually requires the involvement of multiple disciplines—clinical cardiology, hematology, gastroenterology, interventional radiology, and interventional cardiology/cardiac surgery.

CONCLUSIONS

Heyde's syndrome is a cause of gastrointestinal bleeding due to angiodysplastic changes in the digestive tract as a result of severe aortic stenosis. The bleeding from these angiodysplastic lesions is closely related to alterations in von Willebrand factor caused by increased valvular flow. The definitive long-term treatment for this condition is aortic valve replacement.

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CONFLICT OF INTEREST

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AUTHORSHIP CONTRIBUTIONS

Conceptualization: Alejandra González Esquerra, Alexis Pérez Pérez, Yendry Gattorno Aguila, Marlon Durán Cárdenas, Luis Alberto Rodríguez López.
Research: Alejandra González Esquerra, Alexis Pérez Pérez, Yendry Gattorno Aguila, Marlon Durán Cárdenas, Luis Alberto Rodríguez López.
Methodology: Alejandra González Esquerra, Alexis Pérez Pérez, Yendry Gattorno Aguila, Marlon Durán Cárdenas, Luis Alberto Rodríguez López.
Project administration: Alejandra González Esquerra, Alexis Pérez Pérez, Yendry Gattorno Aguila, Marlon Durán Cárdenas, Luis Alberto Rodríguez López.
Writing - original draft: Alejandra González Esquerra, Alexis Pérez Pérez, Yendry Gattorno Aguila, Marlon Durán Cárdenas, Luis Alberto Rodríguez López.
Writing - revision and editing: Alejandra González Esquerra, Alexis Pérez Pérez, Yendry Gattorno Aguila, Marlon Durán Cárdenas, Luis Alberto Rodríguez López.