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ORIGINAL ARTICLE

A Pictorial Review of Lymphocele Treatment: How to Choose the Best Option

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Abstract

Lymphocele represents a quite frequent complication of surgical treatments that involve kidneys, lymphadenectomy, and pelvic organs. It can also arise after pelvic trauma, or due to infectious diseases. Aim of this review is to give a pictorial evaluation on current epidemiology, pathophysiology, clinical presentation, diagnosis of lymphocele, with particular attention to possible treatments, considering the standard management, but also the new available alternatives, which arose in the last years. All studies were identified by searching from electronic databases of PubMed. We used the following keywords to search the database: lymphocele, symptoms, pathophysiology, infection, treatment. All the articles chosen were in English.

Key Words: *Lymphocele; Lymphocele treatment; Scleroteraphy; Surgery; Percutaneous drainage*

Introduction

Lymphocele is defined as a collection of lymphatic fluid, surrounded by a thin fibrotic wall, that lacks epithelial lining [1,2]. It is a relatively infrequent complication after surgical interventions, usually due to iatrogenic injury, in particular after kidney transplantation, lymphadenectomy, and pelvic interventions. As it is usually asymptomatic, it is frequently found during follow-up. A minority of cases are symptomatic. Symptoms are generally due to compression of adjacent anatomical structures and patients can present pain, edema, hydronephrosis, constipation, or deep venous thrombosis [1,3]. The classical and more widespread treatments are surgical or percutaneous, even though in the last years a lot of alternatives have been described in literature. Usually, only symptomatic lymphoceles are treated. The efficacy and the algorithm to choose the best option varies based on presence or absence of infection; hence, the therapeutic strategy should be tailored to the specific case.

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Epidemiology

The epidemiology of lymphoceles constitutes a multifaceted field, primarily shaped by the intricate interplay of surgical and percutaneous interventions, patient characteristics, and underlying health conditions [4]. Surgical procedures involving lymphatic structures, such as lymph node dissections during oncological surgeries or organ transplants, significantly contribute to the genesis of lymphoceles [5]. Incidence rates vary widely, ranging from 1% to 40%, contingent upon the nature and extent of the surgical intervention [2]. Renal transplant recipients, individuals undergoing pelvic lymphadenectomy, and patients subjected to vascular surgeries emerge as particularly susceptible cohorts [2,6,7]. Beyond surgical contexts, trauma, infections, and inflammatory disorders disrupt the normal functioning of the lymphatic system, serving as non-surgical risk factors [8,9]. Older adults exhibit a heightened incidence, potentially attributed to age-related changes in lymphatic function [10]. Gender disparities arise from the prevalence of specific surgical procedures in either sex [2,5]. Understanding these trends is integral to devising targeted preventive strategies and optimizing clinical management protocols. Despite the clinical significance of lymphoceles, challenges persist in accurate diagnosis and reporting. Asymptomatic cases may elude detection, and variability in imaging modalities, such as ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI), can impact the reliability of epidemiological data [2]. Standardizing diagnostic criteria, enhancing awareness among healthcare professionals, and fostering collaborative research efforts are essential steps toward refining our understanding of lymphocele epidemiology and improving patient outcomes.

Pathophysiology

The pathophysiology of lymphoceles involves a complex interplay of factors influencing the normal functioning of the lymphatic system, ultimately leading to the abnormal accumulation of lymphatic fluid. The primary mechanism underlying the formation of lymphoceles is the disruption of the lymphatic vessels, which serve as the conduits for transporting lymphatic fluid. When these vessels are compromised, either by surgery, trauma, or inflammatory/infectious processes, lymphatic fluid accumulates in the interstitial spaces, forming cystic structures known as lymphoceles. At the very base of lymphocele formation is the role of lymphatic fluid composition: lymph, the fluid transported by the lymphatic system, carries immune cells, proteins, and waste products. Disruptions in lymphatic drainage can result in the accumulation of proteins, inflammatory cells, and cellular debris within the lymphoceles. Infection serves as a significant complicating factor in the pathophysiology of lymphoceles. The stagnant nature of lymphatic fluid within these cystic structures provides an ideal environment for microbial proliferation. Bacterial, viral, or fungal infections can complicate the clinical course, leading to symptomatic presentations, increased inflammation, and the potential for secondary complications such as abscess formation [11,12]. Moreover, lymphoceles are not static entities; their evolution over time is a dynamic process influenced by the healing response, tissue repair mechanisms, and ongoing physiological changes post-surgery. Fibrosis, a common response to surgical trauma or inflammation, further impedes lymphatic drainage and contributes to the persistence of lymphatic fluid collections. The structural changes in tissues surrounding the lymphoceles may exacerbate symptoms and pose challenges in their management [13]. Understanding the pathophysiology of lymphoceles is crucial for devising effective

prevention and management strategies. This involves not only addressing the immediate causes, but also considering the broader inflammatory and immunological context.

Clinical Presentation

The clinical presentation of lymphoceles is diverse, encompassing a spectrum of signs and symptoms influenced by the size, location, and complications associated with these fluid collections. Notably, a considerable number of cases remain asymptomatic, discovered incidentally through imaging studies conducted for unrelated reasons [2]. However, symptomatic lymphoceles commonly present with localized swelling or discomfort in the surgical or trauma-affected area [14]. This swelling may be palpable or visible, and its extent depends on the size of the lymphocele and the surrounding anatomical structures. Pain or discomfort is a prevalent clinical complaint associated with lymphoceles. The pressure exerted by the expanding cystic structures on surrounding tissues and nerves contributes to this symptom [15]. Pain may be exacerbated by movement or prolonged standing, reflecting the dynamic nature of lymphoceles and their interaction with the surrounding structures. In cases where lymphoceles are large or in close proximity to nerves, the pain can be severe and may necessitate intervention for relief. Complications further diversify the clinical presentation of lymphoceles [12]. Infection represents a significant concern, particularly when the lymphatic fluid within these cystic structures becomes a favorable medium for microbial proliferation [11]. Infected lymphoceles present with features of inflammation, including localized redness, increased warmth, and tenderness. Systemic signs such as fever may accompany the local manifestations, requiring prompt recognition and appropriate management. Compression of adjacent structures is another notable clinical aspect. Depending on the location of the lymphocele, compression can lead to complications such as ureteral obstruction, vascular compromise, or neurologic symptoms. For instance, pelvic lymphoceles may compress the ureters, causing urinary symptoms, and abdominal lymphoceles may exert pressure on blood vessels, potentially leading to edema or compromised blood flow to surrounding organs [16,17]. The clinical presentation of lymphoceles may also include features suggestive of their impact on organ function. In cases involving abdominal or pelvic lymphoceles, patients may report gastrointestinal symptoms, such as nausea or early satiety, due to compression of the digestive organs [18].

Diagnosis

Diagnostic imaging plays a crucial role in confirming the clinical suspicion of lymphoceles and evaluating their characteristics. Ultrasonography, CT, and MRI are commonly employed to visualize and assess the size, location, and potential complications of lymphoceles [2]. These modalities aid in distinguishing lymphoceles from other fluid collections or masses, guiding appropriate management decisions. Most lymphoceles are asymptomatic, they resolve spontaneously, and they are only diagnosed accidentally, during follow-up. When they are symptomatic usually, they are discovered for compression symptoms (like pain, abdominal fullness, leg swelling, constipation, deep venous thrombosis or renal function deterioration) [2].

Diagnosis can be performed by ultrasound, when the lymphocele is superficial, or CT/MRI, when it is located deeply [3]. Ultrasound has the advantages of being non-invasive, safe, and easily repeatable. In the ultrasound setting, lymphoceles appear as ipo/anechoic fluid collections of various dimensions, sonographically indistinguishable from other fluid collections, like urinoma and

seroma. Unenhanced and contrast-enhanced CT usually shows well-defined collections of hypoattenuating fluids (generally with Hounsfield Units close to water) [19,20].

Treatment

Management strategies for clinically significant lymphoceles vary based on the size, symptoms, and complications. Asymptomatic lymphoceles, that are accidentally found, usually do not have indications for treatment: asymptomatic cases may be managed conservatively with observation, although for some Authors lymphoceles that persist beyond 3 months after surgery must be treated to prevent possible infection [19,21,22]. On the other hand, symptomatic lymphoceles require treatment [19,23]. Symptomatic or complicated lymphoceles may require intervention, ranging from percutaneous drainage under imaging guidance to more invasive procedures like sclerotherapy or surgical excision.

Surgery

Surgical methods include open or laparoscopic surgery. Open surgery has long been considered the gold standard treatment of symptomatic lymphoceles. Laparotomy is used to explore the abdominal cavity and to marsupialize the lymphocele [1,2,22].

During open surgery and internal marsupialization lymphocele is drained into the peritoneal cavity internally. Open surgery treatment has good success rates, but also relatively high mortality and morbidity. Another great disadvantage of this treatment is its applicability to only sterile lymphoceles as well as its long recovery period, like other open surgical interventions. Surgical external lymphocele drainage was a possible choice in the past, but with several inconveniences, like long hospital stay, high recurrence rates (up to 25%), and relatively high infection risk [20,21].

On the other hand, laparoscopic treatment is feasible, allowing to position a drainage into the lymphocele, even though it suffers from an increased risk of ureteral injury (up to 7%) [20].

Sometimes, laparotomy remains the only treatment for resistant or recurrent/infected lymphoceles, or in case of lymphoceles not suitable for percutaneous approach [2]. In particular, laparoscopic surgery is used in the treatment of renal transplant-related lymphoceles; however, despite shorter hospital stay, patients are still exposed to risks of general anesthesia and transition to open surgery in case of complications.

Recurrence rate of open surgery is 16%, while recurrence rate of laparoscopic fenestration is 8%. Conversion rates from laparoscopic to open surgery are around 12%. Overall complication rate of laparoscopic surgery is 14%, while they are 30% for open surgery [22].

Percutaneous Techniques

The percutaneous techniques are usually of the field of interventional radiology and include simple aspiration (that has an elevated rate of recurrence, around 80-90%), catheter drainage insertion (which could be maintained for several days or up to some weeks), and percutaneous catheter drainage with sclerotherapy (the most effective percutaneous technique). The latter can be done with injections of several sclerosing agents, with comparable success rates to surgical intervention [2,20,22,24]. In addition, with percutaneous aspiration/catheter drainage only, there is a moderate risk of infection (25-50%) [2].

Ethanol and povidone-iodine are the two most frequent sclerosing agents; ethanol is the most effective (and the cheapest) of the two, that leads to dehydration and coagulation of proteins; on the other hand, povidone-iodine

causes sclerosis by chelation of proteins with a presumed antioxidative effect, also decreasing the chance of infection due to its antiseptic properties [2,24].

Other less used sclerosants are acetic acid, sodium tetradecyl sulfate, tetracycline, doxycycline, bleomycin (strong irritant agents that creates inflammatory response, which promotes adhesion formation), fibrin glue or other sealants [20-22].

Patients that undergo percutaneous treatments are routinely monitored during the procedure. The procedure can be performed during local anesthesia, or under conscious sedation with the help of an anesthesiologist. A fasting of at least 6 hours is required [20].

Seldinger technique is commonly used for percutaneous puncture of lymphoceles, under ultrasonography and/or fluoroscopy guidance. Then, a guide-wire is advanced in the lymphocele, and subsequently a pigtail catheter (8–14 F) is placed over the wire into the cavity. Contrast medium can be injected into the lymphocele through the drainage to rule out the presence of leakage. If there is extravasation, sclerotherapy is not indicated to avoid complications [20,22]. Subsequently, to prevent dilution of the sclerosant, the internal fluid of the lymphocele is aspirated as much as possible. Then, the sclerosant is injected and left in the cavity for a total of 5 to 20 minutes. During this time, the position of the patient should be modified to ensure that the entire internal surface of the lymphocele wall comes in contact with the sclerosant (supine, prone, left and right decubitus). The injected sclerosant is then aspirated as much as possible [22]. In the case of a large or multiloculated lymphocele two or more catheters can be placed [20].

Follow-up could be performed at 1, 3, 6 months and at 1 year after the percutaneous drainage, and yearly thereafter, by ultrasound or CT depending on its location, even though there is no indication on follow-up, which depends on single-centers experience [20].

Percutaneous catheter drainage is an easy method and can be combined with transcatheter sclerotherapy to increase its therapeutic efficiency. The major drawback of percutaneous methods is the relatively long treatment duration, as mean duration varies between 10 and 30 days in the literature; however, it can be performed in outpatient or day hospital settings [1,20].

Outcome of Sclerosant Agents

The use of sclerosant agents has a better outcome when compared to simple drainage with or without percutaneous catheter [2]. Selection of sclerosing agents is usually dependent on radiologist‘s preference [22]. A great lymphocele volume is associated with lower success of sclerotherapy, due to dilution of the sclerosant [22]. Ethanol and povidone-iodine are the two most commonly used sclerosing agents. Success rates with ethanol are high (85-97%) and recurrences are very rare (3-7%). Povidone-iodine is a readily available agent, with lower success rates (60-90%) and higher recurrence rates (10-40%) compared to ethanol, but overall success rate increases after treatment of recurrent lymphoceles, with outcomes similar to those for ethanol (88-100%) [2,20]. Antibiotics (tetracycline and doxycycline) can also be used with overall success rates >90%. Bleomycin is reserved for resistant and recurring lymphoceles, with excellent success [1,2,20]. Fibrin glue has 75 and 25% success and recurrence rates, respectively [20]. Polidocanol is an effective and well-tolerated sclerosant agent that showed good results when applied to post-surgical lymphoceles [25,26].

Most relevant complications of sclerosant agents include allergy reactions, infections and,

for povidone-iodine, nephrotoxic acute renal failure [20]. Povidone-iodine and ethanol have similar infection rates [2]. To prevent the spread of infection, percutaneous drainage could be preferred to surgical drainage [2].

Other Treatments

There are some other treatments described in literature, some newer and widespread, others more pioneering. One of them is glue embolization to close lymphatic leaks. Usually N-butyl cyanoacrylate (NBCA) glue-based embolization, usually mixed with lipiodol, is used for treating lymphatic leaks refractory to conservative treatment and sclerotherapy. Success rate of NBCA embolization is 80-100% [22]. Generally, lymphangiography is mandatory before embolization, to identify the site of leakage and the target site of embolization [1,22,27]. Several recent studies described the effectiveness of intranodal embolization, with injections of diluted NBCA in the lymph node, immediately caudal to the leaking site.

Ozawa and colleagues described 9 patients treated for a groin lymphocele with this technique: a lymphangiography with iodinated contrast medium was firstly performed, and then diluted NBCA was injected in the target site. Despite a small sample size, they obtained clinical success with a median of two treatment sessions; median treatment period was 2 days (range from 1 to 13 days), with no early complications [27].

A very new surgical technique is lymphovenous anastomosis: it consists in linking a damaged lymphatic vessel (or a vessel running into an area where the flow is impaired), to a nearby vein. Nowadays it is a common choice for treatment of mild to moderate secondary lymphedema, but also for lymphocele and lymphorrhea prevention after surgery. Scaglioni and colleagues showed that lymphocele affecting the thigh and not responding to classical treatment can be successfully treated by microsurgical lymphaticovenous anastomosis or combined with muscle flap in order to reconstruct the missing volume [28].

Focassio and colleagues described a case of a patient treated with negative pressure wound therapy for a lymphocele after excision of an inguinal mass. The device is composed of foam medication or alcohol foam medication. The device is covered with adhesive stripe and the effluent of the wound is collected in a little bag attached to the vacuum pump, with adjustable negative pressure. [29]. They describe lymphocele excision with ligation of lymphatic vessels, followed by negative pressure wound therapy appears to be a safe and effective approach [29]. The robotic approach is another option, and it grants safe and feasible drainages, being a definitive treatment for infected and/or symptomatic lymphoceles, even though very few studies focused on this approach [30].

Soga and colleagues described an endoscopic approach through which a post-ovarian surgery lymphocele was treated by puncture, using a 19-gauge needle, and then positioning a double-pigtail plastic stent, without complications [31].

Discussion

Percutaneous treatment should be considered as the first-line treatment modality for lymphoceles, due to its effectiveness, widespread applicability, ease of procedure and low complication rate. In cases of infection, appropriate antibiotic therapy is instituted alongside drainage procedures. When lymphocele does not respond or recurs after percutaneous treatment, a surgical treatment is unavoidable [19,23]. A first differentiation should be done between treatment of infected or not-infected lymphocele. The treatment of infected lymphoceles is challenging. The only administration of broad-spectrum antibiotics is usually not sufficient, but it may help to avoid surgical intervention [2].

Percutaneous drainage may be of benefit as it also prevents inflammation from spreading into the abdominal cavity. The role of surgery is the last chance in case of failure of other treatments [2].

Some studies showed that infected collections were more likely to resolve with percutaneous drainage alone, due to inflammatory changes that render the lymphocele adhesive [22].

According to Kim and colleagues, the technical success rate obtained with percutaneous technique (percutaneous catheter drainage with or without injection of sclerosant agents) was 100% and clinical success rate was 79.1-91.2%, depending on the presence of infected or not-infected lymphocele. The catheter placement time was not significantly different in both the pre- and post-sclerotherapy period, when compared. Several studies have reported that sclerotherapy is a safe and effective treatment in addition to simple percutaneous drainage for non-infected lymphoceles. Treatment of infected lymphoceles is different: infected lymphoceles are not candidates for surgical marsupialization, due to infection that can spread into the peritoneal cavity; these cases could be treated by percutaneous drainage only. Kim and colleagues also note that the total drainage volume of infected lymphoceles was significantly smaller, compared to non-infected lymphoceles, that suggested infection could obliterate the lymphatic leakage through a mechanism similar to that of sclerotherapy (inflammation and subsequent fibrosis of the lymphocele). Moreover, they observe that the drainage volume decreased significantly after sclerotherapy in infected lymphoceles, but not in non-infected lymphoceles. The treatment of sclerotherapy in infected lymphoceles is a safe treatment to decrease the drainage volume and it can lead to reduced catheter placement time. Patients treated only with percutaneous drainage showed comparable results with those treated with additional sclerotherapy, in infected and non-infected lymphoceles. Percutaneous drainage alone is an effective treatment in lymphoceles with gradually decreasing size and drainage volume over time [21].

According to data collected by Ten Hove and colleagues, embolization seems to be the best option for treatment, considering its high success rate and low recurrence rate; however, in the great majority of these studies embolization was never the first performed treatment [1]. An important advantage of embolization over sclerotherapy is that embolization is not contraindicated for ruptured lymphoceles that freely communicate with other spaces, like peritoneum [3].

Conclusion

Percutaneous catheter drainage with or without sclerotherapy must be considered the first line treatment method, due to its safety and effectiveness, with a high success rate, also for infected postoperative lymphoceles. Open surgery and peritoneal marsupialization had been the gold standard in the treatment of pelvic lymphoceles for decades; laparoscopic surgery represents an alternative to classic surgery. Nowadays other techniques are available and described in literature, but without sufficient sample population to have a significant comparison with classical treatments; therefore, new studies are needed.

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