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Original Article

Lymphocele: a clinical analysis of 19 cases

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Abstract: Purpose: To summarize the clinical manifestations, diagnosis, and treatment of lymphocele. Materials and methods: 19 cases of lymphocele diagnosed by postoperative pathology from January 2003 to September 2012 were retrospectively analyzed, especially the general information, clinical manifestations, imaging, operations, and pathological findings. Results: In 19 cases, the common locations were in retroperitoneal, abdominal wall, and neck. There were no typical clinical manifestations with lymphocele. 6 cases visited hospital because of pain, while 13 cases were diagnosed incidentally with imaging or surgery. Fourteen cases undergoing CT were all displayed as cystic lesion. In 12 of 14 cases undergoing type-B ultrasonic, the masses were shown to be cystic lesion without special signs. 19 cases were all treated by surgical resection, and testified to be lymphocele with pathological analysis. The sensitivity of D2-40 was 89.5% (17/19) in our study. Conclusions: Lymphocele is very rare with no specific clinical manifestations. The preoperative diagnosis was based on imaging examinations, while definite diagnosis was based on the pathological, and (or) immunohistochemical examination with D2-40. The prognosis of lymphocele is good after it is removed completely.

Keywords: Lymphocele, cystic lymphangioma, clinical analysis, lymphatic cyst

Introduction

Lymphocele, also known as cystic lymphangioma, is a rare disease, and mainly reported in some case reports. There are no typical clinical manifestations, and most patients were diagnosed incidentally with imaging or surgery. Therefore, diagnosis is challenging. Surgical resection is still considered as the most effective approach for lymphocele, and prognosis is favorable. 19 cases of lymphocele in our hospital from January 2003 to September 2012 were summarized retrospectively. Basic information, clinical, and radiologic imaging, diagnosis, management, and follow-up of these patients were described.

Material and methods

We reviewed all cases from files of the department of pathology in the period from January 2003 to September 2012 and identified 19 cysts as lymphoceles. This study was approved by IRB of Drum Tower Clinical Medical College of Nanjing Medical University. The informed consent for participation in the study was obtained from participants. We then reviewed the clinical and radiologic data, treatment, and pathological findings of these cysts. Age and gender of patients, cyst location, and clinical symptoms at presentation were recorded (**Table 1**). 11 of 19 patients had no previous local trauma or surgery and unremarkable medical history, while 8 patients underwent operations (**Table 1**).

We reviewed the findings of the different imaging techniques, including computed tomography (CT, n=14), type-B ultrasonic (n=14), magnetic resonance imaging (MRI, n=1). Type-B ultrasonic, CT, and MRI imaging findings were evaluated with respect to cyst margins, echogenicity, density or signal intensity, contrast enhancement. Histopathological examination

Table 1. Clinical characteristics of 19 patients with lymphoceles sort by gender and age

Patient	Gender	Age (year)	Location	Clinical symptoms	Operation history
N1	Female	14	The gap between spleen and pancreas	pain	None
N2	Female	18	Abdominal wall	None, discovered in imaging examination	None
N3	Female	30	Adrenal gland	None, discovered in physical examination	None
N4	Female	38	Abdominal wall	None, discovered in physical examination	Cesarean section
N5	Female	40	Uterine round ligament	None, discovered intraoperative	Cesarean section
N6	Female	45	Kidney	Pain	None
N7	Female	47	Retroperitoneal	None, discovered intraoperative	Cesarean section
N8	Female	57	Pancreatic tail	Pain	Bilateral mastectomy
N9	Female	57	Gastric curvature	None, discovered intraoperative	None
N10	Female	58	Retroperitoneal	Pain	None
N11	Female	61	Ovarian	None, discovered in physical examination	Resection of uterine myoma
N12	Male	22	Submandibular gland	None, discovered in imaging examination	Septoplasty orthotics through nasal endoscopy
N13	Male	35	Mesentery of small intestine	Pain	Cholecystectomy
N14	Male	38	Penis	None, discovered in physical examination	Resection of hepatocellular carcinoma
N15	Male	46	Neck	None, discovered in imaging examination	None
N16	Male	48	Neck	None, discovered in physical examination	None
N17	Male	52	Hepatic portal	None, discovered in imaging examination	None
N18	Male	59	Maxillary sinus	Pain	None
N19	Male	66	Retroperitoneal	None, discovered intraoperative	None

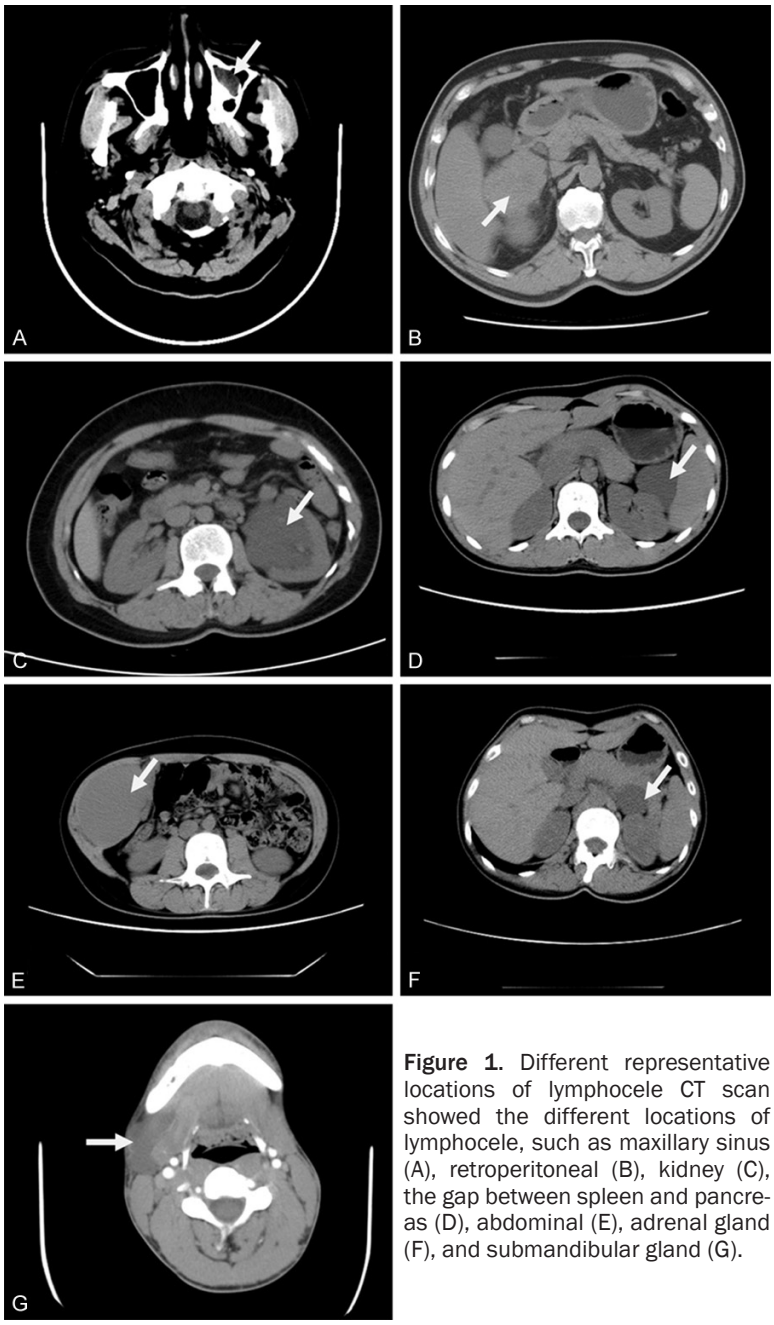

Figure 1. Different representative locations of lymphocele CT scan showed the different locations of lymphocele, such as maxillary sinus (A), retroperitoneal (B), kidney (C), the gap between spleen and pancreas (D), abdominal (E), adrenal gland (F), and submandibular gland (G).

of surgical specimens was carried out using standard hematoxylin and eosin staining (HE), as well as special immunohistochemical techniques. Immunohistochemical staining was performed using a Dako EnVision System according to the manufacturers instruction, with primary antibodies including D2-40, CD10, CD34, CK, CD31, CR, and HBME1. Diaminobenzidine was used as the chromogen. Treatment of these lymphoceles, patient management, and follow-up of patients were also recorded.

Results

Patients and lymphoceles

There were 19 patients with histologically proved lymphoceles (8 men and 11 women, age ranging from 14 to 66 years, with mean age 46 years). Tumors ranged from 0.3 to 20 cm. The common location was retroperitoneal (n=3), abdominal wall (n=2), and neck (n=2) (**Table 1**; **Figure 1**). The lymphocele in 11 patients without operation history was considered to be congenital. Three patients undergoing cesarean had lymphocele in uterine round ligament, retroperitoneal, or abdominal wall, which meant the lymphocele may be related with cesarean. However, the lymphocele in other patients was not relevant with operation because the location is quite different from the surgical sites.

All cases were diagnosed as lymphocele through postoperative pathologic and (or) immunohistochemical examination. Symptoms were related to location or size of cyst. 13 of 19 cases had no symptom and discovered incidentally in physical examination (n=9) or intraoperative exploration (n=4), while 6 cases presented with pain.

Imaging characteristics: well-defined, homogeneous low density without enhancing

CT is the most frequent imaging technique performed for studying these cysts. CT images were available in 14 of 19 patients. Of these, 2 patients had the cyst originating in retroperitoneal, 2 in abdominal wall, 2 in neck, 1 in pancreatic tail, 1 in hepatic portal, 1 in maxillary sinus, 1 in mesentery of small intestine, 1 in kidney, 1 in submandibular gland, 1 in adrenal gland, and 1 in the gap between spleen and

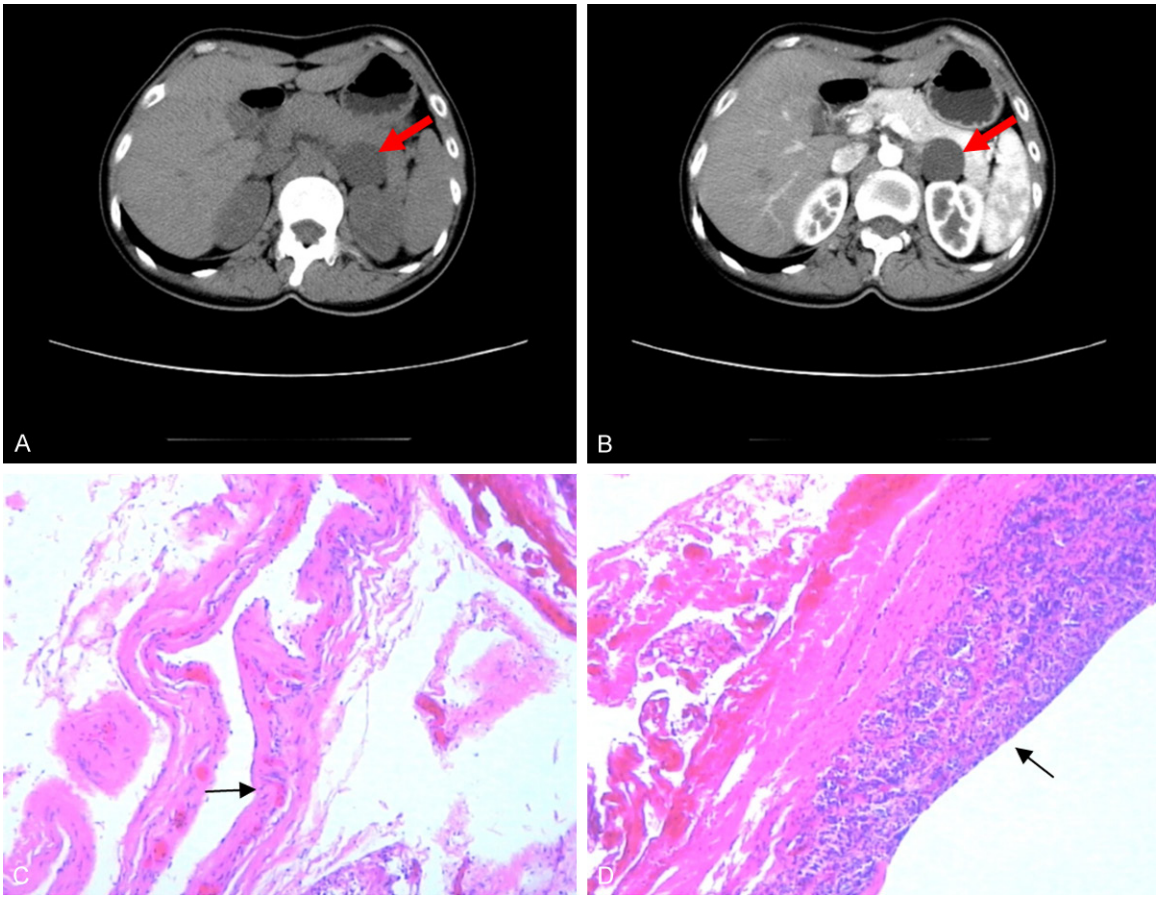

Figure 2. A 30-year-old female with an abdominal mass discovered in physical examination and proved to be lymphocele of adrenal gland. Masses were presented as well-defined, homogeneous low density (A), and no enhancement after iodinated contrast administration (B). The representative H.E. images were showed under 40 (C) and 100 (D) folds.

pancreas. Some representative images were shown (**Figure 1**). In all 14 images (100%) tissue masses were presented as well-defined, homogeneous low density and no enhancement after iodinated contrast administration (**Figure 2**). 14 of 19 patients underwent type-B ultrasonic scan. In 12 patients (85.7%) cystic lesions were showed. In 12 cases, 10 cases (83.3%) were with echo-free, clear and irregular nodules while 2 cases (16.7%) were with hypoechoic, clear and irregular nodules (**Figure 3**). MRI was performed in only one patient who presented pancreatic tail lymphocele and showed with abnormal signal shadow.

Patient management, pathology, and follow-up

All cases underwent surgical resection with no serious complications and postoperative mortality was nil. Resections included incidentally resection with other operations in 4 cases, open surgery in 9 cases, and laparoscopic surgery in 6 cases. All cases were clearly diagnosed as lymphocele through postoperative pathologic examination (**Figure 2**) or immunohistochemical examination. The immunohistochemical findings were summarized. D2-40 is a specific marker for lymphatic endothelial cell differentiation, with a positive rate of 89.5% (17/19) in our study. Some other markers were also tested for differential diagnosis, such as CD10, CD34, CK, CD31, HBME1, and CR. Their positive rate is 5.3% (1/19), 42.1% (8/19), 0 (0/19), 26.3% (5/19), 10.5% (2/19), 15.8% (3/19) respectively. The representative immunohistochemical pictures of the patient with abdominal lymphocele were shown in **Figure 4**. The mean follow-up period ranged from 6 to 60 months in 19 patients. All patients reviewed type-B ultrasonic and CT every 3-6 months and remained alive and disease free.

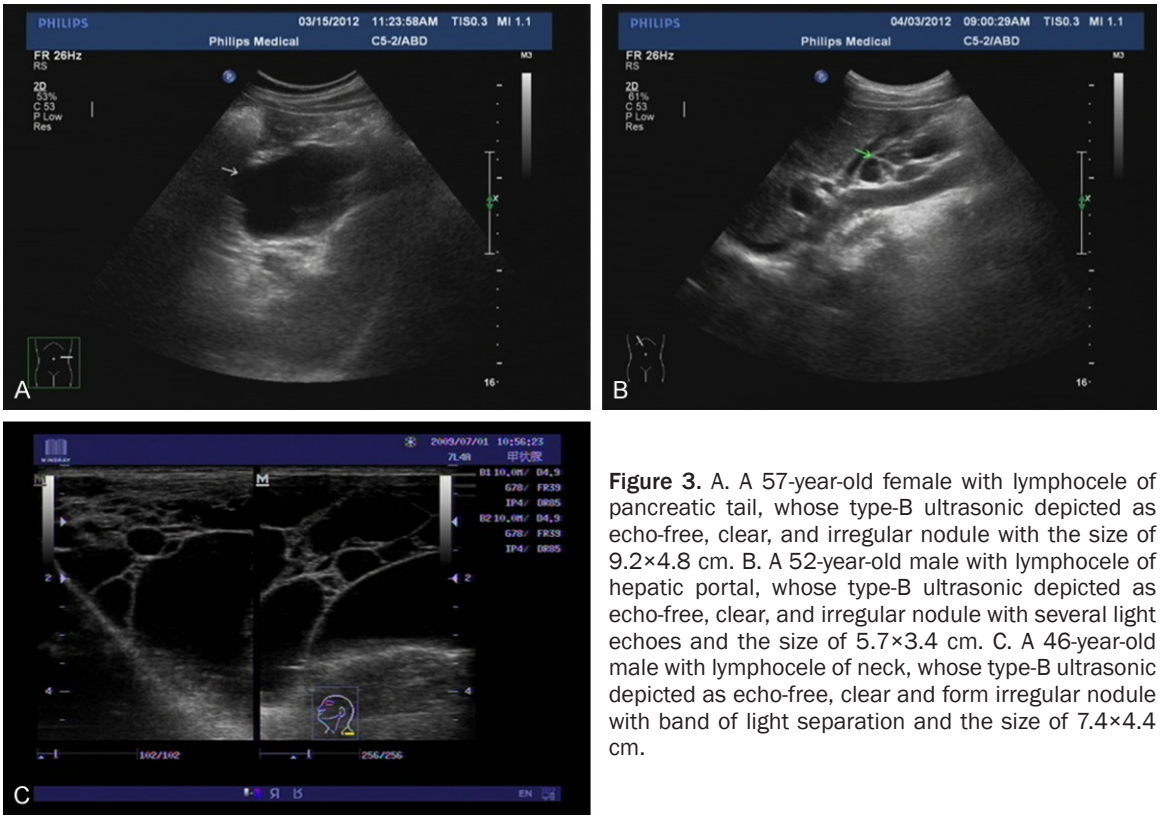

Figure 3. A. A 57-year-old female with lymphocele of pancreatic tail, whose type-B ultrasonic depicted as echo-free, clear, and irregular nodule with the size of 9.2×4.8 cm. B. A 52-year-old male with lymphocele of hepatic portal, whose type-B ultrasonic depicted as echo-free, clear, and irregular nodule with several light echoes and the size of 5.7×3.4 cm. C. A 46-year-old male with lymphocele of neck, whose type-B ultrasonic depicted as echo-free, clear and form irregular nodule with band of light separation and the size of 7.4×4.4 cm.

Discussion

Lymphocele, also known as cystic lymphangioma, is a congenital benign hamartoma. In the embryonic period, mesoderm fissures of the venous plexus fuse and form large primitive lymph sacs, draining into the central venous system. Later, lymph sacs gradually degrade or develop into the venous system in parallel with the lymphatic system. If the primitive lymph sacs do not connect with venous system, then the lymphocele emerges. Besides, lymphocele can also be caused by lymphatic injury usually secondary to lymphadenectomy in surgery [1-3]. In our study, 11cases were regarded as congenital lymphocele. 8 cases (42.1%) had surgery history, of which, 3 cases occurred in the original surgery sites, suggesting surgery was considered as the underlying aetiology. It is worth noting that pelvic surgery is easy to be complicated by lymphocele. Lymphocele, which is a very rare cystic mass and occurs at any age, especially younger age, is often present in neck (75%), axilla (20%), mediastinum (1%), subdiaphragmatic and so on [4, 5], as well as in some rare parts, such as omentum majus, retroperitoneal, mesenterium, back, lesser omentum, aorta abdominalis and so on. We reviewed the clinical, radiologic, treatment and pathology data from 19 cases of these cysts that were diagnosed at our hospital from January 2003 to September 2012. In our series of patients, the common locations are retroperitoneal, abdominal wall, and neck. Rare locations such as hepatic portal, submandibular gland, maxillary sinus, ovarian, adrenal gland, gastric curvature, pancreatic tail, penis, or uterine round ligament have not been reported.

The symptoms associated with lymphocele are usually vague and nonspecific [6-8]. The nonspecificity of the symptoms is a contributing factor in delayed diagnosis associated with lymphocele. Oppression and pain may appear due to the growth of the cyst. Because most lymphoceles are incidental findings and others present with nonspecific clinical symptoms, there is no standard diagnostic protocol. Most patients are diagnosed incidentally in physical examination or intraoperative and a small number of patients see a doctor present with nonspecific symptoms such as pain, discomfort and oppression. In our series, 13 of 19 cases had no symptom and discovered in physical

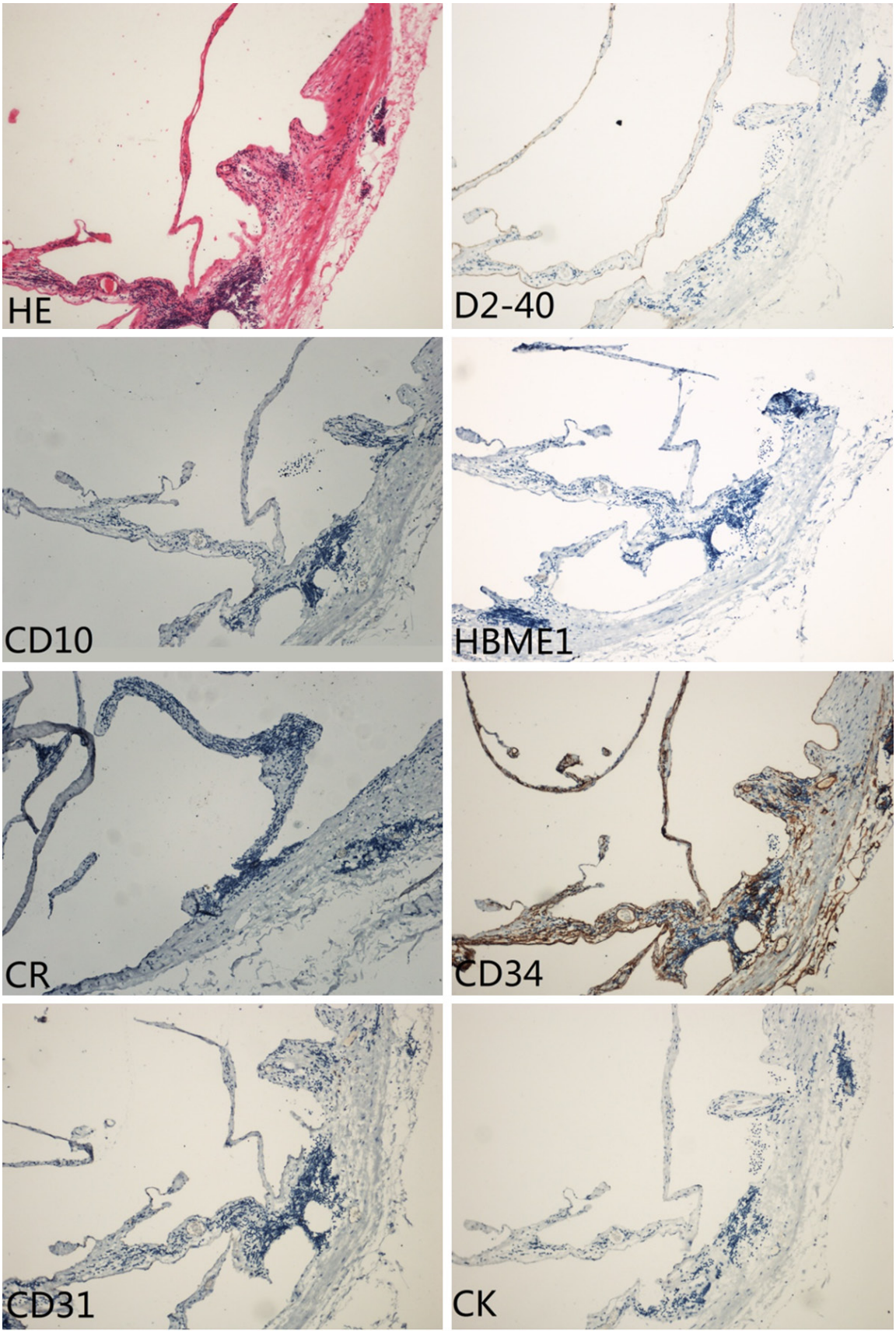

Figure 4. The representative immunohistochemical imaging was presented with HE, D2-40 (+), CD10 (-), HBME1 (-), CR (-), CD34 (+), CD31 (-), CK (-).

Table 2. Immunohistochemical phenotype of the 19 cases

Patient	D2-40	CD10	CD34	CK	CD31	HBME1	CR
Lymphocele in the gap between spleen and Pancreas (N1)	(+)	(+)	(+)	(-)	(+)	(-)	(-)
Abdominal lymphocele (N2)	(+)	(-)	(-)	(-)	(-)	(-)	(-)
Adrenal lymphocele (N3)	(+)	(-)	(+)	(-)	(+)	(-)	(-)
Abdominal lymphocele (N4)	(+)	(-)	(+)	(-)	(-)	(-)	(-)
Uterine round ligament lymphocele (N5)	(+)	(-)	(-)	(-)	(-)	(+)	(+)
Kidney lymphocele (N6)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
Retroperitoneal lymphocele (N7)	(+)	(-)	(-)	(-)	(-)	(-)	(-)
Pancreatic tail lymphocele (N8)	(+)	(-)	(-)	(-)	(-)	(-)	(-)
Gastric curvature lymphocele (N9)	(+)	(-)	(+)	(-)	(+)	(-)	(-)
Retroperitoneal lymphocele (N10)	(+)	(-)	(+)	(-)	(+)	(-)	(-)
Ovarian lymphocele (N11)	(+)	(-)	(+)	(-)	(-)	(+)	(-)
Submandibular gland lymphocele (N12)	(+)	(-)	(-)	(-)	(-)	(-)	(-)
Mesentery of small intestine lymphocele (N13)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
Penis lymphocele (N14)	(+)	(-)	(+)	(-)	(-)	(-)	(-)
Neck lymphocele (N15)	(+)	(-)	(-)	(-)	(+)	(-)	(-)
Neck lymphocele (N16)	(+)	(-)	(-)	(-)	(-)	(-)	(+)
Hepatic portal lymphocele (N17)	(+)	(-)	(+)	(-)	(-)	(-)	(-)
Maxillary sinus lymphocele (N18)	(+)	(-)	(-)	(-)	(-)	(-)	(-)
Retroperitoneal lymphocele (N19)	(+)	(-)	(-)	(-)	(-)	(-)	(+)

examination (n=9, 47.4%) or intraoperative (n=4, 21.1%), while 6 cases (31.2%) presented with pain. Preoperative diagnosis based on clinical data is difficult because the patients were without specific presentation. However, by analysis of the utility of the frequently ordered diagnostic studies that were performed before surgical exploration, CT, type-B ultrasonic, and MRI can contribute to preoperative diagnosis [2, 6, 9-11]. On CT studies these cysts are normally seen as well-defined, round or oval and density uniformity cystic masses and no enhancement after iodinated contrast administration, sometimes, pouch wall can be enhanced mildly as minor hairline. In our series, 14 cases who made CT examination and all (100%) were seen as tissue masses well-defined, homogeneous low density and without enhancement after iodinated contrast administration. On type-B ultrasonic studies these cysts are normally depicted as cyst with no echoes and Doppler signals inside. Doppler signals are sometimes detected in pouch wall and separation. High-frequency color Doppler ultrasonography can definite cyst size, spot, and proximity relation with a high sensitivity. In our series, type-B ultrasonic were performed in 14 patients and lesions were discovered in 12 cases (85.7%, 12/14) depicted as echo-free, clear and form irregular nodules in 10 cases and hypoechoic, clear, and form irregular nodules in 2 cases, 4 cases with band of light separation. Therefore, CT is more sensitive to detect lesion than type-B ultrasonic. The MRI features of lymphocele are described as well-defined, round or oval and density uniformity cystic masses and long signal intensity on T1 and T2-weighted images. In our series, just 1 patient accepted MRI examination, characterized by clear, uniform density of abnormal signal shadow. Han et al [12] reported that lymphocele could get a good demonstration by lymphoscintigraphy SPECT/CT, but this technology was expensive.

It is difficult to diagnose these cysts before operation, because they are lack of specific clinical manifestations and low in morbidity. Despite imagine examination can help in the diagnosis and fine needle aspiration biopsy can improve the diagnosis accuracy [13], it has to rely on pathological and immunohistochemical examination to diagnose definitely. In our series, all cases were diagnosed through the postoperative pathologic and immunohistochemical examination summarized in **Table 2**. D2-40 is a specific marker for lymphatic endothelial cell differentiation [14, 15], with a positive rate of 89.5% in our study.

Surgery has been the mainstay of therapy for lymphocele to prevent the cyst to carry on the nature to increase to have the oppression symptom or prevent infection due to cyst rupture [16]. Laparoscopic management is safe, feasible, and effective option for lymphocele [17, 18]. Karcaaltincaba et al [1] proposed that percutaneous methods with emphasis on percutaneous techniques particularly in conjunction with sclerotherapy could be considered as the first-line treatment modality for lymphoceles due to its effectiveness, ease of procedure, and low complication, especially for infected lymphoceles. Choudhrie et al [19] also proposed that the first step in the management of symptomatic lymphocele should be percutaneous drainage, which can optimize patients who may require surgery, besides, laparoscopic marsupialization offers superior definitive treatment of lymphoceles with the least recurrence rates. As a result, it is critical to diagnose lymphocele before therapies. Todokoro et al [20] reported that lymphaticovenular anastomosis (LVA) should be considered as a therapy for lymphocele because of its low invasiveness and its effectiveness in re-establishing circulation of lymphatic flow. However, further studies should be performed to assess and compare theses treatments. The 19 patients in our study all underwent surgical resection with 4 cases of incidentally resection in other operation, 9 cases of excision by open surgery, and 6 cases of excision by laparoscopic surgery. Laparoscopic surgery is the best treatment for lymphocele in abdominal and pelvic cavity.

Lymphatic cyst is a benign disease and complete resection can get a good curative effect [17, 21]. It may recurrence if removed incompletely, but it will not become malignant generally. Up to now, all cases in our study accompanied by good prognosis without recurrence.

Prevention of lymphocele is also important. It is necessary to accurately follow-up the patient who has undergone an operation at risk for the appearance of lymphatic complications and, even better, to assess clinically and by lymphoscintigraphy the patient before surgical operation [22]. And all tissues close to vessels must be ligated to prevent lymphocele. Gauthier et al [23] proposed that medical methods such as somatostatin analogs and nutrition treatment which could prevent lymphoceles formation after pelvic and lumboaortic lymphad enectomy.

In conclusion, lymphocele is a rare disease with no specific clinical manifestations. CT, type-B ultrasonic, and MRI play an important role in the diagnosis for lymphocele, while, pathological examination is the gold standard diagnostic tool. Surgery has been the mainstay of therapy for lymphocele and prognosis is favorable if removed completely.

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Disclosure of conflict of interest

None.

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