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Management of severe symptomatic abdominal lymphatic malformation complicated by abscess formation, protein-losing gastroenteropathy, and bleeding

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Abstract

Background: The optimal strategy for the management of patients with severe symptomatic abdominal lymphatic malformation (ALM) complicated by abscess formation, protein-losing gastroenteropathy, and bleeding has not yet been established. The present study aimed to determine an appropriate management for patients with severe symptomatic ALM, particularly for those with abdominal complications.

Materials and methods: Eight infants and young adults who underwent emergency surgery for ALM in our department, between the years 1997 and 2020, were selected for the study. We also evaluated and compared the operative procedures, operative timing, and postoperative surgical outcomes.

Results: Emergency resection was performed in all patients with bleeding. Some patients presented with ALMs that invaded the adjacent organs. Resections that included the involved organs were necessary to achieve full resolution in three patients. After evaluating the diagnostic modalities for symptomatic ALM, we also performed elective surgery for patients without bleeding.

Conclusions: Clinicians should be aware of severe symptomatic ALM with or without bleeding, as well as its associated complications, in order to select the best surgical management plan.

Keywords: Abscess formation, Bleeding, Management, Protein-losing gastroenteropathy, Severe symptomatic abdominal lymphatic malformation

Background

Lymphatic malformation is a rare benign disease that occurs mainly in pediatric patients, and approximately 80–90% of patients are diagnosed within the first few years of their life [1, 2]. Patients experiencing lymphatic malformations in the neck and axillary area are approximately 70% and 20%, respectively [3–5]. Abdominal lymphatic malformations (ALM) account for approximately 3–9.2% of all lymphatic malformations [6].

The common symptoms in patients with ALM are abdominal pain and distention. Although ALM lesions are histologically benign, they have a life-threatening potential when they increase in size and encroach upon adjacent structures [7]. Some studies have reported severe and complicated cases of ALM, where the clinical presentation included infection, rupture with hemorrhage, volvulus, intestinal obstruction, torsion, and peritonitis [8].

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As a first line of treatment for ALM patients with complications, surgical intervention, including radical surgical excision, remains the treatment of choice. Emergency surgery is required for patients with ALM in order to prevent their condition from deteriorating to an irreversible stage [8]. However, complete surgical resection of lymphatic malformations is impossible because of the nature of the lesion, which has a propensity to infiltrate tissue planes. Thus, recurrence of lymphatic malformations and nerve injury are common complications after surgical resection [9].

Studies are yet to establish the optimal strategy for the management of severe symptomatic ALM complicated by abscess formation and protein-losing gastroenteropathy (PLGE). The diagnosis with the optimum timing of intervention to sufficiently manage the deteriorated general condition, technical difficulty of complete resection, occurrence of postoperative complications, and lymphatic malformation recurrences are also yet to be established. Delayed intervention for severe symptomatic ALM may affect patients' quality of life, leading to treatment difficulties.

The present study included eight patients with severe ALM with bleeding, abscess formation, and PLGE. To the best of our knowledge, studies that have explored the available treatment options for different categories of ALM are absent. Therefore, our study aimed to determine an appropriate management plan for patients with severe symptomatic ALM, especially for those with complications, such as abscess formation, chylous ascites, and PLGE.

Materials and methods

Selection of patients

Eight infants and young adults who underwent emergency surgery for ALM in our department, between the years 1997 and 2020, were selected for the study. We retrospectively reviewed the case notes and pathological reports of the eight patients and considered the general condition requiring emergency treatment as "severe". All ALM cases in this study underwent early, delayed, or definitive surgery.

Operative procedure, assessment of operative timing, and postoperative surgical outcomes

The operative indications were abdominal pain or fever because of bleeding, abscess formation, and protein-losing gastroenteropathy without bleeding. The surgical procedure was determined based on the type of ALM, patient age, general condition, clinical course, laboratory data, and invasion into adjacent organs. We preoperatively distinguished between bleeding and non-bleeding conditions using physical findings, blood tests, and imaging tests.

In ALM patients with bleeding, definitive surgery was performed before deterioration of the general condition. In contrast, ALM without bleeding was further subdivided into two, and symptomatic ALM patients without bleeding underwent laparotomy or drainage after evaluation of the final diagnosis.

This study was approved by the institutional review board of Hokkaido University Hospital, Japan (approval number: 018–0067). All patients provided informed consent prior to study participation.

Results

Symptomatic ALM patients with bleeding

Clinical characteristics and preoperative complications

Table 1 shows preoperative clinical and biochemical characteristics at the time of referral.

Patients (five males and one female) with bleeding were 2–15 years old, with a mean age of 6.2 years, and their clinical symptoms included abdominal pain, abdominal distension, palpable mass, fever, syncope, or melena. Lymphatic malformations with bleeding occurred in the retroperitoneum, pancreas, small bowel, and transverse colon mesenteries; however, preoperative complications were not observed.

Operative management, postoperative complications, and surgical outcomes

For ALM patients with bleeding, we performed definitive surgery a day after admission, and the operative findings revealed that the ALM invaded the ileum, uncinate process of the pancreas, and jejunum. In case 1, the ALM encased the trunk of the superior mesenteric artery (SMA) and superior mesenteric vein; therefore, the ALM could not be detected. We performed complete resection in all patients with bleeding. Resection of the involved organs, such as the jejunum, ileum, ileocecum, and uncinate process of the pancreas, was necessary for the total resolution of ALM in three patients. Postoperative treatments, such as blood transfusion or cardiovascular drug support, were not required in this group, and postoperative complications in patients with bleeding were not observed. All patients survived without ALM recurrence.

Symptomatic ALM patients without bleeding

Clinical characteristics and preoperative complications

ALM without bleeding consisted of two pathophysiological categories: abscess formation and chylous ascites with PLGE, comprising one male and one female patient aged 9 and 19 years, respectively. The clinical symptoms were abdominal pain, fever, anasarca, and tetany, with a retroperitoneal origin of ALM. Preoperative complications

Table 1 Clinical characteristics, presentations, and preoperative complications in ALM patients

Patient No	Age (years)	Sex	Symptoms	Site	Size (cm)	Complications	WBC (/mm^3)	CRP (mg/dL)	Hb (g/dL)	TP/Alb (g/dL)
1	15	M	Syncope, melena, abdominal mass	Small bowel mesentery	19	Cystic bleeding	3400	0.24	6.7	6.7/-
2	6	F	RLQ pain, mass	Retroperitoneum	NA	Cystic bleeding	16,800	NA	NA	NA
3	2	M	Abdominal pain, abdominal distention	Retroperitoneum	NA	Cystic bleeding	6500	NA	NA	NA
4	6	M	Fever, abdominal pain	Small bowel mesentery	NA	Cystic bleeding	5100	1.25	11.7	6.6/3.8
5	6	M	Abdominal pain	Retroperitoneum, uncinate process of pancreas	7.5	Cystic bleeding	NA	17.2	3.7	7.6/4.8
6	2	M	Fever, abdominal pain	Transverse colon mesentry	15	Cystic bleeding	NA	22.8	10.9	6.9/3.2
7	19	F	Fever, abdominal pain, anasarca, tetany	Retroperitoneum	NA	PLGE	29,100	< 0.02	13.2	3.0/1.4
8	9	M	fever, abdominal pain	Retroperitoneum	11	abscess	17,800	42.2	10.9	6.7/-

PLGE, protein-losing gastroenteropathy; *ALM*, abdominal lymphatic malformation; *RLQ*, right lower quadrant; *NA*, not applicable

Table 1 shows the preoperative clinical and biochemical characteristics at the time of referral

included protein-losing enteropathy, chylous ascites (total protein: 3.0 mg/dL), and abscess formation.

Operative management, postoperative complications, and surgical outcomes

Table 2 shows the operative management of the patients with ALM. In case 7, a large mesenteric and retroperitoneal mass invaded the second portion of the duodenum, resulting in PLGE and chylous ascites. Initially, ALM drainage and intralesional OK-432 sclerotherapy were performed; however, this strategy was unsuccessful (Fig. 1). Subsequently, an upper gastroduodenal endoscopy revealed enteral chylous leakage in the second portion of the duodenum. We performed partial

Table 2 Operative management of ALM patients

Patient No	Age, years	Site	Invasion of adjacent organs	Multi-step surgery	Treatment	Outcome/follow-up (years)
1	15	Small bowel mesentery	Jejunum, SMA/SMV encasement	-	Resection, including resection of jejunum	Alive (18)
2	6	Retroperitoneum	None	-	Resection of lymphangioma	Alive (22)
3	2	Retroperitoneum	None	-	Resection of lymphangioma	Alive (17)
4	6	Small bowel mesentery	Ileum	-	Resection, including resection of ileum	Alive (9)
5	6	Retroperitoneum, uncinate process of pancreas	Uncinate process of pancreas	-	Resection, including resection of uncinate process of pancreas	Alive (6)
6	2	Transverse colon mesentery	None	-	Resection of lymphangioma	Alive (6)
7	19	Retroperitoneum	Duodenum	+	Abscess drainage, sclerotherapy → partial resection → lymphatic duct ligation → Denver shunt	Alive (12)
8	9	Retroperitoneum	Ileocecum	+	Abscess drainage → resection, including resection of ileocecum	Alive (9)

ALM, abdominal lymphatic malformation; *SMA*, superior mesenteric artery; *SMV*; superior mesenteric vein

Table 2 shows the operative management of patients with ALM

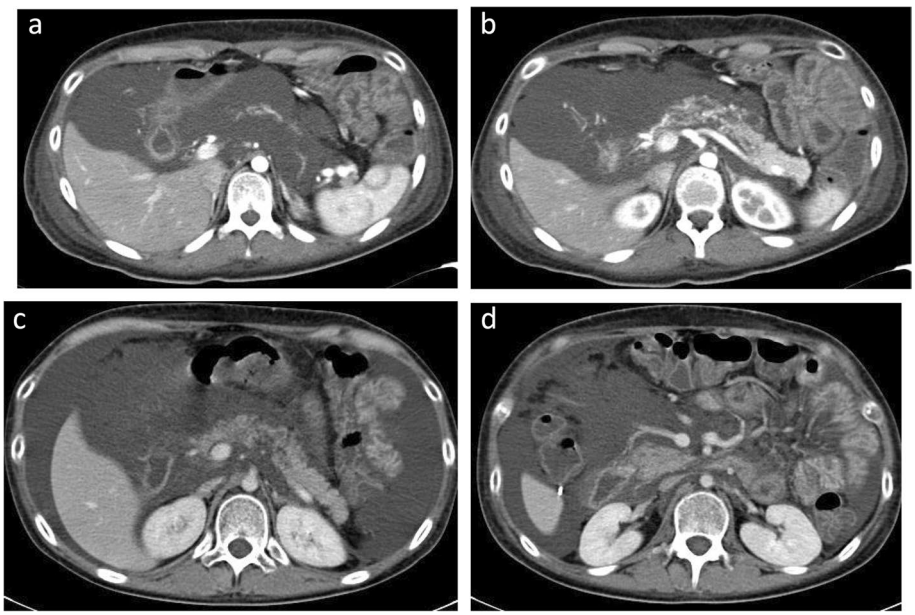

Fig. 1 Enhanced CT findings of case 7. Case 7 enhanced CT finding with chylous ascites with PLGE. **a**, **b** CT findings before intralesional sclerotherapy using OK-432. **c**, **d** CT findings after intralesional sclerotherapy using OK-432

resection of the retroperitoneal lymphatic malformation around the second portion of the duodenum as the second surgical maneuver. Consequently, a peritoneovenous shunt (Denver shunt) was implanted to control chylous ascites and hypoproteinemia, and the patient survived for 12 years. In case 8, the retroperitoneal mass infiltrated the ileocecum, and the patient presented with a high fever and elevated blood C-reactive protein levels (42.2 mg/dL). After drainage of the percutaneous abscess, his fever reduced. Subsequently, complete surgical resection of the lymphatic malformation, including the ileocecum, was performed using laparotomy. The postoperative course of both patients remained uneventful, and ALM did not recur.

Discussion

The primary treatment for ALMs is definitive surgical resection even when the patients are asymptomatic because ALMs have massive potential for growth, leading to complications such as infection and invasion to the adjacent organs [10]. In ALM patients with intestinal invasion or involvement of the main branch of the mesenteric artery or nearby organs, segmental resection of the ALM is usually a definitive surgical treatment. Recurrence is a known characteristic of ALM, but is uncommon in cases where the mesenteric artery or nearby organs are involved. Considering the surgical approaches for patients with ALM, the laparoscopic approach has been used in both adults and children [11–14]. However, complete resection is technically difficult in patients with involvement of vital organs or the SMA trunk. Alternative interventions for direct treatment of unresectable ALM include sclerotherapy, radiotherapy, and drainage. Preoperative diagnosis is currently easier with the widespread use of diagnostic modalities, such as ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI). However, obtaining an accurate preoperative diagnosis [15] is difficult, especially in patients with severe symptomatic ALM and complications. When ALM with complications presented with life-threatening manifestations, a decision regarding the requirement of emergency surgical resection was made. It is important to consider which surgery would be more advantageous to patients, either emergency resection after prompt diagnosis or elective surgery with sufficient evaluation. In this study, patients with severe symptomatic ALM who had bleeding and those with non-bleeding complications such as abscess formation and PLGE underwent emergency resection. Based on these findings, we developed an algorithm for the management of symptomatic patients with ALM, at our institute (Fig. 2).

Several studies have reported anemia with ALM [16]. Firstly, anemia because of chronic gastrointestinal blood loss is an unusual presentation in ALM, and some symptoms in patients with persistent bleeding into the lumen of intestines from the cyst lead to dyspnea, abdominal

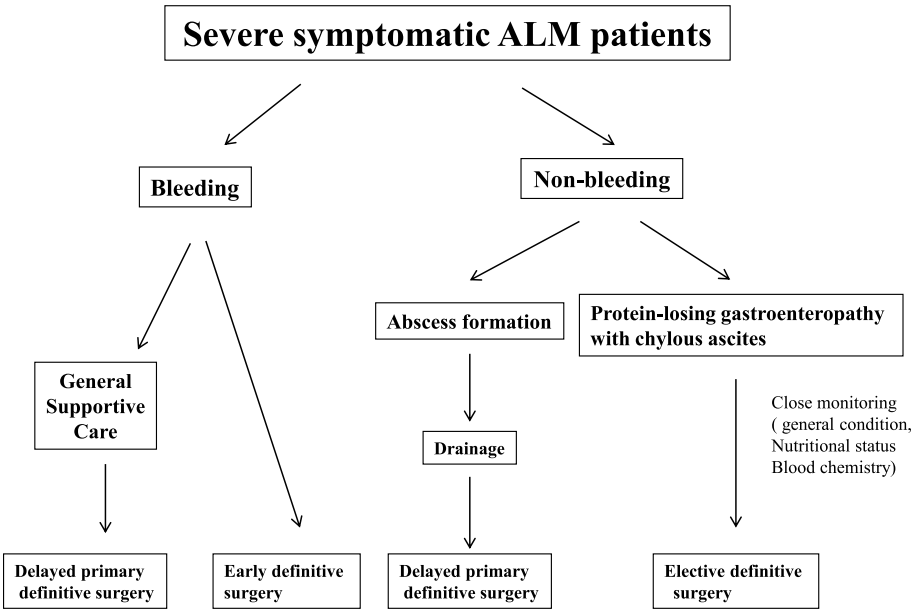

Fig. 2 Algorithm for the management of a symptomatic ALM patient at our institute. Severe symptomatic ALM patients who had bleeding underwent emergency resection, and those with non-bleeding complications such as abscess formation and PLGE with chylous ascites were scheduled for delayed primary surgery. Based on these findings, we developed an algorithm for the management of symptomatic ALM patients at our institute

pain, anemia, and melena. Secondly, bleeding into the abdominal cavity may cause acute abdomen. There are three possible explanations for ALM-related bleeding: firstly, bleeding into the lymphatic malformation due to trauma or other causes; secondly, bleeding from a veno-lymphatic communication that may be a result of erosion of the venous plexus by the proliferating endothelium; and thirdly, irritation of the surrounding mucosa caused by lymph [17]. We observed an acute abdomen in most patients with bleeding, especially in case 1. We assessed the general condition, and in patients who did not require general supportive care, we performed imaging studies. US, CT, and MRI revealed hyperintense liquid components in the bleeding lesions of the ALM. In addition to imaging studies, evaluation of the wall structure and assessment of coexisting intra- and extra-intestinal lesions are required to determine the operative procedure for symptomatic ALM. In rare instances, emergency surgical resection should be performed immediately after diagnosis to prevent life-threatening events such as hypovolemic shock in patients with massive intra-cystic bleeding [18].

Only a few studies on ALMs with abscess formation have been reported [19]. Abscesses formed in ALM because of two reasons. First, compression of the intestinal tube with enlargement of the ALM leads to infection of the lymph by partial ileus and secondary enteritis. Second, congestion and blocking of the lymph lead to impaired drainage and stasis. We performed drainage of the abscess in a patient (case 8) with a deteriorated condition for whom surgical resection was planned. Patient 8 had a high fever and deteriorated general condition. Therefore, we chose to delay the surgery. The treatment strategies (surgical procedures and timing) for an abscess are important; however, ALM infection does not always require emergency resection. Such a delay would allow for the resolution of the inflammatory adhesion [20]; however, resection of the ALM should not be overly delayed after abscess formation has been diagnosed. In this study, we performed a second-look operation after percutaneous drainage of the abscess and resolution of the general condition in case 8. This led to successful results, such as complete resection of the mass. This indicates that appropriate timing of elective resection is vital after abscess drainage based on patient recovery or preservation of the organ.

Complications such as chylous ascites, PLGE, and hypoproteinemia, as observed in case 7, are very severe and difficult to treat. The ALM widely extended around the duodenum, invading the intestinal wall and causing leakage of the lymph into the duodenum, which is referred to as PLGE. Therefore, we selected cyst drainage and intralesional sclerotherapy. Intralesional sclerotherapy is generally regarded as an adjuvant treatment for unresectable lymphatic malformation [10, 21]. It uses a sclerosing agent that irritates the endothelial lining of the lymphatic malformation. This leads to inflammation, fibrosis, and involution [22]. OK-432, in addition to bleomycin, is currently the most commonly used sclerosing agent [9]. Several studies using OK-432 as a sclerosant have shown promising results for lymphatic malformation [9, 23–25]. Success rates in cystic lymphatic malformation are 43–63% for complete regression, with approximately 84% significant lesion regression. Contrarily, a poor response rate including no change was found to be 16–23%. To the best of our knowledge, elucidation of the complications and recurrence rates in patients with ALM treated with OK-432 [7], and the combination of chylous ascites and PL, has yet not been studied. In our case, duodenal lymph fistula owing to massive retroperitoneal ALM led to PLGE. In cases of combined chylous ascites and PLGE, conservative therapies such as intake of medium-chain triglycerides and total parenteral nutrition are recommended as first-line treatments, without OK-432 sclerotherapy [2]. In cases where conservative therapy is ineffective, we recommend volume reduction of the ALM, lymph fistula or lymph duct ligation, and a subsequent Denver shunt procedure. Cochran et al. reported that total parenteral nutrition (TPN) is safe, and exploratory laparotomy, in addition to some treatments, is appropriate for ALM patients who do not improve after 1 or 2 months of TPN [26].

We performed resection of the duodenal lymph fistula during laparotomy in case 7 because conservative therapies were ineffective. It was impossible to perform definitive resection of the ALM because the chylous ascites increased and general condition deteriorated. Subsequently, the patient was administered palliative treatment with home-based medical care and a Denver shunt was implanted. Previously, palliative surgical treatment including partial ALM resection and marsupialization has been used in a patient without combined chylous ascites and PLGE [27]. Palliative treatment is usually performed for ALM patients with infection and lymphatic fistula [28].

The Denver shunt transfers fluid from the peritoneal space to the circulatory system, allowing patients to maintain critical protein and nutrient levels. Peritoneovenous Denver shunts are beneficial in both malignant and non-malignant ascites [29, 30]. In a Japanese study, peritoneovenous shunts were effective for refractory chylous ascites in childhood [31]. In our study, the tip of the Denver shunt produced a thrombus in the superior vena cava, and 3 months after the initial insertion of it, the shunt was completely obstructed. The rate of shunt occlusion has been reported to be 9–19% in Japanese

patients [32]. In our study, after re-implantation of the Denver shunt, we administered warfarin to the patient. After a prolonged hospital stay, the patient's condition improved, and she survived for 12 years at home. Therefore, we assume that the Denver shunt may be effective in ALM patients with chylous ascites and PLGE.

The number of cases in this study was too small to draw any conclusions. Further studies are required to delineate an optimal management strategy for patients with severe symptomatic ALM. Based on our experience, we propose an optimal strategy for treating severe symptomatic ALM to minimize surgical complications (Fig. 1). Madsen et al. showed the effectiveness of sclerotherapy for volume reduction and durable symptom resolution in abdominal lymphatic malformations [33]. However, in ALM patients with bleeding, surgery is a better treatment strategy than sclerotherapy. In infants and adolescents with severe symptomatic ALM with bleeding, we propose that early definitive surgery is required before the general condition deteriorates. In patients with ALM and abscess formation, the drainage procedure for the abscess should be performed under strict supervision and delayed primary definitive surgery after drainage should be performed as early as possible. Contrarily, in patients with ALM and uncontrolled bleeding, prompt and emergency surgeries are required. For patients with PLGE and chylous ascites, we should monitor closely the general condition, nutrient status, and blood chemistry. Subsequently, elective definitive surgery should be performed.

Conclusion

In conclusion, clinicians should be aware of severe symptomatic ALM with or without bleeding, as well as its associated complications, in order to select the best surgical management plan.

Abbreviations

ALM: Abdominal lymphatic malformation; PLGE: Protein-losing gastroenteropathy; SMA: Superior mesenteric artery; US: Ultrasonoraphy; CT: Computed tomography; MRI: Magnetic resonance imaging; TP: Total protein; Alb: Albumin; TPN: Total parenteral nutrition.

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Authors' contributions

S.H. and T.O. designed the study; H.M., M.A., T.K., K.O., and M.M. collected the data; H.O. wrote the manuscript; S.H. and A.T. critically reviewed the manuscript and supervised the study process. All authors have read and approved the final manuscript.

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Availability of data and materials

Available upon request.

Declarations

Ethics approval and consent to participate

This study was approved by the institutional review board of Hokkaido University Hospital, Japan (approval number: 018–0067). All patients provided informed consent prior to study participation.

Consent for publication

The author Hitoshi Ono gives consent for publication in Annals of Pediatric Surgery.

Competing interests

The authors declare no competing interests.

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