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【 CASE REPORT 】

Obscure Gastrointestinal Bleeding Caused by a Small Intestinal Lymphatic-venous Malformation: A Case Report with a Literature Review

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Abstract:

A 44-year-old woman presented with severe anemia. We strongly suspected gastrointestinal bleeding; however, esophagogastroduodenoscopy, colonoscopy, and computed tomography showed no bleeding sources. Video capsule endoscopy revealed an actively bleeding submucosal lesion within the jejunum. Double-balloon enteroscopy revealed a 20-mm continuously bleeding submucosal lesion in the distal jejunum. We suspected small intestinal vascular malformation and performed surgical resection. The resected specimen pathologically comprised dilated, thin-walled lymphatic channels and blood vessels involving the small intestinal submucosa. Therefore, the patient was diagnosed with small intestinal lymphatic-venous malformation. Postoperatively, the patient recovered well, and recurrence was not observed.

Key words: capsule endoscopy, enteroscopy, gastrointestinal bleeding, vascular malformation, small intestine

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Introduction

A lymphatic-venous malformation (LVM), also called a hemolymphangioma, is a vascular disease characterized by both lymphatic and venous malformations (1, 2). An LVM most commonly presents on the surface of the body (3), whereas a limited number of gastrointestinal LVMs (especially those of small intestinal LVMs) have been reported because of its low morbidity (4). Furthermore, reaching a definitive diagnosis is challenging, considering the absence of specific clinical findings.

We herein report a patient with small intestinal LVM presenting with obscure gastrointestinal bleeding along with a review of the related literature.

Case Report

A 44-year-old woman presented to her family physician with a 1-month history of general fatigue. A physical examination revealed conjunctival pallor and tarry stool. Blood tests revealed severe anemia; her hemoglobin level was 4.0 g/dL (reference range, 13.0-14.6 g/dL), and other parameters were within the near-normal range (Table 1). She received a blood transfusion and was referred to our hospital for a further evaluation.

Although gastrointestinal bleeding was suspected, neither esophagogastroduodenoscopy nor colonoscopy detected a bleeding source. Furthermore, enhanced computed tomography (CT) revealed no obvious abnormal findings. We therefore decided to perform video capsule endoscopy (VCE) to investigate the small intestine, which revealed a submucosal lesion with active bleeding detected in the jejunum

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Table 1. **Laboratory Results.**

Parameter	Result	Normal range
White blood cell count	4,300×10³/mL	3,200-8,500×10³/mL
・Neutrophils	68.5%	48.0-61.0%
・Lymphocytes	24.7%	25.0-45.0%
・Monocytes	4.9%	4.0-7.0%
・Eosinophils	1.4%	1.0-5.0%
・Basophils	0.5%	0.0-1.0%
Hemoglobin	4.0 g/dL	13.0-14.6 g/dL
Mean corpuscular volume	102.2 fL	83.0-99.0 fL
Platelet	46.1×10⁴ g/dL	13.0-34.9×10⁴ g/dL
Ferritin	8.7 ng/mL	3.6-114.0 ng/mL
Blood urea nitrogen	17.9 mg/dL	9.0-22.0 mg/dL
Creatinine	0.8 mg/dL	0.4-1.1 mg/dL
Total bilirubin	0.4 mg/dL	0.2-1.3 mg/dL
Alkaline phosphatase	111 U/L	120-340 U/L
Lactate dehydrogenase	152 U/L	110-225 U/L
Aspartate aminotransferase	20 U/L	10-35 U/L
Alanine aminotransferase	23 U/L	10-35 U/L
C-reactive protein	0.02 mg/dL	0.0-0.5 mg/dL

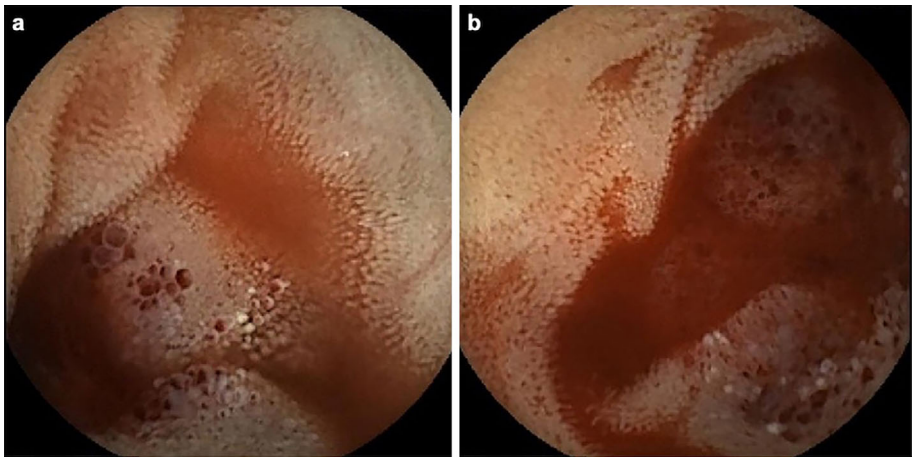

Figure 1. **Video capsule endoscopy presenting a submucosal lesion with active bleeding in the jejunum (a, b).**

(Fig. 1a, b). Double-balloon enteroscopy using an antegrade approach revealed a 20-mm submucosal lesion with dense white spots on the mucosal surface and continuous bleeding in the distal jejunum (Fig. 2a, b). Based on these findings, we considered LVM (hemolymphangioma), lymphangioma, cavernous hemangioma, and lipoma as differential diagnoses.

We marked a site proximal to the lesion by inking and clipping - without performing a biopsy because of the high risk of bleeding aggravation - and partial small bowel resection was emergently performed with a definitive diagnosis and curative intent. During operation, a reddish polypoid lesion measuring 15×15 mm was observed near the inking spot at the serosal side of the jejunum (Fig. 3a). A macroscopic finding at the mucosal side of the resected specimen revealed a soft and elastic lesion measuring 20×15 mm (Fig. 3b, arrows). The lesion pathologically comprised dilated, thin-walled vascular channels involving the small intestinal submucosa, which was a mixture of D2-40-positive lymphatic and CD31- and CD34-positive venous malformations on an immunohistochemical analysis (Fig. 4a, hematoxylin and eosin stain ×40; 4b, D2-40 stain ×40; 4c, CD31 stain ×40; 4d, CD34 stain ×40). Based on these findings, the patient was diagnosed with a small intestinal LVM, according to the International Society for the Study of Vascular Anomalies (ISSVA) classification (5). Postoperatively, the patient recovered well, and recurrence was not observed.

Discussion

An LVM is classified as a complex-combined vascular malformations according to the ISSVA classification and is

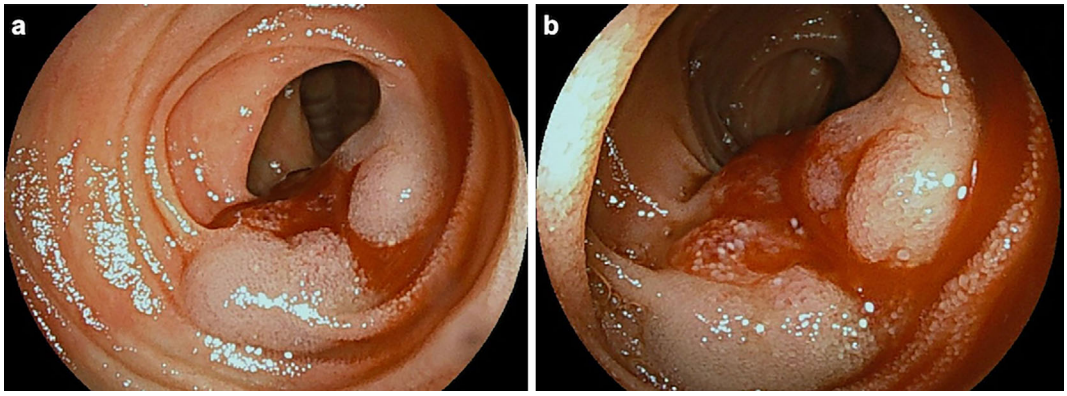

Figure 2. **Double-balloon enteroscopy using an antegrade approach presenting a 20-mm submucosal lesion with continuous bleeding in the distal jejunum (a, b).**

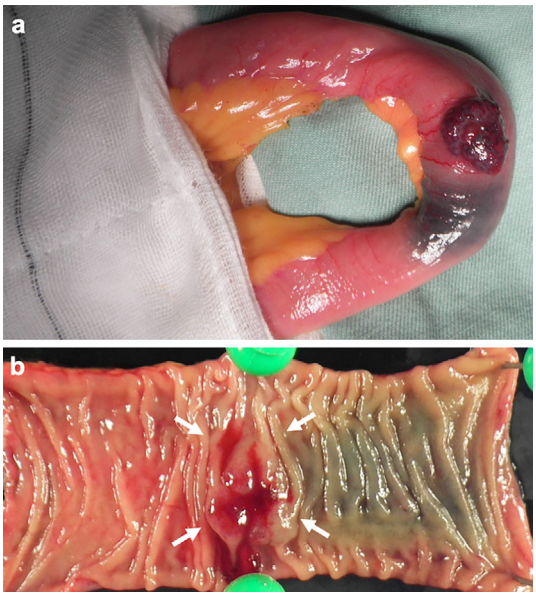

Figure 3. **Intraoperative findings revealing a reddish polypoid lesion measuring 15×15 mm near the inking spot at the serosal side of the jejunum (a). Macroscopic findings of the surgically resected specimen showing an elastic and soft lesion measuring 20×15 mm (b, arrows).**

also called hemolymphangioma. It originates from the mesenchymal tissue and is histologically composed of both lymphatic and vascular components (6, 7). LVM formation is mostly congenital, although its exact development process is yet to be ascertained. Some researchers consider LVM to be a congenital malformation of the lymphatic vascular system, whereas others think that it may be induced by lymphatic damage as a result of trauma or surgery (8, 9). In our patient, the possibility of a primary LVM was considered because the patient had no history of intestinal surgery or trauma; she may have had an asymptomatic LVM for many years and only been eventually diagnosed because of active bleeding from the lesion.

An LVM arising from the small intestine is extremely rare. To our knowledge, only 10 cases of small intestinal LVMs have been reported (Table 2) (1, 4, 10-17), with most cases occurring in women. The main symptoms at the initial diagnosis are anemia and melena, and the lesion is mainly located in the jejunum. Thus, the diagnosis is usually challenging because of its low incidence and lack of specific findings.

LVM generally presents as a solid or cystic lesion. The cystic part may develop owing to the expansion and fusion of the vascular cavity, whereas the solid part may be a residual extruded vascular tissue (18). For lesions with abundant blood vessels, enhancement can be demonstrated on CT findings, especially in the venous and delayed phases (19). However, in our case, we observed no abnormalities in the small intestine on enhanced CT. This may be due to the relatively small size of the lesion, low degree of lesion vascularization, or slow blood flow caused by vascular malformations (4). Among the 11 LVM cases presented in Table 2, enhanced CT was performed in 4 cases. Consequently, an LVM lesion could be detected in only 2 cases (sensitivity 50%).

Based on previously reported cases, VCE and enteroscopy are valuable in detecting small intestinal LVMs. Endoscopically, LVMs are often white to yellow in color and have a submucosal tumor-like morphology. The surface is smooth but may have a fine granular appearance with white spots. Larger lesions may have multiple irregular bumps and dense white spots on the lesion surface (4). Other differential diagnoses include lymphangioma, cavernous hemangioma, and lipoma. The color difference aids in distinguishing these lesions from cavernous hemangioma and lipoma, whereas differentiation from lymphangioma is difficult, as its endoscopic findings are very similar to those of LVM (20, 21).

A pathological examination is still required for a definitive diagnosis, but an endoscopic biopsy may cause or aggravate bleeding because of abundant vascular components in the lesion. Therefore, we should avoid performing an endoscopic biopsy, considering the possibility of a small intestinal LVM, as in this case. The LVMs pathologically comprised dilated, thin-walled lymphatic channels and blood vessels involving the small intestinal submucosa. Further identification is possible with immunohistochemical analyses

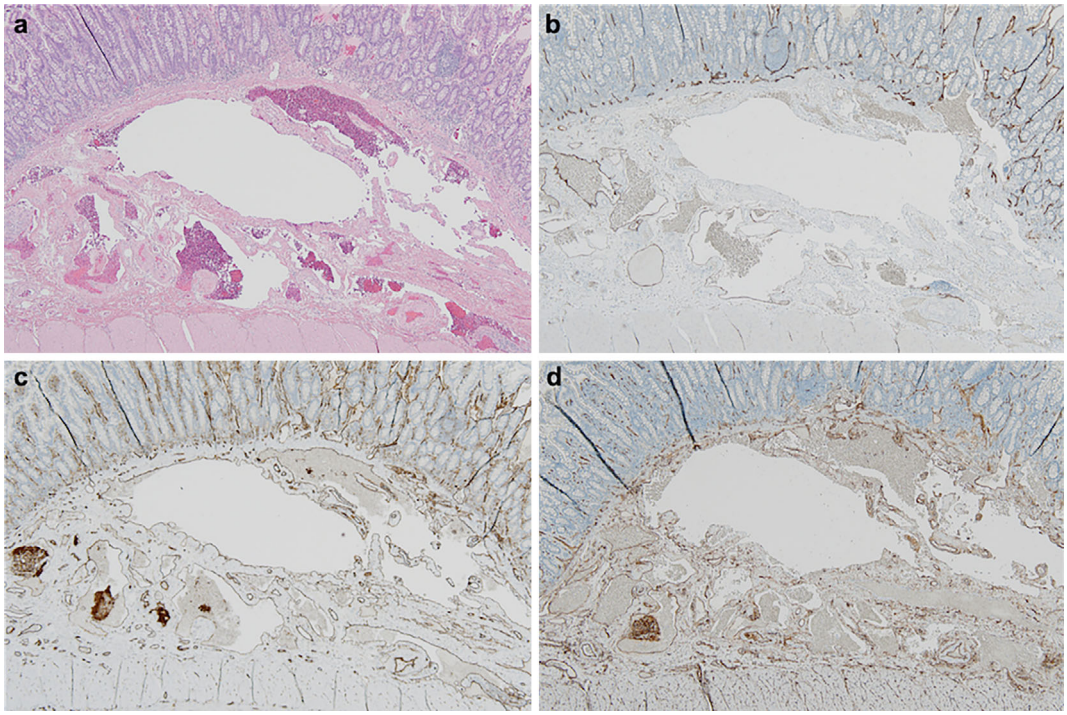

Figure 4. **A pathological examination showing dilated, thin-walled vascular channels involving the small intestinal submucosa, which are a mixture of D2-40-positive lymphatic and CD31-and CD34-positive venous malformations on immunohistochemical analysis (a, Hematoxylin and Eosin staining ×40; b, D2-40 staining ×40; c, CD31 staining ×40; d, CD34 staining ×40).**

Table 2. **Case Series of Small Intestinal Lymphatic-venous Malformation in English Literature.**

Case No.	Reference	Age, years	Sex	Clinical symptoms	Location	Tumor size	Diagnostic modality	Treatment
1	(10)	57	Female	Melena	Jejunum	50 mm	Enteroscopy	Surgical resection
2	(1)	24	Female	Anemia	Duodenum	50 mm	EGD	Surgical resection
3	(11)	43	Female	Anemia	Duodenum	40 mm	VCE, enteroscopy	Surgical resection
4	(12)	45	Female	Melena	Jejunum	80 mm	VCE, enteroscopy	Surgical resection
5	(13)	70	Male	Melena	Jejunum	20 mm	VCE, enteroscopy	Surgical resection
6	(14)	20	Female	Melena	Jejunum	100 mm	CT, enteroscopy	Surgical resection
7	(15)	42	Male	Melena	Jejunum	Not described	VCE, enteroscopy	Endoscopic injection sclerotherapy
8	(16)	55	Female	Abdominal discomfort	Jejunum	30 mm	CT, enteroscopy	Surgical resection
9	(17)	74	Female	Melena	Jejunum	6 mm	Enteroscopy	Surgical resection
10	(4)	37	Female	Melena	Ileum	65 mm	Enteroscopy	Surgical resection
11	-	44	Female	Anemia	Jejunum	20 mm	VCE, enteroscopy	Surgical resection

EGD: esophagogastroduodenoscopy, VCE: video capsule endoscopy, CT: computed tomography

in such cases; D2-40 staining is positive in lymphatic endothelial cells, while CD31 and CD34 staining is positive in vascular endothelial cells.

Both surgical and non-surgical treatments can be performed in cases with small intestinal LVM. The non-surgical treatments include cryotherapy, laser therapy, and radiother-

apy. However, these are not considered superior to surgical treatment, as their recurrence rates are relatively high (15). Thus, most previous studies reported that surgical resection was the preferred treatment option for small intestinal LVMs (Table 2). In contrast, Xiao et al. reported that jejunal hemolymphangioma with bleeding could be treated using endoscopic sclerotherapy; consequently, the lesion disappeared, and only a few white spots remained on the mucosal surface at the one-year postoperative follow-up examination by endoscopy (15). Furthermore, endoscopic injection sclerotherapy was reportedly applied to small intestinal hemangiomas without complications (22). Therefore, further studies may reveal that endoscopic sclerotherapy is acceptable as a standard treatment option for small intestinal LVMs instead of surgical resection.

In conclusion, small intestinal LVM is rare disease but can cause life-threatening gastrointestinal bleeding. Despite its low incidence, this disease should be considered when obscure gastrointestinal bleeding is observed in a patient.

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

The authors state that they have no Conflict of Interest (COI).

References

1. Antonino A, Gragnano E, Sangiuliano N, Rosato A, Maglio M, De Palma M. A very rare case of duodenal hemolymphangioma presenting with iron deficiency anemia. Int J Surg Case Rep **5**: 118-121, 2014.
2. Ahmad K, Vad H, Christensen TD. Mediastino-hepato-renal cystic lymphangiomas-diagnostic and surgical considerations. J Thorac Dis **6**: E173-E175, 2014.
3. Kosmidis I, Vlachou M, Koutroufinis A, Filiopoulos K. Hemolymphangioma of the lower extremities in children: two case reports. J Orthop Surg Res **5**: 56, 2010.
4. Yang SX, Zhou YH, Zhang J, et al. Haemorrhagic ileal haemolymphangioma: a case report and review of the literature. J Int Med Res **49**: 300060520986677, 2021.
5. Enjolras O. Classification and management of the various superficial vascular anomalies: hemangiomas and vascular malformations. J Dermatol **24**: 701-710, 1997.
6. Zhang Y, Chen XM, Sun DL, Yang C. Treatment of hemolymphangioma of the spleen by laparoscopic partial splenectomy: a case report. World J Surg Oncol **12**: 60, 2014.
7. Chen G, Cui W, Ji XQ, Du JF. Diffuse hemolymphangioma of the rectum: a report of a rare case. World J Gastroenterol **19**: 1494-1497, 2013.
8. Zhang X, Sheng X, Liu F, Jian R, Li L, Luo R. Hemolymphangioma of the chest wall: a rare case report. Oncol Lett **3**: 816-818, 2012.
9. Li Y, Pang X, Yang H, Gao C, Peng B. Hemolymphangioma of the waist: a case report and review of the literature. Oncol Lett **9**: 2629-2632, 2015.
10. Fang YF, Qiu LF, Du Y, Jiang ZN, Gao M. Small intestinal hemolymphangioma with bleeding: a case report. World J Gastroenterol **18**: 2145-2146, 2012.
11. Gómez-Galán S, Mosquera-Paz MS, Ceballos J, Cifuentes-Grillo PA, Gutiérrez-Soriano L. Duodenal hemangiolymphangioma presenting as chronic anemia: a case report. BMC Res Notes **9**: 426, 2016.
12. Blanco Velasco G, Tun Abraham A, Hernández Mondragón O, Blancas Valencia JM. Hemolymphangioma as a cause of overt obscure gastrointestinal bleeding: a case report. Rev Esp Enferm Dig **109**: 213-214, 2017.
13. Iwaya Y, Streutker CJ, Coneys JG, Marcon N. Hemangiolymphangioma of the small bowel: a rare cause of chronic anemia. Dig Liver Dis **50**: 1248, 2018.
14. Yang J, Zhang Y, Kou G, Li Y. Jejunum hemolymphangioma causing refractory anemia in a young woman. Am J Gastroenterol **115**: 810, 2020.
15. Xiao NJ, Ning SB, Li T, Li BR, Sun T. Small intestinal hemolymphangioma treated with enteroscopic injection sclerotherapy: a case report and review of literature. World J Gastroenterol **26**: 1540-1545, 2020.
16. Teng Y, Wang J, Xi Q. Jejunal hemolymphangioma: a case report. Medicine (Baltimore) **99**: e18863, 2020.
17. Ito Y, Osuga T, Kawasaki K, Ikura Y. Jejunal hemorrhage due to hemolymphangioma successfully detected and controlled by double-balloon enteroscopy. Clin Case Rep **9**: e05153, 2021.
18. Dong F, Zheng Y, Wu JJ, Fu YB, Jin K, Chao M. Hemolymphangioma: a rare differential diagnosis of cystic-solid or cystic tumors of the pancreas. World J Gastroenterol **19**: 3520-3523, 2013.
19. Mao CP, Jin YF, Yang QX, Zhang QJ, Li XH. Radiographic findings of hemolymphangioma in four patients: a case report. Oncol Lett **15**: 69-74, 2018.
20. Gaeta L, Murino A, Koukias N, et al. A rare cause of small-bowel bleeding: haemorrhagic small-bowel lymphangioma diagnosed by antegrade double-balloon enteroscopy. Endoscopy **50**: E86-E87, 2018.
21. Wu TL, Hsu HT, Yen HH. Jejunum lymphangioma: a rare case of obscure gastrointestinal bleeding with successful endoscopic therapy. Endoscopy **53**: E307-E308, 2021.
22. Igawa A, Oka S, Tanaka S, Kunihara S, Nakano M, Chayama K. Polidocanol injection therapy for small-bowel hemangioma by using double-balloon endoscopy. Gastrointest Endosc **84**: 163-167, 2016.