Lymphatic Reconstruction Following Sarcoma Surgery

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1. Abstract

1.1. Introduction: Oncologic surgery often comprises lymph node removal, especially in aggressive tumors such as sarcoma. If the tumor is localized in areas of important lymphatic conducts or lymph nodes, patients may suffer from lymphedema or lymphatic fistulas. In this case series we present three consecutive patients with lymphedema and/or lymphatic fistula following sarcoma resection and the surgical treatment.

1.2. Methods and Results: Three patients with lymphedema and/or lymphatic fistula following sarcoma resection were included. All patients presented lymphedema stage II-III of the affected extremity and two had additional lymphocele. Lymphovenous anastomosis (LVA) on the knee or upper ankle joint was performed in all patients beyond lymphocele resection. LVA showed regression of lymphedema in all patients. Moreover, complete healing of lymphatic fistulas and dissolution of lymphocele was observed in the affected patients. No postoperative complications occurred.

1.3. Conclusion: Performing LVA showed successful regression of lymphedema, dissolution of lymphocele and healing of lymphatic fistulas. Prophylactic LVA may be considered in tumor resections in areas at risk of lymphatic injury to prevent lymphatic complications.

2. Introduction

Oncologic surgery comprises many medical disciplines and therapeutic approaches. Surgical resection is an important aspect in cancer treatment and often involves additional lymphadenectomy of sentinel lymph nodes and downstream lymph node stations [1]. In some cases, radiotherapy is performed for local disease control and to increase functional outcomes [2]. However, despite lymph node resection [3], radiation increases the risk of lymphatic vessel damage and lymphatic complications [4]. In fact, radiotherapy was shown to decrease the proliferative potential of lymphatic tissue, to promote lymph node fibrosis and mechanical insufficiency of lymph vessels [4].

Especially sarcomas are tumors characterized by an aggressive growth pattern, early metastasis and poor prognosis [5-7]. In this regard, a safe tumor resection and lymphadenectomy of affected lymph nodes are crucial [5-7], but often lead to lymphatic complications [8, 9]. An incidence of lymphedema of about 29% has been found following limb salvage of extremity soft tissue sarcoma [9]. Number of resected lymph nodes [10-12], tumor localization on the thigh, tumor depth and size > 5 cm were identified as risk factors for the development of lymphedema [8, 9]. For local disease control, patients frequently undergo radiotherapy [13] and as mentioned before, this contributes as well to the development of lymphedema. In lymphedema, compression therapy and manual
lymphatic drainage are some examples of conservative treatment that can ameliorate symptoms. Yet if symptoms persist and no improvement can be achieved, surgery may be indicated. Surgical therapy includes lymphovenous anastomosis (LVA) [14] or vascularized lymph node transfer.

Moreover, the occurrence of lymphoceles is also a common problem in oncologic surgery [15, 16] and radiotherapy has been identified as a risk factor [16]. Furthermore, a lymphocele diameter greater than 6 cm has been found to be a risk factor for infection [17]. Additionally, the development of a lymphocutaneous fistula contributes to the risk of infection as well [18]. In lymphoceles, complete resection and clipping of afferent lymph vessels indicated [19, 20]. However, in recent years, there has been increasing evidence that LVA is an effective therapy in the treatment of lymphocele as well [21].

By presenting this case series, we aimed to highlight the importance of rapid recognition of risk factors for lymphatic vessel injury and lymphatic complications in order to suggest patients the adequate surgical treatment and to prevent worsening of symptoms. Moreover, we wanted to describe the efficacy of LVAs in the treatment of lymphocele.

3. Materials and Methods

Three patients (one female, two males) were included in this case series. They were operated at the University Hospital of Regensburg, Germany, between 2019 and 2020. The study was approved by the local Ethics’ Committee (No. 19-1491-104). Informed consent for data elaboration was obtained from all patients and the study was carried out in accordance with the Declaration of Helsinki. A special consent for the use of images was collected as well from all presented cases.

3.1. Surgical Treatment

If patients suffered from lymphedema, LVA was usually performed on the knee and/or upper ankle joint of the affected extremity. To identify the appropriate localization of LVA, ICG and patent blue dye were injected preoperatively: On the evening before surgery, 250 µl of ICG were injected intra- and subcutaneously into the first and fourth interdigital space of the foot on the affected leg and patients were asked to move the leg and/or walk to assure appropriate distribution. In the morning of the surgery day, 250 µl of Patent blue were additionally injected into the same injection points. In fact, preoperative ICG lymphography is a well-established tool to identify functional lymphatic vessels. Thanks to a near-infrared camera, injected ICG can be visualized and a normal linear pattern indicates functional lymphatic vessels, whereas an abnormal dermal backflow pattern is an indicator of damaged lymphatics and lymphedema [22]. Patent blue dye injection enables the visualization of functional lymphatics for the naked eye and has therefore proven to be simple and effective way for mapping suitable subdermal lymphatic vessels [23].

Once the correct LVA localization was found, the skin was incised, and functional lymphatic vessels were visible thanks to patent blue dye. After subcutaneous dissection and preparation of functional lymphatic vessels, an equivalent vein was prepared for anastomosis. After clipping of the lymphatic vessels and the veins as well as the exclusion of venous backflow, the LVA was performed with 11-0 sutures. Functionality of the anastomosis was proven via ICG-fluorescent imaging (Figure 1). Thereafter, layer-by-layer closure of the wound was performed, and a splint was applied to prevent excessive movement after loose bandaging of the extremity. Manual lymphatic drainage and compression therapy were prescribed postoperatively.

Figure 1: Intraoperative ICG. (A) The native picture of an end-to-side anastomosis is shown. (B) The near infrared mode and the (C) merged mode of the camera system provide proof of the functionality of the anastomosis.

If patients suffered from lymphocele, lymphocele resection and lymphatic vessel clipping were performed. To localize the lymphatic vessels to be clipped, ICG and patent blue dye were injected at the beginning of surgery to identify the afferent lymph vessels. After localization of afferent lymphatic vessels, clipping was performed, and the lymphocele capsule was resected if possible.

Postoperatively, patients were instructed to continue with compression therapy and manual lymphatic drainage. Patients were controlled one, three and six weeks, three months, six months, and one year postoperatively.
4. Results

Patients had an age range between sixty-four and seventy-nine years and suffered from lymphatic complications including lymphedema, lymphatic fistula and/or lymphocele following sarcoma resection of the lower extremity. Two patients suffered from liposarcoma and one from clear cell sarcoma. Two patients had additional resection of inguinal lymph nodes and two patients underwent radiation therapy following tumor resection. All sarcomas presented at least one recurrence after first resection. All patients presented lymphedema stage II or III of the affected extremity and two patients had lymphocele of the affected groin. One of the patients with the lymphocele had an additional lymphatic fistula. Lymphocele resection and lymph vessel clipping was performed in all patients with lymphocele and LVA was performed in all patients. LVAs were performed medially on the knee, the lower leg, and/or the upper ankle joint. An overview of these data is given in (Table 1 and Table 2).

Table 1: Demographic data of patients. The case series included one woman and two men aged between 64 and 79 years. They suffered from clear cell sarcoma, pleomorphic liposarcoma and liposarcoma of the lower extremities.

<table>
<thead>
<tr>
<th>Cases no.</th>
<th>Sex</th>
<th>Age</th>
<th>Sarcoma type</th>
<th>Sarcoma localization</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>female</td>
<td>64</td>
<td>clear cell sarcoma</td>
<td>right knee</td>
</tr>
<tr>
<td>2</td>
<td>male</td>
<td>79</td>
<td>pleomorphic liposarcoma</td>
<td>left thigh</td>
</tr>
<tr>
<td>3</td>
<td>male</td>
<td>69</td>
<td>liposarcoma</td>
<td>right thigh</td>
</tr>
</tbody>
</table>

Table 2. Lymphatic complications and lymph surgery. Two patients were affected by stage II lymphedema and one patient of stage III lymphedema. Two patients presented additional lymphocele. LVA was performed in all patients and lymphocele was resected in the affected patients including afferent lymph vessel clipping.

<table>
<thead>
<tr>
<th>Cases no.</th>
<th>Lymphedema stage</th>
<th>Lymphatic complications</th>
<th>Lymph surgery procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>II</td>
<td>lymphedema</td>
<td>LVA lower leg medially and upper ankle joint</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lymphocele resection, lymph clippings (7x), LVA left knee medially and upper ankle joint</td>
</tr>
<tr>
<td>2</td>
<td>III</td>
<td>lymphedema, lymphocele, lymphocutaneous fistula</td>
<td>LVA right knee medially</td>
</tr>
<tr>
<td>3</td>
<td>II</td>
<td>lymphedema, lymphocele</td>
<td></td>
</tr>
</tbody>
</table>

In the postoperative controls, all lymphoceles were dissolved, and the lymphatic fistula was completely healed. Regression of lymphedema was observed in all patients. All patients underwent manual lymphatic drainage daily for the first three weeks and then it was gradually reduced to one/two times a week. Compression therapy was prescribed as well for at least six months.

5. Case Presentation

5.1. 1st Case: Our first case was a sixty-four years old woman who suffered from clear cell sarcoma of the right knee. Metastatic lesions were present in the inguinal lymph nodes. After several resections of the tumor and recurrent tumor, as well as the removal of the inguinal lymph nodes, the patient developed stage II lymphedema of the right leg. She was admitted to our clinic five years after the last resection and LVA was planned. LVA was performed medially on the lower leg and in the area of the upper ankle joint. Postoperatively, successful lymphedema regression was observed (Figure 2).

Figure 2: Pre- and postoperative pictures of case 1. (A and C) After sarcoma resection of the left knee, the patient presented lymphedema stage II of the left leg. (B and D) Following LVAs on the lower leg medially and of the upper ankle joint ventrally, lymphedema regression was observed, especially around the ankle and the calf (white arrows).

5.2. 2nd Case: Our second case was a seventy-nine years old man with lip sarcoma of the left thigh. Due to tumor recurrence, radiotherapy was performed after repeated resection, and the patient developed a lymphocele and a lymphatic fistula of the left groin. ICG fluorescent imaging confirmed this diagnosis (Figure 3). Moreover, stage III lymphedema with tension bullae appeared on the left leg. Three years later, the lymphocele was resected and covered with a vertical rectus abdominis muscle (VRAM)-flap. However, the lymphocele did not dissolve and got infected and the
patient presented to our clinic. Lymphocele resection and lymph vessel clipping of seven lymph vessels were performed as a first surgical step. Nevertheless, the lymphocele, the lymphatic fistula and the lymphedema persisted, so LVA was planned four months later. Three LVAs were performed on the left knee and the area of the upper ankle joint. Surprisingly, after only three weeks, the lymphatic fistula was completely healed, and the lymphocele was dissolved. Moreover, the lymphedema was significantly regredient and the tension bullae had completely disappeared (Figure 4).

5.3. 3rd Case: Our third case was a sixty-nine years old male patient with liposarcoma and of the right thigh and after initial resection, tumor recurrence was found. Concomitantly with tumor resection, inguinal lymph node resection was performed. Moreover, the patient underwent adjuvant radiation therapy. After a few months, lymphocele of the right groin and lymphedema of the right leg appeared. As a first surgical step, lymphocele resection and lymph vessel clipping of two lymphatic vessels were performed and LVA was performed on the right knee. Postoperatively, lymphedema and lymphocele regression were confirmed (Figure 5).

Figure 3: ICG-fluorescent imaging of the lymphocele. ICG-fluorescent imaging displays abnormal lymphatic backflow pattern as well as coloration of the drainage fluid (black arrows) from the inguinal lymphocele of case 2. A part of the VRAM flap can be observed as well.

Figure 4: Pre- and postoperative pictures of case 2. (A and C) The patient suffered from lymphatic fistula and lymphocele of the left groin, from which liposarcoma was previously resected and the tissue defect was covered by a VRAM flap. Moreover, the patient had stage III lymphedema of the left leg and presented severe tension bullae on the lower leg. (B and D) After lymphocele resection, lymph vessel clipping and LVAs on the knee (medially) and the upper ankle joint, the lymphatic fistula completely healed, and the lymphocele gradually dissolved. Moreover, lymphedema decreased (white arrows) and tension bullae were completely absent.

Figure 5: Pre- and postoperative pictures of case 3. (A and C) Following liposarcoma resection of the right thigh, the patient suffered from lymphocele and lymphedema. The lymphocele was resected and LVA was performed on the right knee. (B and D) Postoperatively, the lymphocele dissolved, and lymphedema was regredient.

6. Discussion

In this case series, we presented three patients with secondary lymphedema, lymphocele and/or lymphocutaneous fistula following sarcoma resection. LVA was performed in all patients: in one patient as a singular surgical intervention and in two patients in addition to lymphocele resection with moderate outcome. LVA successfully led to a reduction of lymphocele and healing of fistulas. Lymphedema decreased in all patients. No complications or lymphedema recurrence was observed in the weekly and monthly controls after surgery.

In the western world, the most common cause of secondary lymphedema are cancer-related treatments such as surgical resection, radiotherapy and chemotherapy [24-28]. This represents an additional biopsychosocial burden for patients, as aesthetic appearance, basic movements, sports, adequate fitting of clothes and
other daily activities are impaired, leading to significantly reduced social well-being [29]. Thus, it is important to mention lymphatic complications in patient education and to inform them on treatment options.

Complex decongestive therapy is the first step in lymphedema treatment, including compression therapy, manual lymphatic drainage, exercise and skin care [30, 31]. The use of diuretics has been proven to be ineffective and is not indicated in lymphedema treatment [32]. On the contrary, diuretics may worsen lymphedema by accelerating fibrosis via concentration of proteins in the extracellular space [32].

Yet if conservative treatment remains ineffective, surgical treatment is indicated. In this regard, ablative surgical procedures such as liposuction [33] or tissue excision have been described [34], but are not an option of first choice, but rather indicated in advanced lymphedema, when fibrotic tissue transformation has occurred and physiological surgical procedures such as lympholymphatic bypass, LVA or vascularized lymph node transfer are not expected to provide any relief [24]. The surgical gold standard in the treatment of lymphedema includes LVA [35, 36], vascularized lymph node flap transfers [37, 38] and lymphatic vessel transplantation [39]. However, lymphatic vessel transplantation may result in lymphedema of the donor site and thus, LVA and the transfer of vascularized lymph node flaps is generally preferred.

The LVA technique used in our patients was the sleeve-in techni-que. However, other techniques such as the “octopus” technique have been referred to as an effective measure [40]. In a systematic review of Scaglioni et al. it is reported that approximately 50-100 % of patient’s experience limb circumference decrease and cellulitis episodes are reduced following LVA [14]. Conversely, in a systematic review of Rosian et al., report that no conclusions on effectiveness of LVAs can be made due to the methodological shortcomings of available studies [41].

Cancer treatment is mostly discussed in an interdisciplinary tumor board preoperatively. In this regard, it should be important to discuss potential complications and to rapidly recognize their onset. Especially lymphatic complications should be treated appropriately since the beginning and if tumors are localized in areas of potential lymphatic damage, preventive lymphatic surgery such as LVA may be planned [42]. For instance, simultaneous microsurgical breast reconstruction and vascularized lymph node transfer are possible [43]. In this surgical procedure, the adipocutaneous flap supplied by the deep inferior epigastric vessels is utilized to reconstruct the breast connecting the vascular supply to the internal thoracic vessels [43]. The lymph nodes surrounding the contralateral superior epigastric vessels can be harvested and placed in the axilla [43]. LVA may be performed as well as preventive measure in vast tumor and lymph node resections.

7. Conclusion
LVA provides successful regression of lymphedema and dissolving of lymphatic fistulas. Lymphedema is a diagnose worth recognizing in time to suggest the adequate treatment and prevent the patients from undergoing the sequelae of the disease. Moreover, prompt treatment of lymphatic fistulas may prevent infections and carriage of drains. In this regard, prophylactic LVA may be considered in resections in areas at risk of lymphatic injury and complications.

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References


