Case Reports in Women's Health 40 (2023) e00559

Contents lists available at ScienceDirect

Case Reports in Women's Health

journal homepage: www.elsevier.com/locate/crwh

Recurrent severe anemia associated with a jejunal arteriovenous malformation in pregnancy: A case report

Kazuhiko Oka [a,*], Akihiro Hasegawa [a], Hayato Mikuni [b], Ryosuke Miyazaki [b], Tomotaka Kumamoto [c], Yasuhiro Takeda [c], Natsuko Ukai [d], Takako Kiyokawa [d], Osamu Samura [a], Aikou Okamoto [a]

[a] Department of Obstetrics and Gynecology, The Jikei University School of Medicine, Tokyo, Japan
[b] Department of Gastroenterology, The Jikei University School of Medicine, Tokyo, Japan
[c] Department of Surgery, The Jikei University School of Medicine, Tokyo, Japan
[d] Department of Pathology, The Jikei University School of Medicine, Tokyo, Japan

ARTICLE INFO

Keywords:
Pregnancy
Small intestinal arteriovenous malformation
Anemia
Gastrointestinal hemorrhage
Case report

ABSTRACT

Background: Small intestinal arteriovenous (AV) malformations may cause gastrointestinal hemorrhage, occasionally leading to anemia; however, they are rarely seen in pregnancy. This report presents a case of a pregnant woman who had recurrent severe anemia that was attributed to a small hemorrhagic intestinal arteriovenous malformation.

Case Presentation: A 24-year-old pregnant woman (gravida 2, para 1) presented with a low hemoglobin concentration (3.6 g/dL) in her first pregnancy and underwent an emergency cesarean section at 36 weeks due to non-reassuring fetal status. In her second pregnancy, she was hospitalized at 30 weeks with epigastric pain and nausea. A low hemoglobin level (6.6 g/dL) and scant fecal occult blood were revealed upon examination. She was referred to the hospital for further evaluation and pregnancy management. Recurrent blood transfusions were required; however, neither hematemesis nor obvious fecal hemorrhage was observed. At 31 weeks, a cesarean section was performed owing to persistent anemia. Postoperative small intestinal capsule endoscopy and flexible fiberoptic proximal small intestinal endoscopy revealed a suspected bleeding small intestinal arteriovenous malformation. The patient underwent partial resection of the small intestine on hospitalization day 16. Histopathological examination confirmed a small intestinal arteriovenous malformation. The patient had a good postoperative course and was discharged on hospitalization day 24.

Conclusions: Small intestinal arteriovenous malformations can bleed during pregnancy. They can go undetected if they spontaneously shrink postpartum. In severe anemia during pregnancy, hemorrhage from small intestinal arteriovenous malformations should be included in the differential diagnosis and promptly investigated even in the absence of gastrointestinal symptoms.

1. Introduction

Small intestinal arteriovenous malformations (AVMs) are dilated and thickened arteriovenous (AV) anastomoses. They occur between relatively large arteries and veins and can cause hemorrhage [1]. Small intestinal bleeding accounts for approximately 5% of all gastrointestinal hemorrhages, and vascular lesions account for 23–52% of small intestinal bleeds [2,3]. Although small bowel endoscopy and dynamic contrast-enhanced computed tomography (CECT) are powerful and readily available diagnostic tools, small intestinal bleeding may go

Abbreviations: aPTT, activated partial thromboplastin time; AV, arteriovenous; AVM, arteriovenous malformation; CECT, contrast-enhanced computed tomography; CTA, computed tomographic angiogram; Hb, hemoglobin; LBW, low birth weight; MCA-PSV, middle cerebral artery peak systolic velocity; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; NICU, neonatal intensive care unit; PT, prothrombin time; RBC, red blood cell; WCC, white cell count.

* Corresponding author at: Department of Obstetrics and Gynecology, The Jikei University School of Medicine, Nishi-Shimbashi 3-25-8, Minato-ku, Tokyo 105-8461, Japan.

E-mail address: okaokamono@yahoo.co.jp (K. Oka).

https://doi.org/10.1016/j.crwh.2023.e00559
Received 2 September 2023; Received in revised form 20 October 2023; Accepted 24 October 2023
Available online 25 October 2023

undetected if the bleeding is minimal or spontaneously resolves. Bleeding from AVMs in the brain, lungs, and kidneys has been reported during pregnancy; however, small intestinal bleeding is exceedingly rare [4].

This report presents the case of a pregnant woman with severe anemia that was attributed to bleeding from an AVM of the small intestine, which was treated by surgical resection after postpartum diagnosis.

2. Case Presentation

The patient was a 24-year-old pregnant woman (gravida 2, para 1). She underwent an emergency cesarean section at 36 weeks in her first pregnancy due to an extremely low hemoglobin (Hb) level (3.6 g/dL) and non-reassuring fetal status. Postoperative upper endoscopy revealed no evidence of gastrointestinal bleeding, and the anemia spontaneously resolved. In her second pregnancy, she was hospitalized at 30 weeks with epigastric pain and nausea. An extremely low Hb level (6.6 g/dL) and scant fecal occult blood were revealed upon examination. She was referred to the hospital for further evaluation and pregnancy management.

The patient was conscious throughout admission, and the following clinical parameters were noted: blood pressure, 123/75 mmHg; pulse, 103 b/min; temperature, 37.2 °C; and respiratory rate, 16 b/min. On examination, her abdomen was soft and non-tender. Rectal examination produced only a small number of dark red spots without obvious hematochezia. Transabdominal ultrasonography at 30 weeks and 4 days of gestation revealed an estimated fetal body weight of 1685 g (0.6SD), no obvious anomalies, and a middle cerebral artery peak systolic velocity (MCA-PSV) of 44.1 cm/s (1.06 MoM). Nonstress testing revealed a fetal heart rate of 150 bpm with a reactive pattern.

Laboratory test results were as follows: white cell count (WCC), 135 $\times$ 10^9/L; red blood cell (RBC) count, 183 $\times$ 10^{12}/L; Hb, 6.1 g/dL; platelet count, 262 $\times$ 10^9/L; hematocrit, 17.6%; mean corpuscular volume (MCV), 96.2 fL; mean corpuscular Hb (MCH), 33.3 pg/cell; mean corpuscular Hb concentration (MCHC), 34.7 g/dL; reticulocyte count, 6.0%; total bilirubin, 0.1 mg/dL; prothrombin time (PT), 100%; activated partial thromboplastin time (aPTT), 24.9 s; and fibrinogen, 296 mg/dL. These findings indicated normocytic anemia with elevated reticulocyte count; therefore, hemorrhage-related anemia was suspected. No coagulopathy or obvious hemolytic or hematopoietic findings were observed.

The patient received 22 units of RBC solutions over the first 5 days of admission; however, the Hb levels were fluctuating with no evidence of coagulopathy (Fig. 1). Additionally, the patient was asymptomatic. Hence, the cause of her anemia during pregnancy was uncertain. Considering her previous pregnancy, further progression of maternal anemia was anticipated; therefore, a cesarean section was performed at 31 weeks and 1 day of gestation. A live female infant weighing 1503 g (41.1 percentile) was delivered, and the Apgar scores at 1 and 5 min were 8 and 8, respectively. Intraoperative findings showed no obvious abnormalities, such as retroplacental hematoma or bloody amniotic fluid.

A CECT of the maternal thorax and abdomen was performed on the 6th day of admission, and an upper gastrointestinal endoscopy was performed on the 8th day; however, there were no obvious bleeds or active lesions.

On the 12th day of admission, lower gastrointestinal endoscopy was performed. Although no bleeding lesions were observed, clots accumulated throughout the colon; therefore, a small intestinal hemorrhage was suspected. On the 14th day of admission, capsule endoscopy was performed, which revealed jejunal bleeding (Fig. 2). Following the capsule endoscopy, a flexible fiberoptic small bowel endoscopy was performed, and the bleeding source was suspected to be an AVM approximately 200 cm distal of the ligament of Treitz (Fig. 3a). Tattooing was performed on the other side of the lesion, and hemostasis by clipping was achieved (Fig. 3b); nevertheless, there was a high likelihood of rebleeding.

Partial resection of the small intestine was performed on the 16th day of admission. The ink was observed within the jejunum, 160 cm distal of the ligament of Treitz, and a cluster of reticulate dilated blood vessels was seen within the serosa. Postoperative histopathological examination revealed vascular hyperplasia from the mucosal lamina propria to the submucosa, hemorrhage, and fibrinous precipitation from the mucosa to the submucosa. These findings indicated a diagnosis of a small intestinal AVM (Fig. 4a and b).

The patient had a good postoperative course as the anemia quickly improved, and she was discharged on the 24th day of admission. The newborn was discharged without any complications on the 75th day of admission.

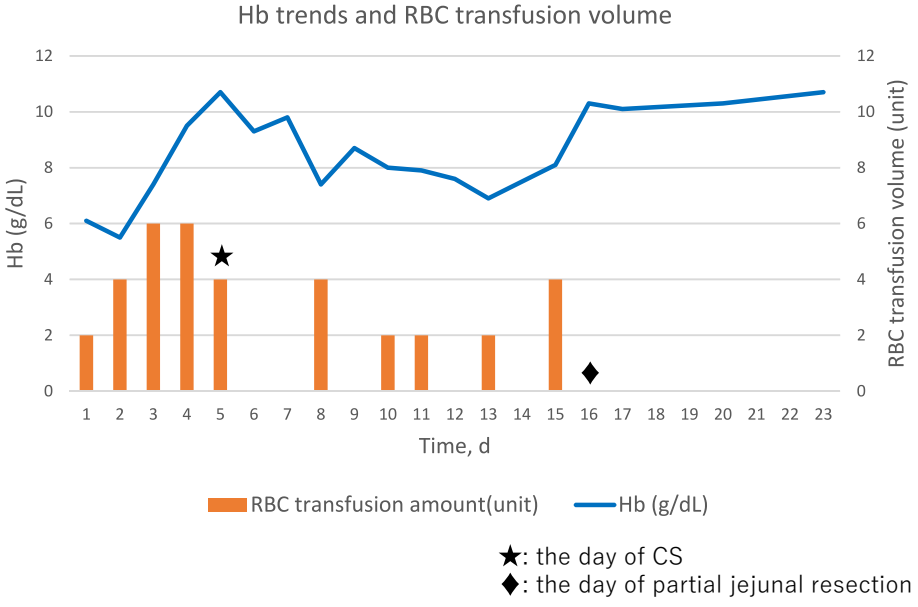

Fig. 1. Hemoglobin trend and transfusion volume after admission.
After admission, the patient received a massive blood transfusion; however, the hemoglobin levels did not improve.

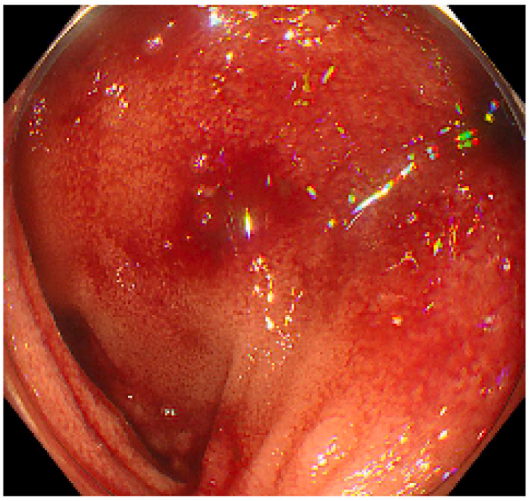

Fig. 2. Findings of small intestinal capsule endoscopy.
Small intestinal capsule endoscopy shows bleeding from the jejunum.

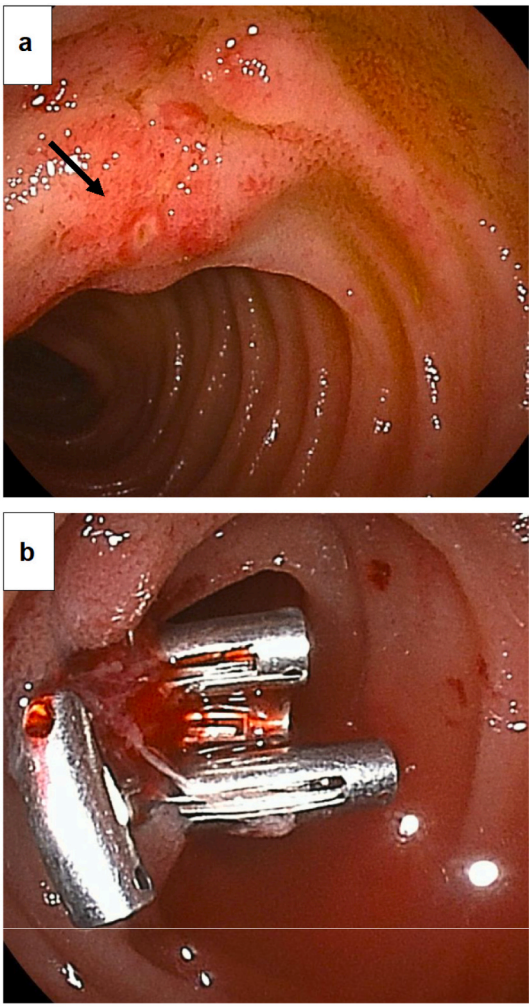

Fig. 3. Findings of small bowel endoscopy.
(a) Small bowel endoscopy shows the source of bleeding (black arrow) suspected to be an arteriovenous malformation observed approximately 200 cm distal of the ligament of Treitz.
(b) Hemostasis by clipping.

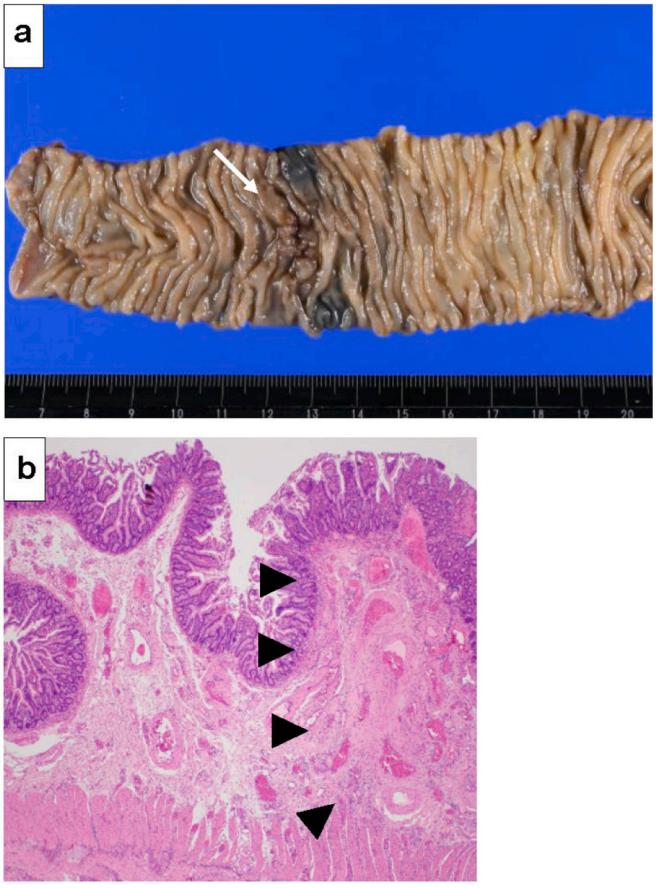

Fig. 4. Histopathological examination of the resected small bowel specimen.
(a) The resected specimen shows a circumferential granular mucosa (white arrow).
(b) Histopathological findings of the resected specimen show vascular hyperplasia from the mucosal lamina propria to the submucosa, hemorrhage, and fibrinous precipitation from the mucosa to the submucosa (black arrowheads) (H&E, ×40).

3. Discussion and Conclusions

Small intestinal bleeding from an AVM during pregnancy is extremely rare but should be included in the differential diagnosis of recurrent severe anemia during pregnancy. However, making this diagnosis is difficult. The following points can be given as reasons. First, AVM-associated small intestinal bleeding often presents with few symptoms; thus, accurate diagnosis and early treatment are challenging. The symptoms include gastrointestinal bleeding and anemia; however, bleeding is often intermittent, and cases without abdominal pain are common. Second, the diagnostic accuracies of the special investigations for this disease are low. Small bowel endoscopy and dynamic CECT are useful methods; however, the diagnostic yields of double-balloon and capsule endoscopy for unexplained gastrointestinal bleeding are 56% and 62%, respectively. Therefore, the diagnostic accuracies are not very high [5]. In addition, the longer the time interval between the bleeding episode and small intestinal endoscopy, the lower is the diagnostic yield. This indicates that lesions can resolve spontaneously and that small lesions are difficult to recognize without evidence of active bleeding [6]. In the present case, few symptoms were observed despite persistent anemia, and no other findings could explain the cause of the severe anemia. Therefore, arriving at a definitive diagnosis was difficult since the small intestinal bleeding from the AVM was not sudden, and the anemia developed gradually with the hemorrhaged blood being absorbed within the gastrointestinal tract.

To the best of the authors' knowledge, only one case of bleeding from a small intestinal AVM during pregnancy has been reported previously [3]. In that case, anemia was observed in the first trimester; however, it improved with oral iron therapy alone, and the patient did not have signs or symptoms of bleeding during the follow-up. However, in the third trimester, she presented with hematochezia and required frequent blood transfusions from 29 weeks of gestation. An emergency cesarean section was performed at 36 weeks and 6 days because of severe anemia and the mother's acute confusion caused by hyperammonemia. After the cesarean section, a jejunal AVM was diagnosed based on a computed tomographic angiogram (CTA) finding, and the lesion was managed using interventional radiology and surgery. The authors indicated that a pregnancy complicated by an AVM of the small intestine is characterized by a lack of symptoms during the pregnancy and the possibility of severe anemia after the second trimester, during which the circulating plasma volume increases and hormonal dynamics change. In addition, in both cases, a diagnosis of AVM of the small intestine was made postpartum. Capsule endoscopy, flexible fiberoptic small bowel endoscopy, and CECT are highly invasive investigations for pregnant women and carry a high burden of radiation exposure. Therefore, it is very difficult to diagnose small intestinal AVM prenatally.

In contrast, bleeding from AVMs of other organs during pregnancy is more likely to occur in the second or third trimester. For instance, hemorrhages in the brain and lungs have been reported to occur at 25 and 27 weeks, respectively [7,8]. This may be due to a marked increase in the circulating plasma volume after the second trimester of pregnancy, an increase in progesterone levels during pregnancy (which relaxes the smooth muscle of vessel walls), and an increase in estrogen levels (which promotes angiogenesis) [7]. Severe and recurrent anemia in the second or third trimester is a key sign to suspect an AVM of the small intestine in the pregnant patient.

As part of the differential diagnosis of severe anemia in pregnancy, renal anemia, leukemia, hemolysis, and bone marrow failure were ruled out, since there was no normocytic anemia with elevated reticulocyte levels and other findings were normal. Therefore, despite the lack of symptoms, the possibility of acute bleeding from the gastrointestinal tract was considered. In general, although flexible fiberoptic upper gastrointestinal endoscopy is considered relatively safe during pregnancy, the indications for other investigations are limited to cases in which bleeding is strongly suspected [9]. In this case, there were almost no gastrointestinal symptoms, and the situation did not strongly suggest gastrointestinal bleeding. Considering the adverse effects of frequent blood transfusions, such as coagulopathy, electrolyte abnormalities, and allergic reactions, and the neonatal prognosis at 31 weeks of gestation, a close examination of the bleeding was not performed until after delivery.

Small intestinal bleeding from an AVM during pregnancy is extremely rare, and its diagnosis is difficult. Small bowel hemorrhage should be included in the differential diagnosis in cases of severe anemia during pregnancy, especially after the second trimester.

Contributors

Kazuhiko Oka conceived the form and structure of this report, wrote the initial version, and revised the manuscript.

Akihiro Hasegawa conceived the form and structure of this report, wrote the initial version, and revised the manuscript.

Hayato Mikuni contributed to patient care, acquiring and interpreting the data, and revising the manuscript.

Ryosuke Miyazaki contributed to patient care, acquiring and interpreting the data, and revising the manuscript.

Tomotaka Kumamoto contributed to patient care, acquiring and interpreting the data, and revising the manuscript.

Yasuhiro Takeda contributed to patient care, acquiring and interpreting the data, and revising the manuscript.

Natsuko Ukai contributed to acquiring and interpreting the data and revising the manuscript.

Takako Kiyokawa contributed to acquiring and interpreting the data and revising the manuscript.

Osamu Samura conceived the form and structure of this report and revised the manuscript.

Aikou Okamoto conceived the form and structure of this report and revised the manuscript.

All authors approved the final submitted manuscript.

Funding

This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Patient consent

Written informed consent for publication was obtained from the patient.

Provenance and peer review

This article was not commissioned and was peer reviewed.

Acknowledgments

The authors would like to thank Editage (www.editage.jp) for English language editing.

Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

References

[1] E. Sakai, K.K. Ohata, A. Nakajima, N. Matsuhashi, Diagnosis and therapeutic strategies for small bowel vascular lesions, World J. Gastroenterol. 25 (2019) 2720–2733, https://doi.org/10.3748/wjg.v25.i22.2720.

[2] C.A. Briley Jr., D.S. Jackson, I.S. Johnsrude, S.R. Mills, Acute gastrointestinal hemorrhage of small-bowel origin, Radiology. 136 (1980) 317–319, https://doi.org/10.1148/radiology.136.2.6967614.

[3] N. Ohmiya, T. Yano, H. Yamamoto, D. Arakawa, M. Nakamura, W. Honda, et al., Diagnosis and treatment of obscure GI bleeding at double balloon endoscopy, Gastrointest. Endosc. 66 (Suppl. 3) (2007) S72–S77, https://doi.org/10.1016/j.gie.2007.05.041.

[4] H. Clarke, T. McCormack, E. Paul, J. Ford, Arteriovenous malformation as a cause for acute confusion and gastrointestinal bleeding in a primigravida pregnancy, BMJ Case Rep. 14 (2021), e239723, https://doi.org/10.1136/bcr-2020-239723.

[5] C.W. Teshima, E.J. Kuipers, S.V. van Zanten, P.B. Mensink, Double balloon enteroscopy and capsule endoscopy for obscure gastrointestinal bleeding: an updated meta-analysis, J. Gastroenterol. Hepatol. 26 (2011) 796–801, https://doi.org/10.1111/j.1440-1746.2010.06530.x.

[6] S. Shinozaki, H. Yamamoto, T. Yano, K. Sunada, T. Miyata, Y. Hayashi, et al., Long-term outcome of patients with obscure gastrointestinal bleeding investigated by double-balloon endoscopy, Clin. Gastroenterol. Hepatol. 8 (2010) 151–158, https://doi.org/10.1016/j.cgh.2009.10.023.

[7] A.S. Gershon, M.E. Faughnan, K.S. Chon, R.A. Pugash, J.A. Clark, M.J. Bohan, et al., Transcatheter embolotherapy of maternal pulmonary arteriovenous malformations during pregnancy, Chest. 119 (2001) 470–477, https://doi.org/10.1378/chest.119.2.470.

[8] J. Takahashi, K. Iihara, A. Ishii, E. Watanabe, T. Ikeda, S. Miyamoto, Pregnancy-associated intracranial hemorrhage: results of a survey of neurosurgical institutes across Japan, J. Stroke Cerebrovasc. Dis. 23 (2014) e65–e71, https://doi.org/10.1016/j.jstrokecerebrovasdis.2013.08.017.

[9] S. Nurten, Gastrointestinal endoscopy in pregnancy, World J. Gastroenterol. 20 (2014) 15241–15252, https://doi.org/10.3748/wjg.v20.i41.15241.