Lymphovenous bypass surgery for the treatment of Kaposi sarcoma-associated lymphoedema:

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Key words

Kaposi sarcoma, lymphovenous anastomosis, lymphovenous bypass, lymphoedema

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Abstract

Lymphoedema is a sequela of Kaposi sarcoma (KS) that often does not respond adequately to chemoradiotherapy and complete decongestive therapy (CDT). Lymphovenous bypass (LVB) is an option for patients whose lymphedema persists despite conservative treatment. We present the case of a 59-year-old man with a diagnosis of KS due to human immunodeficiency virus (HIV), who presented with progressive, bilateral lower-extremity swelling refractory to CDT. This patient's lymphoedema was successfully treated with LVB, illustrating the applicability of LVB for the treatment of KS-associated lymphoedema.

Kaposi sarcoma (KS) is an angioproliferative neoplasm associated with infection by KS-related herpesvirus (KSHV, also known as human herpesvirus-8 [HHV-8]; Etemad and Dewan, 2019). Infection often occurs from salivary transmission.

The wide clinical spectrum of KS suggests multiple mechanisms of pathogenesis, which are classified into epidemiological subtypes: classic, iatrogenic, African endemic and epidemic HIV/AIDS (Schneider and Dittmer, 2017). In all subtypes of KS, lymphoedema may be present due to altered lymphatic drainage and destructive inflammation caused by HHV-8 infection of endothelial cells (Pantanowitz and Duke, 2008; Santos et al, 2013; Schneider and Dittmer 2017; Cesarman et al, 2019). Although early antiretroviral therapy has made the development of lymphoedema secondary to KS less common, the condition still presents in up to 57% of affected individuals and remains debilitating (Volkow-Fernández et al, 2022).

Lymphovenous bypass (LVB), also referred to as a lymphovenous anastomosis, is a minimally invasive supermicrosurgical procedure to treat lymphoedema. This intervention is considered in cases that cannot be controlled by conservative therapy alone, such as compression wraps and manual lymphatic drainage (Kareh and Xu, 2020).

Here, the authors present the successful treatment of KS-associated lymphoedema refractory to conservative treatment using LVB.

Materials and methods

Case report

The patient was a 59-year-old Caucasian man with no known past medical history who was referred for evaluation of bilateral lower-extremity swelling. The swelling had been present for 10 years with episodes of recurrent cellulitis requiring IV antibiotics.

The patient's initial medical workup led to a diagnosis of HIV in 2008, with associated KS, as determined by an inguinal lymph node biopsy. The patient received seven rounds of chemotherapy, with evidence of recurrence and subsequent radiation treatment. In 2009, while undergoing a course of chemotherapy, the patient developed lymphoedema. He was treated with garments and a lymphoedema compression pump. However, the patient discontinued use of both the pump and the stockings due to lack of improvement with this therapy. His oedema continued and impaired his ability to ambulate comfortably and wear shoes. He expressed interest in pursuing an alternative method of treatment that would provide better outcomes when used in coordination with complete decongestive therapy (CDT).

On examination, the patient was noted to have oedema extending from below the knees to the dorsum of both feet (*Figure 1*), with worse swelling of the right lower extremity compared to the left. Open wounds, pitting and adiposity were present in bilateral lower extremities. Computed tomography of the chest, abdomen and pelvis, as well as venous duplex ultrasonography results,

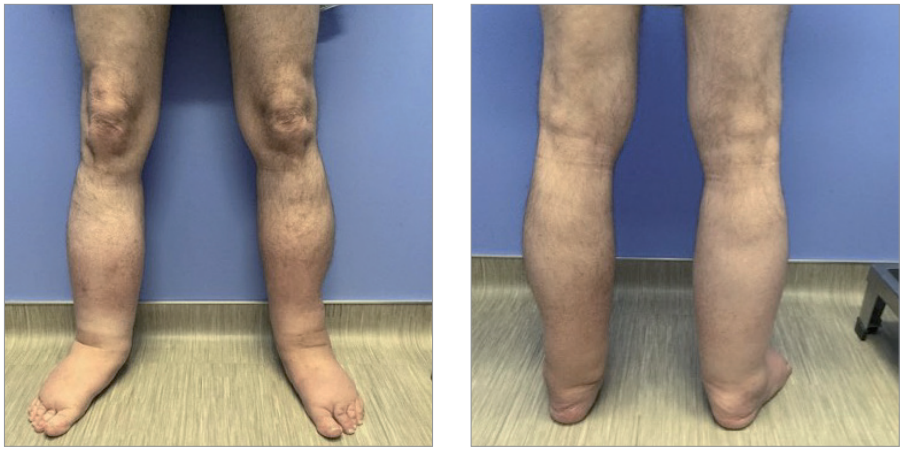

Figure 1. Left: Anterior view of bilateral lower-extremity swelling, demonstrating more severe lymphoedema on the right side. Right: Posterior view.

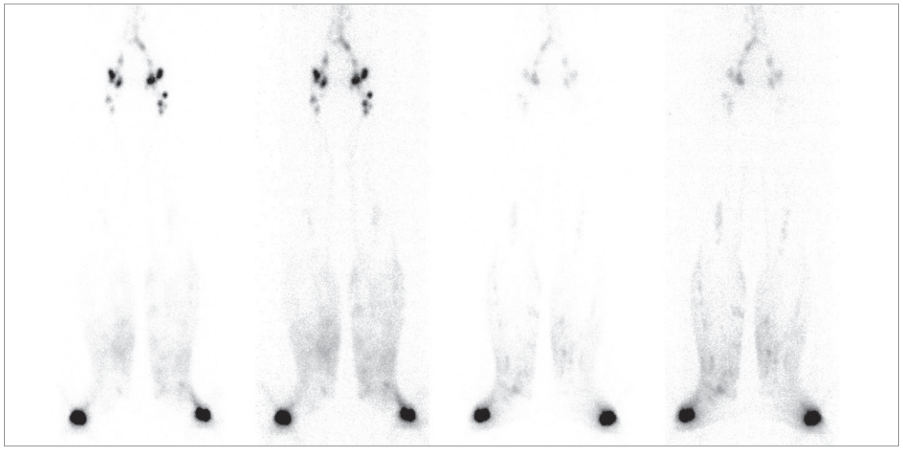

Figure 2. Lymphoscintigraphy results of a 59-year-old patient presenting with bilateral lower-extremity swelling. Results showed marked bilateral lower-extremity oedema with lymphangiectasia and backflow bilaterally.

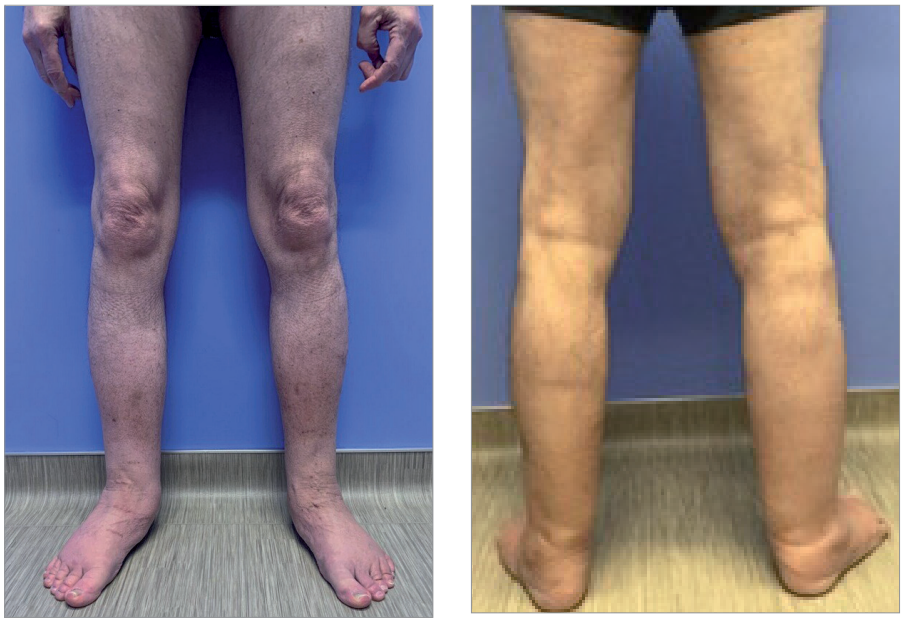

Figure 3. Left: Anterior view of 21-month postoperative results after three LVB surgeries, showing significant improvement bilaterally. Right: Posterior view.

were normal. Lymphoscintigraphy of the lower extremities showed backflow and lymphangiectasia bilaterally (*Figure 2*).

The patient underwent right lower-extremity LVB using supermicrosurgical techniques. In brief, indocyanine green was injected in the foot and an infrared camera was used to map out the lymphatic channels. Prominent dermal backflow was seen at the level of the calf. Therefore, the lymphatics were bypassed distal to this point by making an incision at the ankle. Four usable lymphatic vessels and four veins were found in this location, allowing for four LVBs to be performed. The afferent lymphatics and adjacent veins were each cut and anastomoses were performed in end-to-end fashion using 11-0 nylon suture. Lymphazurin blue was injected to confirm appropriate outflow of lymphatic fluid and patency of the bypass.

Next, an incision was made more proximally around the knee, at the site of another lymphatic channel target. This channel was anastomosed to a neighbouring vein, allowing decompression of the lymphatic fluid to prevent backflow. The incisions were subsequently closed and the leg was wrapped with short-stretch bandage.

The patient received regular follow-up with an occupational therapist to institute CDT, which included diligent use of compression stockings and wraps, a lymphoedema pump, and manual lymphatic drainage. At 2 months post-op, the patient reported marked improvement of lymphoedema symptoms in his right lower extremity.

The decision was made to similarly address the patient's contralateral lower-extremity lymphoedema with LVB, 6 months later. He tolerated the procedure well and had no post-op complications. Regular appointments with occupational therapy continued. The patient endorsed significant improvement in lymphoedema symptoms bilaterally; however, he reported persistent swelling around his right foot and ankle. Due to his positive response to prior surgical intervention, additional right lower-extremity bypass surgery was planned. Next, the patient received an additional three distal LVBs through an incision placed medially on the foot.

Since the final surgery nearly 2 years ago, the patient says he has no ambulatory dysfunction or problematic swelling of his lower extremities. The patient is pleased

with his functional improvement, as well as the aesthetic results (*Figure 3*). He is continuing his usual treatment regimen of compression garments, as well as lymphoedema-specific exercise under the supervision of a certified therapist.

Results

At the initial pre-operative appointment, the left lower extremity measured 39.2 cm and 50.0 cm in circumference at the lateral malleolus (LM) and superolateral patella (SP), respectively (*Table 1*). The right lower extremity measured 41.3 cm and 49.3 cm at the LM and SP, respectively.

Three months after the first LVB, the left lower-extremity lymphoedema measured 36.0 cm at the LM and 49.0 cm at the SP; the right lower-extremity measured 40.5 cm at the LM and 47.5 cm at the SP.

Two years after two additional LVB surgeries, the left lower extremity measured 31.8 cm and 43.0 cm at the LM and SP, respectively; the right lower extremity measured 35.0 cm and 43.0 cm at the LM and SP, respectively.

Total reduction in limb circumference on the left side at 40 months post-op was 18.9% at the LM and 14.0% at the SP. Similar results were seen on the right side, with a reduction of 15.3% at the LM and 12.8% at the SP.

At appointments with occupational therapists, recordings of lower-extremity circumference were taken for the metatarsal heads (forefoot), the arch of the foot, the heel and ankle (Y-heel), and at 4 cm increments starting from the base of the heel and moving proximally along each lower limb (*Table 2, overleaf*). Summing the squares of the limb's circumference measurements at each time point generates an estimate of limb volume to compare the overall reduction in swelling between the first and subsequent follow-up appointments with occupational therapy. *Figure 4* shows a comparison of the progress for each lower-extremity's volume measurements along with the points at which LVB was performed. The final, measured reduction in volume was 25% and 26% for the left lower extremity and right lower extremity, respectively.

Table 1. Lymphoedema measurements.

	Left lower extremity		Right lower extremity	
	Lateral malleolus	Superolateral patella	Lateral malleolus	Superolateral patella
Pre-operative	39.2 cm	50.0 cm	41.3 cm	49.3 cm
3 months post-op	36.0 cm	49.0 cm	40.5 cm	47.5 cm
9 months post-op	34.6 cm	47.6 cm	36.3 cm	47.8 cm
15 months post-op	33.3 cm	46.0 cm	36.3 cm	46.2 cm
40 months post-op	31.8 cm	43.0 cm	35.0 cm	43.0 cm
Difference (%)	−18.9%	−14.0%	−15.3%	−12.8%

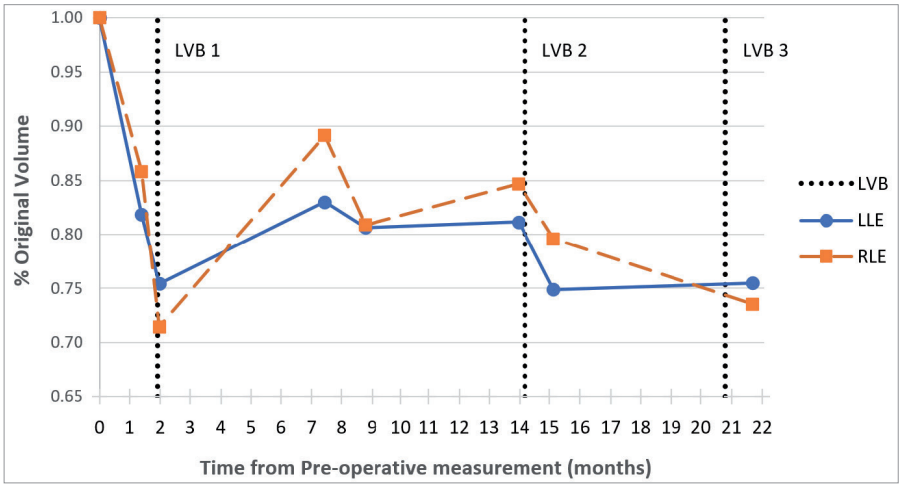

Figure 4. Overall volume measurements of left lower extremity (LLE) and right lower extremity (RLE) after three LVB surgeries.

Discussion

KS comprises a spectrum of disease, however all forms may present with lymphoedema due to altered lymphatic drainage, regional lymph node involvement, increased inflammatory cytokines, or lymphatic vessel obstruction caused by HHV-8-induced proliferation of endothelial cells (Pantanowitz and Duke, 2008; Santos et al, 2013; Schneider and Dittmer 2017; Cesarman et al, 2019). Reports demonstrate that treatment of KS with chemoradiotherapy results in modest reduction of lymphoedema symptoms; however, most patients continue to have burdensome swelling (Dean et al, 2017; Schalk and Katsounas, 2019).

This patient had the typical mild improvement of his lymphoedema after chemoradiotherapy, but ultimately had refractory oedema and cellulitis. Other reports have corroborated that the natural course of KS-associated lymphoedema leads to similar complications of cellulitis and hospitalisation (Volkow-Fernández et al, 2022).

It is the authors' opinion that chemotherapy and radiation should routinely be attempted prior to lymphatic surgery. However, patients with KS-associated lymphoedema refractory to conventional therapy may benefit from surgical interventions to redirect lymphatic drainage.

The current mainstays of treatment consist of conservative measures, such as manual lymphatic drainage, physical therapy, compression bandaging and local skin care; these are known collectively as CDT (O'Donnell et al, 2020). Evidence regarding CDT suggests that this treatment modality does result in improved quality of life; however, it does not offer curative potential (Fish et al, 2020). Furthermore, CDT is a labour-intensive regimen that requires lifelong compliance, as well as access to specialised therapists (Schaverien and Coroneos, 2019).

Table 2. Patient measurements before and after each lymphovenous bypass procedure.

Time (months)	Side	Forefoot (cm)	Arch (cm)	Y-heel (cm)	4 cm (cm)	8 cm (cm)	12 cm (cm)	16 cm (cm)	20 cm (cm)	24 cm (cm)	28 cm (cm)	32 cm (cm)	36 cm (cm)	40 cm (cm)	44 cm (cm)	%
1	LLE	26.5	28.5	36.5	35	32.8	34	35.5	38	40.5	41.5	40.8	38.3	35.5	35.4	1.00
	RLE	26.5	28.5	37.5	37	35	35	37	40	42	43	43	40	35.5	35	1.00
2	LLE	25.5	26	33	31.5	30	29.5	30	32.5	34	36	38	37	34	34.5	0.82
	RLE	24.5	26	34.5	32	31.5	32	35.5	36	38	41	39	37	35	35	0.86
LVB #1																
3	LLE	24	25	33	30.5	27	26.5	27.5	29	32	36	38	36.5	34	33	0.75
	RLE	23.5	25	34	31	28	26	27	30	32.5	35	38	37	34	33.5	0.71
8	LLE	25	27	35	33	29	29	29	30	33.5	37	38	37.5	35	36	0.83
	RLE	24.5	29	36	36	32	32	34	36	38.5	39	39	38	37	36	0.89
9	LLE	24	25	33	31	26	27	29	31.5	35	37	38	37.5	36	36	0.81
	RLE	23.5	25.5	33	31	28	29	32	35	38	39	39.5	36.5	36	36	0.81
14	LLE	23.7	23.8	32.4	31.5	25.6	29.9	31.3	33.1	35.7	37.5	36	34.5	35.9	37	0.81
	RLE	24.6	26.8	34.4	33.1	28.6	30.9	35	37	38.2	38.1	38	37.1	35.2	37	0.85
LVB #2																
16	LLE	24	25	32	30.5	26.5	27	28	30	33	36	36	35.5	33	34.5	0.75
	RLE	24	26	34	34	30	30	32	34.5	36	37.5	37.5	35.5	34	35	0.80
LVB #3																
22	LLE	24.5	25	33	33.5	25.5	25.5	27	29	33	35.5	36.5	36	33.5	34.5	0.75
	RLE	24	25	34	33	27	27	27.5	30.5	34	35.5	37	37	35	34.5	0.74

Measurements of the patient's left lower extremity (LLE) and right lower extremity (RLE) circumference, including the metatarsal heads (forefoot), foot arch, heel and ankle together (Y-heel pattern), and at 4 cm increments moving proximally. The first column indicates the time from first pre-op measurement. Each lymphovenous bypass (LVB) is noted in the first column. The final column shows the overall change in volume for each limb compared to each limb's initial measurement at presentation.

Several surgical options exist for patients whose lymphoedema cannot be adequately controlled by conservative measures. Debulking procedures, including suction-assisted lipectomy and excision of excess extremity tissue have been shown to improve skin hygiene and functional status (Kung et al, 2017).

Advances in microsurgical techniques have led to the development of vascularised lymph node transplant (VLNT) and LVB, which attempt to restore normal lymphatic physiology. VLNTs can be used in patients whose native lymph nodes and vessels are too dysfunctional or scarred to proceed with LVB (Kareh and Xu, 2020).

In the setting of HHV-8 infection of endothelial cells seen in KS, conservative lymphoedema treatment typically cannot overcome the severe lymphatic dysfunction (Brambilla et al, 2006). It is hypothesised that advanced surgical options, such as VLNTs and LVBs, are more suitable options when the underlying pathophysiology is an altered lymphatic system (Pantanowitz and Duke, 2008; Santos et al, 2013; Schneider and Dittmer 2017; Cesarman et al, 2019).

LVB has been described in the treatment of numerous pathologies, commonly post-mastectomy lymphoedema, as well as uterine cancer-related and genital lymphoedema (Yamamoto et al, 2011; 2015; 2017). Additionally, LVB has demonstrated efficacy not only in improving lymphoedema after breast cancer therapy, but also in preventing lymphoedema when performed in the prophylactic setting (Chang et al, 2013; Agarwal et al, 2020).

We now report the first case of the successful use of LVB for the treatment of KS-associated lymphoedema. We believe LVB is a versatile tool that can be applied to treat lymphoedema across diverse aetiologies and anatomical locations. Bypasses can be performed on an outpatient basis, with very low risk to the patient yet with the potential for significant improvement in symptoms and quality of life.

After failing disease-directed treatment and conservative management, the authors' patient demonstrated notable functional and aesthetic improvement in his lower-extremity oedema over a relatively short period of time. He had multiple open lymphatic channels, and thus multiple bypasses were able to be executed over 2 years, with the goal of optimising his physiologic ability to reroute lymphatic fluid.

We believe LVB may provide an excellent therapeutic alternative for patients with KS-associated lymphoedema whose symptoms are refractory to conservative treatments. Physicians faced with these challenging patients should be aware of this surgical option and should seek out trained microsurgeons for further evaluation.

Lymphoedema is a common complication of KS, due to HHV-8 infection of endothelial cells and resultant lymphatic system dysfunction. Lymphoedema management in KS traditionally involves

treating the underlying sarcoma with chemotherapeutics and radiation. However, medical therapies only modestly improve functional limb status and symptoms in patients with KS-associated lymphoedema. Microsurgical options, such as LVB, may provide an adjunct to conservative treatment, particularly for patients in whom decongestive therapy has failed.

The authors' successfully applied LVB to improve lower-extremity lymphoedema symptoms and quality of life in a patient who had exhausted other options. As demonstrated by this case, LVB can be an effective alternative for patients with lymphoedema due to KS and should be carefully considered.

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