

Case and Review

Long Survival after Gastrointestinal Bleeding in a New-Onset Heyde's Syndrome Patient Treated with Multiple Endoscopic Hemostatic Procedures and Repeated Transfusions after Aortic Valve Replacement

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Keywords

Heyde's syndrome · Gastrointestinal bleeding · Endoscopic hemostasis · Transfusion · Long survival

Abstract

Heyde's syndrome, which is caused by aortic stenosis and subsequent acquired von Willebrand factor deficiency, is a gastrointestinal bleeding disease. Gastrointestinal bleeding develops in patients with Heyde's syndrome, which may have a different prognosis from general gastrointestinal bleeding; thus, it is important to understand the clinical course. We report a 76-year-old Japanese female who underwent aortic mechanical valve replacement 1 year ago and presented with recurrent gastrointestinal bleeding in angiodysplasia of the sigmoid colon. Endoscopic interventions achieved hemostasis. However, 6 rebleeding events occurred due to a sigmoid colon ulcer and gastric and jejunal angiodysplasia 7 years after first hemostasis. The patient underwent multiple endoscopic hemostatic procedures (upper, lower, and balloon-assisted endoscopy) and repeated transfusions (total of 394 units of red blood cells). The intensive treatment contributed to the survival time of 10 years. In addition, we performed a literature review of the prognosis of patients with Heyde's syndrome.

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Introduction

Gastrointestinal bleeding is a common clinical condition requiring hospitalization and blood transfusion, particularly in patients with severe systemic comorbidities, including cardiovascular diseases such as Heyde's syndrome [1, 2]. The pathogenesis of Heyde's syndrome is characterized by gastrointestinal bleeding caused by arteriovenous malformation and acquired von Willebrand factor (vWF) deficiency resulting from mechanical destruction of vWF multimers as they pass through the narrowed aortic valve. Gastrointestinal bleeding lesions develop in patients with Heyde's syndrome, which may have a different prognosis from general gastrointestinal bleeding; thus, it is important to understand the clinical course.

We report a case of Heyde's syndrome characterized by chronic persistent gastrointestinal bleeding that was treated with multiple endoscopic hemostatic procedures and transfusions, resulting in a survival time of approximately 10 years. We also performed a literature review of the prognosis of patients with Heyde's syndrome.

Case Report/Case Presentation

A 76-year-old woman underwent mitral valve replacement and tricuspid valve in 1989. The patient also underwent aortic valve replacement in 2009 due to advanced aortic stenosis and regurgitation.

A large-volume painless tarry stool occurred in 2010, accompanied by hemorrhagic shock. A complete blood count revealed a hemoglobin level of 11.0 g/dL. The patient required a transfusion to recover her general condition. Early colonoscopy identified the stigmata of a recent hemorrhage for angiodysplasia of the sigmoid colon, and she underwent endoscopic coagulation (Fig. 1A).

Between 2010 and 2016, 6 gastrointestinal bleeding events occurred in a sigmoid colon ulcer, sigmoid and gastric angiodysplasia, and a descending colon polyp, which required the transfusion of 10 units of blood. Endoscopic therapies, including clipping and argon plasma coagulation (APC), successfully treated these gastrointestinal bleeding (Fig. 1B, C).

In 2016, anemia occurred after gastric hyperplastic polyp bleeding due to a *Helicobacter pylori* (*H. pylori*) infection and required 16 units of blood. Endoscopic mucosal resection was performed, and *H. pylori* was eradicated. However, the anemia progressed again in 2017. Capsule endoscopy was performed and revealed jejunal intestinal angiodysplasia. APC was performed using balloon-assisted endoscopy (Fig. 1D). A total of 360 units of blood were transfused between 2017 and 2020 to treat the slowly progressing anemia (Fig. 2).

The patient had a max aortic jet velocity (AV_{\max}) of 3.96 m/s in 2008 before the aortic valve replacement, which improved to 3.04 m/s after surgery in 2009. The AV_{\max} increased to 3.95 m/s in 2010 when gastrointestinal bleeding occurred, and increased to 4.74 m/s in 2012 (Fig. 3). The vWF activity decreased from 113% in 2017 to 100% in 2019. The vWF multimer analysis was normal in 2020; her vascular endothelial growth factor level was 865 pg/mL (normal range: 62–704 pg/mL).

Hematemesis developed in October 2020. A complete blood count revealed progression of anemia (hemoglobin level = 6.8 g/dL), which required 24 units of blood. Upper endoscopy revealed multiple gastric angiodysplasia lesions, and hemostasis was performed twice using APC (Fig. 1E, F). Although hemostasis was achieved, the patient died of acute exacerbation from chronic heart failure in November 2020, 10 years after the initial gastrointestinal bleeding event.

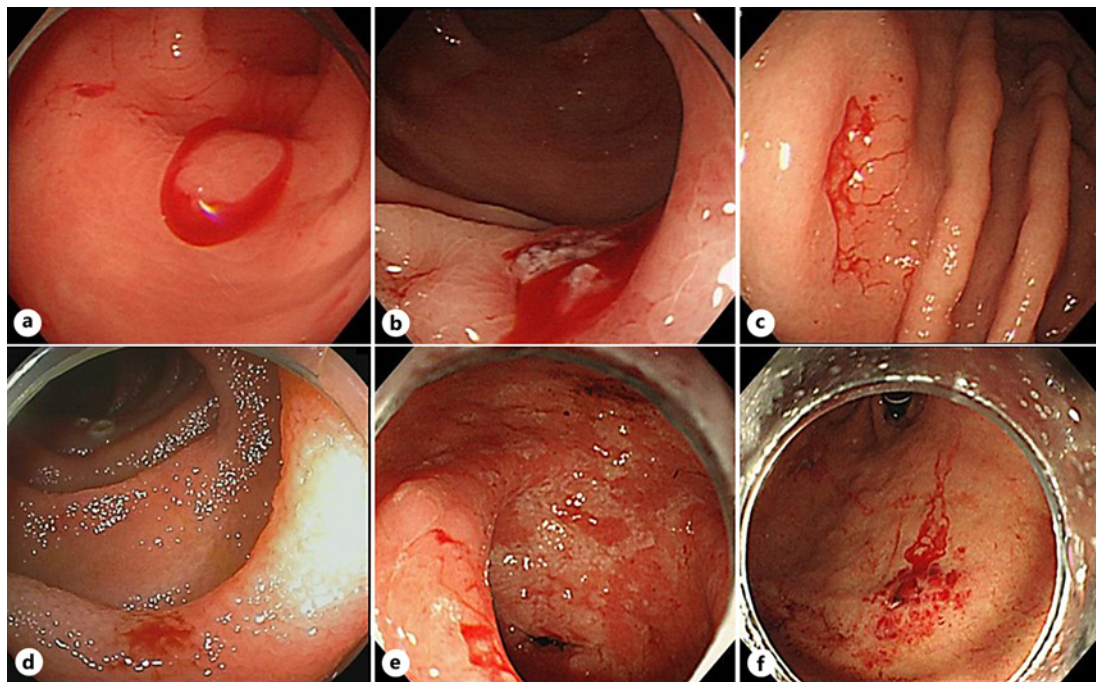


Fig. 1. Gastrointestinal bleeding events. Active bleeding in angiodysplasia of the sigmoid colon in 2010 (A), 2013 (B), and 2016 (C). D Jejunal angiodysplasia in 2017. E, F Active bleeding in gastric angiodysplasia in 2020.

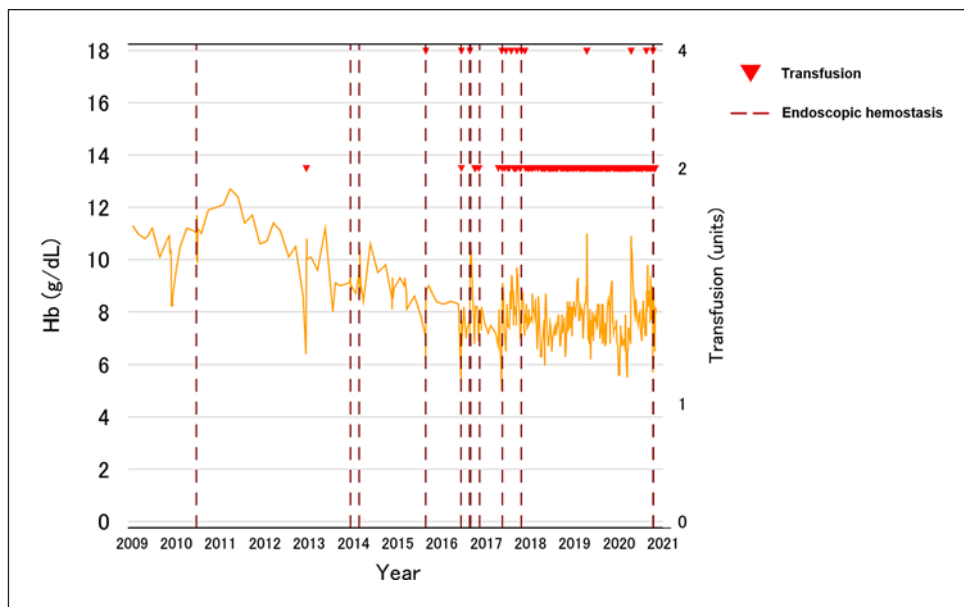


Fig. 2. Clinical course of the patient. Yellow line shows the hemoglobin level.

Discussion/Conclusion

We performed multiple endoscopic hemostatic procedures in a patient with new-onset Heyde's syndrome after aortic valve replacement. The patient survived for approximately 10

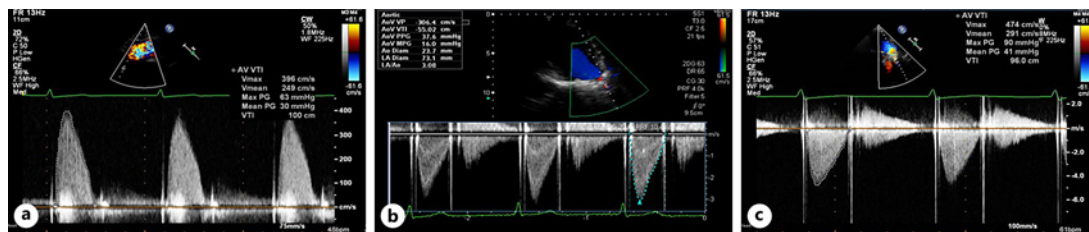


Fig. 3. Changes on echocardiography. **A** Preoperative transthoracic echocardiography shows severe aortic stenosis ($AV_{max} = 3.96$ m/s). **B** Postoperative transthoracic echocardiography reveals improved aortic stenosis ($AV_{max} = 3.06$ m/s). **C** Transthoracic echocardiography shows exacerbation of aortic stenosis ($AV_{max} = 4.74$ m/s).

years after the first gastrointestinal bleeding event. To our knowledge, this is the first report of a long survival time in a new-onset Heyde's syndrome patient after aortic valve replacement.

In 1958, Heyde [1] reported an association between gastrointestinal bleeding and aortic stenosis. The criteria for Heyde's syndrome changed to aortic stenosis with intestinal angiodysplasia and acquired vWF syndrome; our patient met those criteria. Importantly, the time of onset after aortic valve replacement was approximately 1 year, consistent with a previous report [3].

Table 1 shows the previous reports detailing the clinical characteristics and prognoses of patients with Heyde's syndrome. Chukwudum et al. [4] reported a 61-year-old man with upper gastrointestinal bleeding who survived for 36 months. Hudzik et al. [5] reported an 82-year-old man with a bleeding colon who survived 12 months. Our patient survived longer than those in all previous reports [3, 4, 6–18]. However, our patient developed Heyde's syndrome after cardiac surgery, and we could not perform further cardiac interventions. The treatments for Heyde's syndrome include managing cardiac function and gastrointestinal bleeding. Multiple endoscopic hemostatic procedures may contribute to a good response in a patient with Heyde's syndrome. Another potential reason for the long survival of our patient may be the repeated transfusions. Heyde's syndrome is an acquired vWF disease. A severely narrowed aortic valve causes high shear stress and stretching, which impairs function [1]. Multiple transfusions contribute to the recovery of vWF multimer function and activity [19]. In conclusion, multiple endoscopic hemostatic procedures and transfusions may be effective to prolong the survival time of gastrointestinal bleeding patients with Heyde's syndrome.

Statement of Ethics

This study protocol was reviewed and approved by the Institutional Review Board of the University of Tokyo Hospital, Approval No. [2058-2]. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Table 1. Review of the literature on the prognosis of patients with Heyde's syndrome

Author	Age, yr	Sex	Gastrointestinal bleeding site	Hemostasis	Cardiac surgery	New-onset Heyde's syndrome after cardiac surgery	Units of blood transfused	Follow-up period	Prognosis
Our case	76	F	Sigmoid colon, stomach, jejunum	APC, EMR, clipping	AVR	Yes	394	372 months	10 years
Chukwudum et al. [4]	61	M	Upper gastrointestinal tract		AVR	No	2	36 months	nr
Noor and Abadco [7]	72	F	Jejunum	APC		No	7	nr	nr
Famularo and Marrollo [14]	80	F	Jejunum	APC	TVAR	No	nr	3 months	nr
Ahmed and Haque [17]	79	M	Not identified		TAVR	No	nr	nr	nr
Schwaiger et al. [9]	42	M	Small intestine		AVR	No	nr	nr	nr
Omar Then et al. [3]	84	F	Stomach	Clipping	AVR	Yes	3	nr	nr
Garcia et al. [12]	64	M	Jejunum		AVR	No	nr	17 days	nr
Ramachandran et al. [10]	85	M	Duodenum, small intestine		TVAR	No	nr	6 months	nr
Alshuwaykh and Krier [11]	56	F	Small intestine	APC	TVAR	No	4	6 months	nr
Balbo et al. [15]	81	M	Ascending colon		TAVI	No	nr	6 months	nr
Hudzik et al. [5]	82	M	Colon		TAVI	No	nr	12 months	nr
Ilkeli et al. [8]	46	F	Duodenum, ileum, colon	APC	AVR	No	nr	12 months	nr
Ledingham [16]	93	F	Duodenum	IVR		No	10	A few days	A few days
Dos Santos et al. [18]	71	M	Cecum	APC	AVR	No	nr	5 months	nr
Godino et al. [13]	83	F	Duodenum		BAV	No	2	nr	nr
Figuinha et al. [6]	76	M	Ascending colon			No	nr	2 months	2 months

nr, not reported; APC, argon plasma coagulation; IVR, interventional radiology; EMR, endoscopic mucosal resection; AVR, aortic valve replacement; TVAR, transcatheter aortic valve replacement; BAV, balloon aortic valvuloplasty; TAVI, transcatheter aortic valve implantation.

Author Contributions

G. Notoya and R. Niikura contributed to literature review and manuscript writing. M. Ochi performed the management of the patient. A. Yamada contributed to supervision. T. Kawai and K. Koike contributed to final review of the manuscript. The final version of the manuscript was read and approved by all authors.

Data Availability Statement

The Tokyo University IRB does not allow access to the study data on the basis of ethical grounds.

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