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Life-threatening complications in patients with thoracic and abdominal lymphatic malformations

V. P. Prytula [1], Y. O. Rudenko [1], O. M. Gorbatiuk [2], A. Y. Nakonechnyi [3], Y. M. Susak [1]

[1] Bogomolets National Medical University, Kyiv
[2] Shupyk National Healthcare University of Ukraine, Kyiv
[3] Danylo Halytsky Lviv National Medical University

✉ Yevgen Rudenko: erudenko500@gmail.com

V. P. Prytula, http://orcid.org/0000-0001-9023-5898
Y. O. Rudenko, http://orcid.org/0000-0002-7532-1517
O. M. Gorbatiuk, http://orcid.org/0000-0003-3970-8797
Y. A. Nakonechnyi, http://orcid.org/0000-0003-1402-6642
Y. M. Susak, http://orcid.org/0000-0002-5102-485X

The term «lymphatic malformations» (LMs) refers to a wide spectrum of disorders with clinical manifestations that can vary from asymptomatic to life-threatening.

Objective — to analyze the factors and pathological conditions that necessitate the use of emergency surgical procedures in patients with thoracic and abdominal LMs.

Materials and methods. The retrospective study of medical charts of patients with LMs was performed for a period from 2012 to 2021. Among 240 patients with LMs, 55 (22.9%) were diagnosed with lesions of the abdominal or thoracic cavity. 5 (9.1%) required an emergency surgical procedure.

Results. Among 38 patients with abdominal LMs, only one (2.6%) required emergency surgery. This patient underwent laparotomy and subtotal bowel resection for total mesenteric thrombosis. The postoperative period was complicated by short bowel syndrome. Mediastinal LMs were diagnosed in 17 patients, 14 (73.7%) of whom had neck LM extension. In 4 cases, mediastinal LMs were complicated by intrathoracic tension syndrome. It was caused by a lymphatic leak into the pleural cavity in 1 case and by sudden enlargement of LMs, resulting from intracystic hemorrhage, in 3 other cases. A pleural drain with subsequent sclerotherapy was used in a patient with chylothorax. Patients with intracystic hemorrhage underwent thoracotomy and partial LM resection. They also received an injection of a sclerosing agent into the residual cysts. In uncomplicated cases, minimally invasive methods were preferred, with laparoscopic resections of abdominal LMs in 22 (78.6%) patients and sclerotherapy under ultrasound guidance in 7 (36.8%) patients with mediastinal LMs.

Conclusions. Intrathoracic tension syndrome and thrombotic complications are potentially dangerous and life-threatening conditions that pose a risk to patients with visceral LMs and require emergency interventions. Minimally invasive technologies were preferred in uncomplicated cases of thoracic and abdominal LMs, whereas open surgeries were the method of choice in complicated cases.

Keywords
lymphatic malformations, minimally invasive surgery, conversion, lymphorrhea, coagulopathy.

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The term «lymphatic malformations» (LMs) refers to a wide spectrum of disorders with clinical manifestations that can vary from asymptomatic to life-threatening.

LMs are most frequently found in the head and neck, accounting for up to 75% of all cases [1]. Head and neck LMs result in airway compression, a dangerous complication requiring a tracheostomy, and significant cosmetic deformities [16]. According to a Japanese group of authors, up to 14% of head and neck LMs can extend to the superior and anterior mediastinum, which increases the risk of airway obstruction [1, 16]. The incidence of abdominal and thoracic LMs is up to 20% [2], with

5 % and 6 % for each type [3], respectively. In some cases, they may be asymptomatic and incidentally diagnosed during a medical examination for other reasons. In 90 % of cases, LMs are diagnosed in pediatric patients by the age of 2 years due to clinical symptoms [3], some of which require urgent medical care. Other life-threatening complications of extensive vascular malformations may be associated with coagulation disorders [4].

Objective — to analyze the factors and pathological conditions that necessitate the use of emergency surgical procedures in patients with thoracic and abdominal LMs.

Materials and methods

The medical charts of pediatric patients with abdominal and thoracic cystic LMs were retrospectively reviewed, and the cases requiring emergency surgery were revealed. A cohort of 240 patients was studied between 2012 and 2021, and of those, 17 (30.9 %) had mediastinal LMs and 38 (69.1 %) had abdominal LMs. Gender, age of onset, primary clinical symptoms and signs, visualization options, complications, treatment options, and treatment outcomes were analyzed for all patients. Since MRI is the gold standard of pretreatment visualization of LMs, we performed it for all patients before and during treatment. D-dimer and fibrinogen blood tests were mandatory before treatment. The study was conducted according to guidelines implemented in consideration of GCP-ICH and the Declaration of Helsinki. All participants' parents or guardians gave written informed consent.

Results and discussion

LMs of the abdominal cavity were diagnosed in 38 (15.8 %) patients: 22 males and 16 females. In 15 of those patients, LMs were diagnosed before the age of one year; 6 of those LMs were detected during prenatal ultrasound screening. The diagnosis of LMs was made in 16 patients before the age of 18 months, and in 10 patients after the age of 5 years. Ultrasound was used as a screening method to establish the diagnosis of abdominal LM. We used MRI to confirm the diagnosis. According to retrospective analysis data, in most cases (n = 35; 92.1 %), patients received treatment within 6—18 months after the diagnosis of abdominal LMs was confirmed. An increased D-dimer level was detected in 5 (9.1 %) patients; 3 (5.5 %) of those patients had a decreased fibrinogen level. All patients with coagulopathy received low molecular weight heparin at a dose of 100 EM/kg /day before any intervention.

Four hours after the clinical presentation, urgent surgery for acute intestinal obstruction was performed in 3 (7.9 %) cases, and the diagnosis was confirmed in one of them. Treatment options used for abdominal cystic LMs were as follows: pure laparoscopic resections (n = 22; 57.9 %), including 11 (28.9 %) transumbilical segmental resections of the affected bowel; resections via laparotomy (n = 9; 23.7 %); and mTOR inhibitors systemic therapy (n = 1; 2.6 %). In one case, emergency surgery was performed on a child with prenatally diagnosed LM. A female patient was admitted within 22 days after birth with an antenatally identified intraabdominal cystic mass. The patient was born at a gestational age of 41 weeks with a birth weight of 3100 g and a length of 51 cm. A postnatal ultrasound confirmed a large multicystic lesion occupying much of the left side of the abdominal cavity. α-Fetoprotein and β-human chorionic gonadotrophin levels were not abnormally elevated.

The diagnosis was confirmed using an MRI. Afterwards, the newborn manifested a sudden deterioration of her condition, presenting with abdominal distention, marbled skin tone, arterial hypotension (50/30 mm Hg), bilious vomiting, and anxiety. After a short period of preoperative care (nasogastric decompression and intravenous fluid therapy), a laparotomy was performed to discover complete mesenteric thrombosis. The small bowel, affected by cystic LM, presented signs of necrosis, with its mesentery involved. Laparostomy was used to terminate the initial surgery. The planned relaparotomy performed in 48 hours revealed bowel necrosis caused by mesenteric thrombosis. Subtotal small bowel resection and resection of the LM were followed by jejuno-ileoanastomosis. The newborn has about 15 cm of residual small bowel. The patient required total parenteral nutrition for a long period of time due to the development of short bowel syndrome. This postoperative complication is characterized by massive loss of fluid and electrolytes in stool, thus requiring intravenous fluids and parenteral nutrition.

Mediastinal LMs were diagnosed in 19 (7.9 %) patients, with a predominance of head and neck LMs with mediastinal expansion (n = 14; 73.7 %). Other patients had an isolated mediastinal mass (n = 3; 15.8 %) or both mediastinal and abdominal LMs (n = 2; 10.5 %). According to retrospective analysis data, 7 (36.8 %) patients underwent sclerotherapy, which had a positive clinical result. 6 patients were prescribed combined treatment, including sclerotherapy and partial surgical LM resection. 2 (10.5 %) patients were treated using mTOR inhibitors. 4 (21.1 %) patients developed intrathoracic

tension syndrome that required emergency surgery. A lymphatic leak and chylothorax were diagnosed in an 8-month-old newborn. Sudden enlargement of LMs was reported in 3 patients, who were 4, 6, and 14 months old. 4 patients manifested acute respiratory failure (distress) as the first clinical sign that required mechanical ventilation in two of them. Pleural drainage was used to treat a patient with chylothorax. A chest tube was left inside the pleural cavity for two weeks. Then the patient underwent sclerotherapy for cystic LMs. The patient recovered. The follow-up period has lasted for 5 years so far. A thoracotomy with cystic LM resection was performed in 3 other cases, with one sclerosing agent injection into the residual LM cyst. Intraoperatively, it was found that LMs with a predominance of a microcystic component had occupied the entire right hemithorax, collapsed the lower and middle lobes of the right lung, and spread through the upper aperture of the chest into the tissue spaces of the neck. Cysts of a large diameter were filled with hemorrhagic content; fresh blood with clots was detected during aspiration, which was evidence of a sudden increase in the volume of the LM due to hemorrhage into the cyst cavity. The postoperative period was uneventful for all patients, and their follow-up period ranged from 18 to 48 months. 2 patients underwent repeated sclerotherapy for cystic LMs of the neck and superior mediastinum without experiencing any signs of respiratory disorders.

LMs are congenital malformations of the lymphatic system, which have two age peaks for clinical manifestations: before the age of two years and during puberty [3]. Superficial LMs can be initially suspected during the initial examination, and the primary diagnosis can be confirmed by ultrasound. Visceral LMs are the most challenging to diagnose [3, 5], and therefore, have a higher risk of complications. Thoracic LMs can cause airway compression and impaired lymph drainage that result in chylothorax or chyloperitoneum [8]. The enlargement of LMs due to intracystic hemorrhage or infection can elevate intraabdominal or intrathoracic pressure. The two most common causes of chylothorax in children are congenital pulmonary lymphangiectasia and lymphatic malformations of the thorax [15]. Other disorders that lead to chylothorax or pleural effusions include congenital absence or atresia of the thoracic duct, x-linked myotubular myopathy, Gorham-Stout disease, and generalized lymphatic anomaly (GLA) [3].

While formerly thought to be rather benign in their clinical course, the LMs' more recently recognized association with localized intravascular coagulation (LIC) explains many of their related symptoms and complications. LIC was first described in 2008 in patients with slow-flow vascular malformations [4]. It is well-known that extensive vascular malformations are commonly associated with systemic coagulation profile abnormalities [18]. The relative slow flow within the lesion results in thrombosis through the triggering of the fibrinolytic cascade. The extent of the activation and consumption of coagulation factors is characterized by the elevation of systemic D-dimer levels and decreased fibrinogen levels. In our study, an increase in D-dimer levels was observed in 5 patients with extensive LM, whereas acute thrombotic complications occurred in 1 patient. Although coagulation studies are useful for diagnosing LIC, there are not yet any published guidelines regarding its ongoing monitoring [18].

MRI is the gold-standard visualization option to confirm the diagnosis of LM [13]. In specific cases, histology verification is required to confirm it. Lymphatic vessels have a small internal diameter, so it makes the diagnostic process challenging. The effective imaging techniques are still being optimized and developed [14]. Treatment options of choice for LMs are surgical resection or sclerotherapy [7, 9]. Target therapy is used in complicated clinical cases when surgery or sclerotherapy are ineffective or bear a high risk of potential complications [11]. In most cases, treatment is planned and it starts after the patient is fully examined. Additional hemostasis tests help determine anatomical location and structure (mecro-, microcystic, or mixed form) of LMs [1]. It is crucial to order a coagulation panel with D-dimer and fibrinogen levels for all children, considering the potential risks of local coagulopathy, thrombosis, and afibrinogenemic bleeding in the postoperative period [12]. Emergency surgeries are rare anyway. At the same time, acute distress syndrome or intrathoracic tension syndrome resulting from intracystic hemorrhage or chylothorax, as well as thromboembolic complications, are life-threatening and therefore should be considered in treatment strategy planning [13]. Acute compartment syndrome developed in a newborn with giant abdominal LM is described as an indication for an emergency surgical procedure [6]. Abdominal LMs can also be complicated by obturation, intestinal obstruction, intestinal volvulus, constipation, and impaired urinary elimination [9]. Despite the fact that coagulation disorders are common in patients with vascular anomalies, we have not found any available research on acute mesenteric thrombosis as a complication of abdominal LMs. The low speed of blood flow in slow-flow vascular malformations can result in local intravascular coagulopathy that

is manifested by a high D-dimer level, a low thrombocyte count, and/or thrombocytopenia [11].

Minimally invasive methods are preferred for the treatment of uncomplicated LMs, in particular laparoscopic resections [5, 10], which were performed on 57.9 % of patients with abdominal LMs, and sclerotherapy under ultrasound or laparoscopic guidance, which was used in 36.8 % of patients with thoracic LMs. Multidisciplinary team care, minimally invasive techniques, and modern target technologies for patient examination must become an integral part of successful management of patients with LMs [17].

Critical and life-threatening complications require more aggressive surgical tactics, in particular laparotomy or thoracotomy. Despite the use of a sclerosant for sclerotherapy, swelling and enlargement of LMs are observed in the postoperative period [5, 6, 9]. Scleropathy may be dangerous when used in patients with intrathoracic tension syndrome due to the side effects of the sclerotic agents. A thoracotomy was preferred in such cases.

Conclusions

Intrathoracic tension syndrome resulting from intracystic hemorrhage or lymphatic leak (chylothorax) is a critical complication of mediastinal cystic LMs that requires emergency surgery.

Mesenteric and intestinal cystic LMs have the potential to cause total mesenteric thrombosis with subsequent short bowel syndrome.

The highest risk of complications is observed during the first year of life.

Considering the risk of potential critical life-threatening complications, the presence of both mediastinal and abdominal cystic LMs in one patient requires advanced attention and active treatment tactics with a minimal observation period.

Declaration of interests

The authors declare that they have no conflicts of interest.

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Authors contributions

V. P. Prytula: the conception and design of the study; the analysis of clinical data; Y. O. Rudenko: interpretation and statistical analysis of clinical data and literature review; O. M. Gorbatiuk: data collection and analysis; critical revision of the manuscript; A. Y. Nakonechnyi: the design of the study, a literature review, and data analysis; Y. M. Susak: drafting and critical revision of the manuscript.

All authors have read and approved the final version of the manuscript.

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Критичні хірургічні ускладнення у пацієнтів з лімфатичними мальформаціями грудної та черевної порожнини

В. П. Притула [1], Є. О. Руденко [1], О. М. Горбатюк [2], А. Й. Наконечний [3], Я. М. Сусак [1]

[1] Національний медичний університет імені О. О. Богомольця, Київ

[2] Національний університет охорони здоров'я України імені П. Л. Шупика, Київ

[3] Львівський національний медичний університет імені Данила Галицького

Лімфатичні мальформації (ЛМ) — це широкий спектр захворювань, перебіг яких варіює від безсимтомного до стану, який загрожує життю пацієнта.

Мета — проаналізувати чинники, що спричинили потребу в ургентному оперативному втручанні у пацієнтів з ЛМ грудної та черевної порожнини.

Матеріали та методи. Проведено ретроспективний аналіз історій хвороби пацієнтів з ЛМ, які перебували на лікуванні у 2012—2021 рр. Із 240 пацієнтів з ЛМ ураження грудної та черевної порожнини діагностовано у 55 (22,9 %). Потребували термінового оперативного втручання 5 (9,1 %) пацієнтів.

Результати. Із 38 пацієнтів з ЛМ черевної порожнини потреба в ургентному хірургічному втручанні виникла лише в одного. Оперативне лікування в обсязі лапаротомії та субтотальної резекції тонкої кишки проведено з приводу тотального тромбозу мезентеріальних судин. Перебіг післяопераційного періоду ускладнився розвитком синдрому тонкої кишки. Лімфатичні мальформації медіастинальної локалізації виявлено у 19 пацієнтів, з них у 14 (73,7 %) вони супроводжувалися ураженням шийної ділянки. Медіастинальні ЛМ ускладнилися синдромом внутрішньогрудного напруження у 4 пацієнтів, причиною якого в одному випадку було витікання лімфи в плевральну порожнину, у решті — раптове збільшення розмірів ЛМ на тлі крововиливу в порожнину кісти. Для купування хілотораксу проведено дренування плевральної порожнини з наступним склерозуванням ЛМ. У пацієнтів з крововиливом у порожнину кісти виконано торакотомію, часткове видалення ЛМ та введення склерозанта в резидуальні кісти. У неускладнених випадках перебігу ЛМ перевагу віддавали малоінвазивним методам лікування, зокрема лапароскопічному видаленню абдомінальних ЛМ (у 22 (78,6 %) випадках) і склерозуванню медіастинальних ЛМ під ультразвуковим контролем (у 7 (36,8 %)).

Висновки. Синдром внутрішньогрудного напруження та тромботичні ускладнення є потенційно небезпечними ускладненнями ЛМ вісцеральних порожнин, що потребують невідкладного хірургічного втручання. Для лікування неускладнених форм ЛМ грудної та черевної порожнини перевагу віддавали малоінвазивним технологіям, в ускладнених випадках проводили відкриті хірургічні втручання.

Ключові слова: лімфатичні мальформації, малоінвазивна хірургія, конверсія, лімфорея, коагулопатія.

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