

## Case Report

# Bleomycin Sclerotherapy for Severe Symptomatic and Persistent Pelvic Lymphocele

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**Background.** Pelvic lymphoceles are frequently described as a complication of pelvic lymphadenectomy performed for surgical staging of gynaecologic malignancies. **Case Report.** A 72-year-old woman presented with severe symptomatic and refractory lymphocele associated with persistent lower limb lymphedema and recurrent erysipelas. After four CT fluoroscopy scan guided percutaneous catheter drainages, the lymphocele complicated with infection finally resolved with two sessions of bleomycin sclerotherapy. **Conclusion.** Symptomatic persistent lymphoceles require treatment and nowadays the first option is interventional radiologic procedures. Bleomycin is a safe and effective sclerosing agent and therefore should be regarded as a first-line treatment choice.

## 1. Introduction

Lymphocele was first reported in 1950 by Kobayashi and Inoue [1] and it is defined as a lymph filled extraperitoneal collection with a fibromembranous wall devoid of any epithelial lining [2–4]. Therefore, lymphocyst terminology is not appropriate.

The etiopathogenesis is based on the disruption of the lymphatic vessels, which occur for traumatic or surgical reasons. Lymphoceles mainly develop after extraperitoneal surgery and much less frequently after intraperitoneal procedures, because the peritoneum plays a major role in the lymph absorption. The specific characteristics of lymph (namely, the flow tendency after injury due to its reduced clotting factors concentration and the absence of platelets) and of the lymph vessels (namely, the absence of smooth muscle in the vessel wall precluding vasoconstriction) explain the appearance of lymphoceles. These occur mainly after renal transplantation and urogynecologic malignancy related lymphadenectomy. Lymphocele formation after vascular and spinal surgery has been reported less commonly [5–9]. The lymphatic vessels

can remain patent up to 48 hours after injury [10]. Lymphoceles generally develop a few weeks after retroperitoneal surgical procedures; however, late occurrences up to two years have been described [11].

The exact incidence of pelvic lymphoceles is not established; it has a wide variation depending on surgical approach, screening and diagnosis methods, and symptomatology. At pelvic lymphadenectomy for gynaecologic malignancies one can find reports of incidence that range between 18% [2] and 44% [12]. Considering only symptomatic postoperative lymphoceles, Achouri et al. reported an incidence of 34,5% [13]. In the particular case of symptomatic lymphoceles after complete cytoreductive surgery and para-aortic and pelvic lymphadenectomy for ovarian cancer, Gauthier et al. describe an incidence of 28% [14].

When asymptomatic, as most of the cases, spontaneous regression is the natural history [2, 12]. On the other hand morbidity has been described, such as infection and compression of adjacent structures (ureters with hydronephrosis; rectosigmoid with constipation; pelvic nerves with leg/back

pain and urinary frequency; and vessels with genital/lower limb edema and thrombosis/embolism). Complications can emerge, namely, chylous ascites and lymphatic fistula [3, 15, 16].

In the presence of a severe symptomatic pelvic lymphocele, treatment must be offered not only to relieve symptoms and control the functional compromise of adjacent vital structure, but also to prevent a delay of the underlying disease treatment [16–18].

There are several treatment modalities. Nowadays, the first option is interventional radiology procedures (simple aspiration, image guided percutaneous catheter drainage with or without sclerotherapy), leaving surgical treatment for second-line therapeutic [4].

The authors report a case of a severe, symptomatic and refractory pelvic lymphocele successfully treated with bleomycin sclerotherapy.

## 2. Case Report

A 72-year-old woman was referred to our outpatient clinic for an abdominopelvic mass clinically suggestive of ovarian carcinoma. The patient relevant medical and surgical history was obesity (BMI 34.8 kg/m<sup>2</sup>), essential arterial hypertension, diabetes mellitus, dyslipidaemia, and iatrogenic hypothyroidism (total thyroidectomy for a benign condition).

Complete surgical ovarian cancer staging was performed and included total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, infracolic omentectomy, appendectomy, and multiple peritoneal biopsies. Two continuous suction drains were placed at the end of the procedure in both iliac fossae, which were removed on the fourth postoperative day. For systemic thromboprophylaxis reasons she maintained low molecular weight heparin during the 30 days after surgery. Recovery was uneventful with discharge at the fifth postoperative day.

The patient was evaluated on the 13th postoperative day. Definitive diagnosis was grade 2 ovarian mucinous adenocarcinoma, right pelvic ganglia 0/12, left pelvic ganglia 0/27, para-aortic ganglia 0/29, and FIGO surgical staging IAR0. She complained of pain and swelling of the left lower limb. On physical examination she presented left lymphedema and bilateral erysipelas (more pronounced on the left). The abdominopelvic ultrasound revealed a bilateral pelvic lymphocele, the left with 109 \* 56 mm, and the right with 45 \* 21 mm. Bilateral lower limb venous *Doppler* excluded deep venous thrombosis.

After six days of unsuccessful empirical antibiotherapy with flucloxacillin for the erysipelas, she was readmitted. A CT fluoroscopy scan guided percutaneous catheter drainage was performed. Externalization of a clear, slightly yellow-tinged, benign, and sterile fluid was achieved with trocar technique with a 7F Huisman catheter. There was a progressive improvement of the lymphedema and erysipelas, and the drain was removed six days after (last day output 200 mL/24 h with previous medium output/24 h of 850 mL),

with ultrasound confirmation of left lymphocele shrinkage with 51 \* 40 mm; however, six days later she complained of excruciating left inguinal and lower left sided back pain. Imagiologic evaluation by ultrasound and CT pelvic scan revealed recurrence of left lymphocele with 106 \* 54 mm, impairing venous drainage of the inferior limb (Figure 1). Fifteen days after the first drainage, another CT fluoroscopy scan guided percutaneous complete drainage was performed (200 mL), using Seldinger technique with an 8F pigtail catheter, and was removed four days later (last day output 150 mL/24 h with previous medium output/24 h of 550 mL). Twenty-two days after the admission she was discharged with no pain and lymphedema improvement.

Two months after this discharge the patient was readmitted, complaining of pain and swelling of the left inferior limb, anorexia, and vomiting. Abdominopelvic ultrasound showed aggravated left lymphocele with 190 \* 90 mm, compressing the homolateral iliac vessels and ureter with left limb iliac-femoral-popliteal thrombosis. Analytic parameters were compatible with infected pelvic lymphocele and decompensated diabetes, and therefore she was admitted at the intensive care unit. Under low molecular weight heparin and antibiotic therapy (piperacillin/tazobactam) another CT fluoroscopy scan guided percutaneous catheter drainage was performed on the 7th day. Nearly complete aspiration of lymphocele was performed, using trocar technique with a 12F pigtail catheter. There was isolation of ampicillin resistant *Klebsiella pneumoniae*. The pigtail catheter was removed 12 days after, and transition to endovenous cefazolin was performed in order to treat cellulites in the spot of the catheter and erysipelas. Fifteen days after and due to persistent and high output (total of 3100 mL in 4 days) pelvic lymphocele, fluoroscopy scan guided percutaneous catheter (pigtail) drainage was performed. Later, the empty cavity of the lymphocele was filled with contrast medium in order to exclude fistulous communications, which preclude sclerotherapy. 60 000 UI of bleomycin diluted in 50 mL saline was instilled into the lymphocele cavity with occlusion of the catheter, which was left in situ. During this time the patient was mobilized in order to achieve penetrance of the sclerosing agent in all the loci. After 60 minutes of patient mobilization, all the amount of the sclerosing agent was sucked by a syringe from the cavity. The procedure was well tolerated without any complication and was repeated seven days after. Pigtail catheter was removed one week later, after an abdominopelvic CT scan showed reduction of left lymphocele with 71 \* 28 \* 55 mm. She was discharged the linebreak next day.

The patient was submitted to a specific programme of physical rehabilitation to improve the motor dysfunction associated with the inferior limb lymphedema.

A control abdominopelvic CT scan performed one month after the last hospital discharge did not revealed any pelvic collection.

Three years after the surgery the patient remains in oncologic remission with improvement of the left inferior member lymphedema and no imagiologic relapse of the pelvic lymphocele.

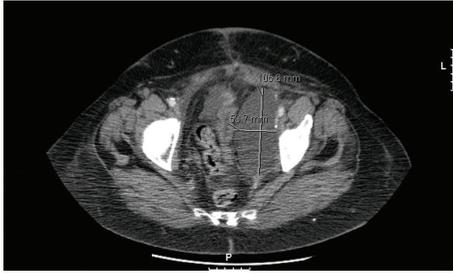


FIGURE 1: Pelvic lymphocele recurrence.

### 3. Discussion

Although divergent results can be found in the literature, many factors are believed to contribute to pelvic lymphocele formation. It may be associated with heparin (some studies showing that the administration near the abdominopelvic region is prone to the occurrence of lymphocele) [19], diuretics, steroids, high body mass index, and surgical technique (extent of lymphadenectomy with the number of lymph nodes removed and the presence of metastases to the lymph nodes) [2, 18, 20–23].

Despite the absence of clear consensus on the risk factors, some surgical measurements may have a potential impact at decreasing the incidence of lymphoceles, such as prefer the laparoscopic approach, ligate the lymph vessels, avoid peritoneal juxtaposing at the end of the procedure [16], and preclude suction drainage tube placement [24] and, when feasible, omentoplasty should be encouraged [16].

In this case, several factors may have contributed to the pelvic lymphocele formation: the high body mass index, the extent of lymphadenectomy, the administration of heparin in the thigh and postoperative suction drainage. In our department, we perform thromboembolic prophylaxis with low-dose subcutaneous heparin to all oncologic patients who are submitted to pelvic surgery. Since the risk of deep vein thrombosis and fatal pulmonary embolism is very high, it justifies its widespread use and overweighs the lymphocele risk. In the past, following radical pelvic and lomboarctic lymphadenectomy, we routinely performed surgical peritoneal juxtaposition and maintained retroperitoneal suction drainage placed at both the iliac fossae for about four days. Actually we still perform thromboprophylaxis during the perioperative period but no longer do the surgical peritoneal approximation or the suction drainage.

Even though almost complete evacuation of the cavity was achieved in each percutaneous drainage, an essential condition to avoid bacterial infection, the repetitive drainages with long term catheter placement and the poor glycaemic control were probably at the basis of the infection. As it is well known, hyperglycaemia in diabetes mellitus is a condition associated with high infection risk.

The treatment modalities describe the surgical approach and percutaneous techniques through interventional radiology (Table 1). The gold standard was open surgery by performing internal marsupialization with drainage into

the peritoneal cavity internally added with omentoplasty. External drainage technique [25], also described, has major drawbacks as long hospitalization, relative high risk of infection, and a high recurrence rate (up to 25%) [3]. Thereby it is no longer a first option. The laparoscopic approach, first described in 1994 by McCullough et al. [26], has a success rate of 95% in the more recent series [27, 28] and nowadays it is the surgical approach of excellence in the literature. The benefits are inherent of every laparoscopic procedure.

The minimal invasive therapeutic options include simple aspiration, simple catheter drainage, and combined catheter drainage with transcatheter sclerotherapy. Simple aspiration should be performed only in small lymphoceles, because of the high risk of recurrence (80–90%) and infection (25%) [3, 29]. Percutaneous catheter drainage has a variable success rate of 70% to 100% [30–34]. The option of adding sclerotherapy has comparable success rates to surgery. Regarding the sclerotherapy, there is no consensus on the optimal sclerosing agent: povidone-iodine, sodium tetradecyl sulphate, sodium azetroate, sodium mortuate, talk, fibrin glue, ethanol, ampicilina, tetracycline, doxycycline, and bleomycin. These act by irritation of lymphocele's walls, inducing local inflammation and fibrosis of the lymphatic channels, obliterating the lymphatic leak. They can be used as a primary treatment or for persistent lymphoceles. Since there is no robust scientific evidence comparing the effectiveness and efficiency of the individual sclerosing substances (success rates range between 62 and 100% and recurrence rates between 3 and 38%), choosing one over another depends on personal preferences and experience [3, 4, 34–50]. The comparable success rate to the surgical approach has shifted the first-line treatment option to this minimal invasive sclerotherapy. This procedure can be performed on an outpatient basis, with no antibioprophyllaxis needed in immunocompetent patients, and is executed under conscious sedation. Ultrasound and CT or MR imaging are useful to diagnose and characterize the lymphocele in respect to location, dimension, and relationship to adjacent structures. But cystograms are ideal for evaluation of the extension of the lymphoceles, to differentiate side to side from juxtaposed lymphoceles from a septate lymphocele and during the intervention it is essential to exclude extravasation outside the cavity of the lymphocele, which is the contraindication to do the sclerotherapy.

Bleomycin is a cytotoxic agent used systemically for the treatment of some malignant neoplasia. Topical use allows the formation of adhesions, making an excellent agent for sclerosis. There are some accumulated experiences using bleomycin for sclerosis of malignant pleural effusions [51, 52] and treatment of lymphangioma [53, 54]. It is not as frequently reported as other agents for lymphoceles sclerotherapy. After the first case of Khorram and Stern of a resistant inguinal lymphocele treated with bleomycin [55], Kerlan et al. reported successful use of this sclerosing agent in four patients, three resistant to other sclerosing agents. They stated that bleomycin should not be considered the agent of choice for sclerosis of postoperative lymphoceles, and it should be reserved for refractory lymphoceles to other sclerosing agents [50]. The reason for this advice is that it is associated with potential side effects, like fever, nausea, vomiting, stomatitis,

TABLE 1: Studies in treatment modalities for pelvic lymphoceles.

| References                  | N   | Treatment modality   | Sclerosing agent | Success rate           | Side effects/complications  |
|-----------------------------|-----|--|------------------|------------------------|---|
| Surgical treatment          |     |  |                  |                        |   |
| Radosa et al., 2013 [27]    | 132 | Laparoscopic drainage  | NA               | 93%                    | Intraoperative 9.8%<br>Postoperative 5.9%   |
| Khoder et al., 2012 [28]    | 105 | Laparoscopic drainage  | NA               | 97%                    | Not mentioned/unknown   |
| Hsu et al., 2000 [57]       | 81  | Laparoscopic drainage  | NA               | 94%                    | Intraoperative (5%):<br>(i) laryngospasm ( $n = 1$ )<br>(ii) inferior epigastric artery injury ( $n = 1$ )<br>(iii) mild renal capsule hematoma ( $n = 1$ )<br>(iv) bladder injury ( $n = 1$ )<br>Postoperative (4%):<br>(i) trocar site hernia ( $n = 1$ )<br>(ii) urinary retention ( $n = 2$ ) |
| Cadrobbi et al., 1999 [58]  | 12  | Laparoscopic drainage  | NA               | 92%                    | 8%:<br>bleeding from the peritoneal window ( $n = 1$ )  |
| Ostrowski et al., 2000 [59] | 9   | Laparoscopic drainage  | NA               | 89%                    | None  |
| Melvin et al., 1997 [60]    | 8   | Laparoscopic drainage  | NA               | 75% (only 6 follow-up) | None  |
| Gill et al., 1995 [61]      | 38  | Open drainage ( $n = 26$ ) versus laparoscopic drainage ( $n = 12$ )         | NA               | 73% versus 100%        | Open drainage (12%):<br>(i) prolonged ileus ( $n = 1$ )<br>(ii) transection of the ureter of a transplant kidney ( $n = 1$ )<br>(iii) pneumonitis ( $n = 1$ )<br>Laparoscopic drainage (8%):<br>cystotomy requiring open repair ( $n = 1$ )   |
| Minimal invasive therapy    |     |  |                  |                        |   |
| Kim et al., 1999 [30]       | 23  | Percutaneous catheter drainage   | NA               | 96%* to 100%**         | 17%:<br>(i) secondary infection ( $n = 1$ )<br>(ii) skin infection ( $n = 2$ )<br>(iii) catheter dislodgement ( $n = 1$ )   |
| Kurata et al., 2003 [31]    | 10  | Percutaneous catheter drainage   | NA               | 90%                    | None  |
| Conte et al., 1990 [32]     | 8   | Percutaneous catheter drainage   | NA               | 88% to 100%**          | None  |
| White et al., 1985 [29]     | 11  | Simple aspiration ( $n = 2$ ) and percutaneous catheter drainage ( $n = 9$ ) | NA               | 82%                    | 27%<br>lymphocele infection ( $n = 3$ )   |
| Jensen et al., 1986 [33]    | 8   | Simple aspiration ( $n = 7$ ) and percutaneous catheter drainage ( $n = 1$ ) | NA               | 75% (only 7 follow-up) | None  |
| Akhan et al., 2007 [34]     | 60  | Percutaneous catheter drainage ( $n = 10$ ) and sclerotherapy ( $n = 50$ )   | Ethanol          | 70% and 98%*           | 12%<br>(i) catheter dislodgement ( $n = 1$ )<br>(ii) secondary infection ( $n = 6$ )  |

TABLE 1: Continued.

| References                      | N  | Treatment modality  | Sclerosing agent                          | Success rate              | Side effects/complications  |
|---------------------------------|----|---|---|---------------------------|---|
| Akhan et al., 2000 [35]         | 38 | Percutaneous catheter drainage ( <i>n</i> = 7) and sclerotherapy ( <i>n</i> = 31)     | Ethanol                                   | 97% to 100%**             | Not mentioned/unknown   |
| Zuckerman and Yeager, 1997 [36] | 32 | Sclerotherapy   | Ethanol                                   | 94%                       | 9%:<br>secondary infection ( <i>n</i> = 3)  |
| Sawhney et al., 1996 [37]       | 14 | Sclerotherapy   | Ethanol                                   | 93% to 100%**             | None  |
| Akhan et al., 1992 [38]         | 8  | Sclerotherapy   | Ethanol                                   | 88% to 100%**             | None  |
| Kuzuhara et al., 1994 [39]      | 4  | Sclerotherapy   | Ethanol                                   | 75%                       | Not mentioned/unknown   |
| Alago et al., 2013 [40]         | 70 | Percutaneous catheter drainage ( <i>n</i> = 52) versus sclerotherapy ( <i>n</i> = 18) | Povidone-iodine                           | 74% to 97%** versus 100%* | 34%<br>(i) pericatheter fluid leakage ( <i>n</i> = 4)<br>(ii) catheter dislodgement ( <i>n</i> = 3)<br>(iii) catheter occlusion ( <i>n</i> = 9)<br>(iv) secondary infection of the collection ( <i>n</i> = 4)   |
| Rivera et al., 1996 [41]        | 19 | Sclerotherapy   | Povidone-iodine                           | 62.5% to 100%**           | 15%:<br>secondary infection ( <i>n</i> = 3)   |
| Montalvo et al., 1996 [42]      | 17 | Sclerotherapy   | Povidone-iodine                           | 82% to 100%**             | Not mentioned/unknown   |
| Cohan et al., 1988 [43]         | 13 | Percutaneous catheter drainage ( <i>n</i> = 6) and sclerotherapy ( <i>n</i> = 7)      | Povidone-iodine                           | 83%*<br>86%               | None  |
| Gilliland et al., 1989 [44]     | 9  | Sclerotherapy ( <i>n</i> = 9)   | Povidone-iodine                           | 89%                       | None  |
| Shokeir et al., 1993 [45]       | 30 | Percutaneous catheter drainage ( <i>n</i> = 9) and sclerotherapy ( <i>n</i> = 21)     | Tetracycline                              | 93%                       | Not mentioned/unknown   |
| Caliendo et al., 2001 [46]      | 21 | Sclerotherapy   | Doxycycline                               | 95%*                      | 27%:<br>minor discomfort or transient mild temperature elevation ( <i>n</i> = 5)  |
| Folk and Musa, 1995 [47]        | 3  | Sclerotherapy   | Doxycycline                               | 67%                       | None  |
| VanSonnenberg et al., 1986 [48] | 14 | Percutaneous catheter drainage ( <i>n</i> = 10) and sclerotherapy ( <i>n</i> = 4)     | Tetracycline<br>povidone-iodine           | 79%                       | Not mentioned/unknown   |
| Mahrer et al., 2010 [4]         | 43 | Sclerotherapy   | Povidone-iodine<br>ethanol<br>doxycycline | 77%*                      | 35%:<br>(i) cellulitis ( <i>n</i> = 1)<br>(ii) severe testicular pain ( <i>n</i> = 1)<br>(iii) ureteral obstruction and increased creatinine level ( <i>n</i> = 1)<br>(iv) acute tubular necrosis ( <i>n</i> = 1)<br>(v) localized peritonitis ( <i>n</i> = 11) |
| Chin et al., 2003 [49]          | 8  | Sclerotherapy   | Fibrin glue                               | 75%*                      | 38%:<br>(i) clogging of drainage catheters ( <i>n</i> = 2)<br>(ii) catheter dislodgement ( <i>n</i> = 1)  |
| Kerlan et al., 1997 [50]        | 4  | Sclerotherapy   | Bleomycin                                 | 100%*                     | 25%<br>transient episode of fever ( <i>n</i> = 1)   |

TABLE 1: Continued.

| References               | N  | Treatment modality  | Sclerosing agent   | Success rate                     | Side effects/complications  |
|--------------------------|----|---|--------------------|----------------------------------|---|
|                          |    |   | Several modalities |                                  |   |
| Atray et al., 2004 [62]  | 36 | Simple aspiration (n = 4),<br>percutaneous catheter drainage (n = 12),<br>sclerotherapy (n = 4),<br>open drainage (n = 8), and<br>laparoscopic drainage (n = 8) | Ethanol            | 100%<br>67%<br>75%<br>88%<br>88% | Sclerotherapy:<br>infection (n = 3)<br>Open drainage<br>infection (n = 1) |
| Ziętek et al., 2007 [63] | 14 | Percutaneous catheter drainage (n = 14)<br>followed by<br>laparoscopic drainage (n = 7)   |                    | 50%<br>86%                       | None  |

N: number of lymphoceles. NA: not applied. \* After multiple sessions. \*\* Considering asymptomatic recurrence.

skin rash, chest pain among others, and cost. The exact incidence of these collateral effects with lymphocele sclerotherapy has not been reported but is probably less compared with intravenous chemotherapy (10% the most frequent side effects). However, in our department we had previous successful experience in treating inguinal lymphocele with bleomycin without major complications and for that reason it was the agent of choice for this particular case. Elsandabesee et al. also reported a safe successful sclerotherapy with bleomycin in a recurrent massive inguinal lymphocele [56].

#### 4. Conclusion

As a potential severe complication following radical pelvic lymphadenectomy, symptomatic lymphoceles should be promptly treated. If daily high volume drainage persists after percutaneous catheter drainage alone, sclerotherapy should be performed. In the absence of robust scientific evidence and expert consensus for the safest and most effective sclerosing agent, individual experience at the management of such situation should guide our options. There is a higher experience with the use of bleomycin in inguinal lymphoceles than in abdominopelvic ones. This case reports adds empirical evidence and reinforces the use of bleomycin as a safe and excellent sclerosing agent. It should be regarded as a first-line agent in refractory abdominopelvic lymphocele.

If it is true that there is no matter of debate regarding the first-line treatment of significant, symptomatic, or complicated lymphoceles by percutaneous techniques through interventional radiology with combined catheter drainage and transcatheter sclerotherapy, the medical community cannot reach a consensual sclerosing agent. Search for the most effective and efficient sclerosing agent is still a continuing process and requires prospective, well-designed randomized studies with comparison of different agents. The present case contributes to the growing experience in this particular matter.

#### Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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