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May-Thurner Syndrome and Lymphedema Reconstruction

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Background: May-Thurner syndrome (MTS) is an anatomical variant that results in compression of the left common iliac vein by the right common iliac artery. Although often asymptomatic, lower extremity swelling/edema, deep venous thrombosis, post-thrombotic syndrome, and eventual lymphedema (due to long-standing venous obstruction) can develop. The clinical management of patients presenting for lymphedema surgery with concomitant or undiagnosed MTS is not well described.

Methods: This review investigates two patients who were evaluated for unilateral lower extremity lymphedema, both of whom were subsequently diagnosed with MTS. Standard imaging (including lymphoscintigraphy, indocyanine green lymphangiography, and magnetic resonance venography) were performed to identify proximal venous obstruction. Treatment was accomplished using vascular surgical management, including stenting of the iliac vein before lymphedema reconstruction with vascularized lymph node transfer and multiple lymphovenous bypass.

Results: Both patients we examined in this review had improvement of lymphedema with vascular surgical management. Literature review reveals that MTS has an incidence as high as 20% in the population, although commonly unidentified due to lack of symptomatology.

Conclusions: There are no studies documenting the incidence of MTS in patients referred for lymphedema surgical management. Routine studies should be obtained to screen for proximal venous obstruction in patients presenting for surgical management of lower extremity lymphedema. Additional research is needed regarding the approach to managing patients with both MTS and lymphedema. Careful observational and prospective studies may elucidate the appropriate time interval between venous stenting and lymphedema microsurgical reconstruction.
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INTRODUCTION

May-Thurner syndrome, also known as iliac vein compression syndrome, is characterized by left common iliac vein compression by the right common iliac artery.[1,2] This finding can be visualized on magnetic resonance venography (MRV) (Fig. 1). Despite frequently presenting in women and on the left side, rare right-sided presentations also occur.[2,3] This condition can present as an asymptomatic anatomic anomaly or result in symptoms including lower limb pain and edema, deep vein thrombosis, claudication, and chronic venous insufficiency. The percent of occurrence in the general population is largely unknown because most patients are asymptomatic; however, estimates are as high as 20%.[2,4] Previous studies have demonstrated an incidence of May-Thurner syndrome in 18%–49% of patients with deep vein thrombosis of the left leg.[4–6] This prevalence warrants further investigation into patients who have lower limb edema, which may be due to undiagnosed May-Thurner syndrome.

At this time there is no standard protocol for the diagnosis and treatment of May-Thurner syndrome.[7,8]

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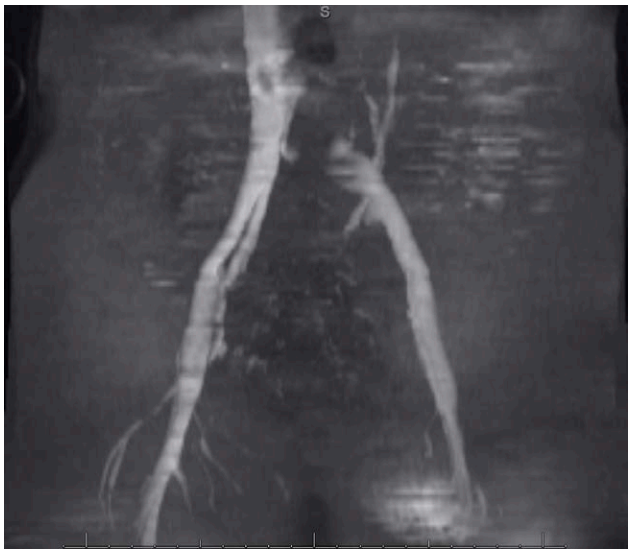

Fig. 1. MRV demonstrating compression of left common iliac vein by overlying iliac artery in case 1.

The techniques currently being employed for diagnosis include color Doppler ultrasound, intravascular ultrasound (IVUS), computer tomography angiogram (CTA), MRV, and contrast venography. Contrast venography with IVUS is the current diagnostic gold standard. These two techniques allow for accurate assessment of the severity and location of the stenosis, which consequently guides the determination of stent use in treatment.[9–11] Current treatment typically involves an endovascular approach with angioplasty and stent placement.[12,13] Although this is generally well-tolerated and improves symptoms, there are complications including recurrent stenosis, in-stent obstruction, and thrombosis.[8,13]

Lymphedema, a common finding in patients with May-Thurner syndrome, is classified as abnormal accumulation of lymphatic fluid in interstitial spaces. The accumulation of lymph leads to downstream effects, including adipocyte proliferation and fibrous tissue deposition.[1,14,15] Lymphedema can be classified as either occurring due to malformation of the lymphatic system (ie, primary) or more commonly occurring as a result of obstruction or destruction of normally formed lymphatic channels (ie, secondary).[15] Various factors can lead to its development including infection, cancer, obesity, hereditary conditions, and many other underlying etiologies.[14] With lymphedema affecting about one in 30 people in the world, it is a prominent health concern requiring medical attention and therapy.[16] First-line treatment typically involves conservative measures, including compression garments and physical therapy.[1] However, when conservative measures are not adequate, microsurgical techniques such as lymphovenous anastomosis (LVA) and vascularized lymph node transfer (VLNT) have recently been proposed to show a significant benefit in patient outcomes.[17–20] This case series aims to describe two patients diagnosed with May-Thurner syndrome during their preoperative work up for lymphedema, who then underwent staged iliac vein stenting followed by vascularized lymph node transfer and multiple lymphovenous bypasses to relieve symptoms of chronic lower extremity lymphedema.

Takeaways

Question: Can traditional surgical treatment for lymphedema be applied to patients with May-Thurner syndrome (MTS)?

Findings: Two patients with MTS underwent successful lymphovenous anastomosis (LVA) and vascularized lymph node transfer (VLNT), with one patient undergoing liposuction. Both patients reported improvements in lymphedema, increases in physical activity, and were aesthetically pleased with their surgical outcome.

Meaning: LVA, LVNT, and liposuction are surgical procedures that have demonstrated to lead to successful patient outcomes in May-Thurner syndrome patients who have lower extremity lymphedema.

Lymphovenous Anastomosis

All patients undergoing planned lymphovenous bypass (LVB) are injected with indocyanine green and isosulfan blue dye at the first and third webspace of the affected limb toes. Additional dyes are injected at the mid-calf and lower thigh levels. The indocyanine green allows for visualization of lymphatic drainage patterns while the blue dye provides intraoperative confirmation of identification of lymphatic channels. Patients are then graded in severity by the Cheng lymphedema grading system.[21] Utilizing this grading system, we decided to perform LVB for grades 1 and 2, and both VLNT and LVB for grades 3 and 4. A vein finder is used to mark superficial veins, and locations where lymphatic channels are found near superficial veins are targeted for exploration and LVB. The number of the lymphovenous bypasses varies from patient to patient and is mainly dependent on anatomic and technical factors related to the proximity and orientation of venous and lymphatic vessels.

At the prior marked locations, multiple small 2-cm incisions are made and deepened down to identified subdermal and subcutaneous vasculature. Using an operative microscope, each surgical site vascular exploration is performed. Appropriate lymphatic and venous vessels are identified, and lymphovenous anastomosis is performed either with standard end-to-end anastomosis or by intussuscepting the smaller lymphatic channel inside the venule with the assistance of a 10-0 nylon or 11-0 nylon "U-stitch." Standard wound closure is performed.

Vascularized Lymph Node Transfer

The vascularized lymph node is harvested from the right supraclavicular region, as described by Maldonado et al.[22] After the neck and superior chest is prepared and draped, an incision is planned 2 cm above the level of the clavicle, lateral to the lateral border of the sternocleidomastoid muscle. The incision is deepened down to the subplatysmal plane and the sternocleidomastoid muscle is dissected and retracted medially. The external jugular vein is identified and used as the lateral extent of dissection.

The right internal jugular vein and the lympho-fatty fascia tissue is dissected enbloc from the lateral border of the internal jugular vein, the contents of Zone 5B of the neck. The proximal and distal transverse cervical artery along with the transverse cervical vein is identified. The lympho-fatty fascia flap is then dissected circumferentially and vasculature is ligated both distally and proximally, once the recipient vessels are prepared. Anastomosis to the vena comitans of the dorsalis pedis is performed at the dorsal foot with the appropriately sized venous coupler. The arterial anastomosis is performed between the proximal dorsalis pedis and proximal transverse cervical artery with 9-0 nylon sutures in preferably end-to-side fashion. If end-to-end arrangement is required, then every effort is made to use the distal transverse cervical artery to the distal cut end of the dorsalis pedis as a flow through flap. The flap is then inset and skin flaps are laid over part of the lymph node flap with absorbable sutures. A full thickness skin graft is harvested from the groin and used to cover the remaining exposed area of the lymph node flap. The skin graft is inset with absorbable suture and nonadherent, noncompressive dressings are applied.

CASE 1

A 70-year-old woman presented for evaluation of left lower extremity lymphedema since approximately 2014 (Fig. 2). The patient had a medical history of vaginal cancer that was treated with surgical resection along with neoadjuvant chemoradiation therapy. She complained of difficulty with ambulation and limitations to activities of daily living. In addition, the patient stated she had left leg pain along with pressure for the past 5 years. Her neurovascular examination was normal and she did not have signs of venous insufficiency apart from limb swelling. The patient's reported height was 5 ft 5 in, weight was 159 lb, and her BMI was 26.49 kg per m^2. At initial visit, lower extremity measurements were taken with the patient sitting. The leg circumference was measured at distances starting at from the tip of the second toe and moving proximally (Table 1). Lymphoscintigraphy was performed and demonstrated dermal back flow patterns involving the left lower extremity from the toes up to the lower-thigh. MRV was performed to evaluate for potential sources of venous obstruction; imaging demonstrated compression of the left common iliac vein in the typical location of May-Thurner syndrome. Before diagnosis, there was no clinical suspicion of May-Thurner syndrome. The patient then underwent pelvic venography with intravascular ultrasound along with angioplasty and stent placement of the left common iliac and external iliac veins with vascular surgery. The patient was observed over a year after undergoing iliac vein stenting, but continued to have residual swelling of her left lower extremity. Due to minimal improvement in her left lower extremity swelling after stenting, the patient was counseled on further surgical management. She underwent lymph node transplant from right supraclavicular lymph nodes and six lymphovenous bypass of left lower extremity. The patient followed up over the course of 12 months, where it was noted that the patient had improvement of her lower extremity swelling and symptoms, but had residual swelling of her thigh, which was felt to be primarily fibroadipose in nature. Twenty-one months later, the patient returned for revision and soft-tissue volume reduction surgery with thigh liposuction. At the patient's most recent follow-up visit, bilateral leg circumferences were taken, and it was determined that the patient had an overall improvement of 21.43% 25-cm proximal to the toes and 5.64% 70-cm proximal to the toes (Table 1, Fig. 3). The patient noted significant increases in physical activity, resolution of lower extremity pain, and was very pleased with her results. In addition, she stated she would continue decongestive wrapping five to six times per week and would continue to exercise several times a week. Once her left lower extremity measurements stabilize, the next step would be to reduce the frequency of her wrapping.

Fig. 2. Case 1: Left lower extremity edema extending from the upper thigh to the foot before surgical evaluation by plastic surgery.

CASE 2

A 33-year-old woman presented for evaluation of left lower extremity lymphedema for the past 10 years, with worsening of symptoms (Fig. 4). The patient had a medical history significant for Hashimoto's thyroiditis, but the

Table 1. Case 1 Lower Extremity Circumferences Pre and Postoperative Measured Proximally from the Toes

Distance Proximal from Toes (cm)	Initial Left Lower Extremity Circumference (cm)	Post-surgical Left Lower Extremity Circumference (cm)	Initial Right Lower Extremity Circumference (cm)	Post-surgical Right Lower Extremity Circumference (cm)
25	28	22	23	23
30	33.25	26	21	22
40	45	35	30.75	30.5
50	45.5	40	32.5	32.5
70	48.75	46	37	37

etiology of her lymphedema was unknown. She did not have signs of lower extremity venous insufficiency apart from limb swelling. The patient's reported height was 5 ft 5 in, weight was 117 lb, and BMI was 19.47 kg per m^2. The patient has been consistent with wrapping her leg at least four times a week, massages her leg daily, and exercises on a treadmill three days a week. At initial visit, lower extremity measurements were taken with the patient sitting. Bilateral leg circumferences were taken and lymphoscintigraphy was performed, which demonstrated dermal back flow patterns involving the left lower extremity from the toes up to the mid-thigh (Table 2). An MRV was then conducted, which suggested moderate compression of the left common iliac vein by the crossing of the right iliac artery, confirming May-Thurner syndrome. Before diagnosis, there was no clinical suspicion of May-Thurner syndrome. The patient then underwent left lower extremity venography with intravascular ultrasound along with percutaneous stent placement of the left common iliac vein with vascular surgery. The patient continued to follow up 2 years after iliac vein stenting and continued to have residual swelling in her left lower extremity. Initially, the patient was apprehensive to engage in further surgical management; however, after counseling, the patient decided that surgical management was her next best step. The patient underwent lymph node transplant from right supraclavicular lymph nodes and two lymphovenous bypass of left lower extremity, as documented in the methods. At the patient's most recent follow-up, 4 weeks after

Fig. 3. Case 1: Reductions in left lower extremity edema 21 months after lymphaticovenous anastomosis, vascularized lymph node transfer surgery, and liposuction.

Fig. 4. Case 2: Left lower extremity edema extending from the lower thigh to the foot before surgical evaluation by plastic surgery.

Table 2. Case 2 Lower Extremity Circumferences Pre and Postoperative Measured Proximally from the Toes

Distance Proximal to Toes (cm)	Initial Left Lower Extremity Circumference (cm)	Post-surgical Left Lower Extremity Circumference (cm)	Initial Right Lower Extremity Circumference (cm)	Post-surgical Right Lower Extremity Circumference (cm)
25	24	22	21	21
30	31	31	22	24
40	40	37	29	29
50	40	39	30	29
70	51	45	34	34

surgery, she indicates that stiffness, discomfort, swelling, and pain has diminished. There was some superficial breakdown of the overlying full thickness skin graft. This was treated with local wound care with daily application of xeroform and gauze to allow re-epithelialization. She still has some limitations with activity, but has begun to walk short distances. Postoperative leg circumferences were measured and it was determined that the patient had an overall improvement of 8.33% 25-cm proximal to the toes and 11.64% 70-cm proximal to the toes in her left lower extremity (Table 2, Fig. 5). The patient stated that she would continue to follow with postoperative decongestive therapy, which consisted of exercising to the best of her ability and wrapping several times a week. Although she has experienced mild improvements, in the short term this is often related to the lymphatic leakage and drainage during the operation that occurs simply from making incisions. She will be followed over time to determine her long-term clinical outcome.

Fig. 5. Case 2: Reductions in left lower extremity edema four weeks after lymphaticovenous anastomosis and vascularized lymph node transfer surgery.

DISCUSSION

Although most patients with May-Thurner syndrome are asymptomatic, the most common presentation is with venous hypertension.[23] In addition, patients may present with episodic swelling and heaviness in the left lower extremity, which may progress to features of chronic venous insufficiency such as leg pigmentation, varicose veins, and venous ulcers.[24] It is unknown whether long-standing May-Thurner syndrome may result in isolated cases of lower extremity lymphedema. Nonetheless, due to its prevalence, it is our protocol to screen for iliac vein compression in patients with lymphedema. There are no current studies that have documented a treatment plan for lymphedema in patients who are found to have May-Thurner syndrome.

Both conservative and surgical techniques are utilized in the treatment of lymphedema.[25] Complete (also known as complex) decongestive therapy is composed of hygiene precautions, lymphatic drainage, compression mechanisms, and exercise.[25,26] It has been shown that Complete decongestive therapy leads to effective reductions in limb volume, improves patient quality of life, and maintains high patient satisfaction, making this treatment the gold standard.[27,28] Intermittent pneumatic compressions are cuffs that are intermittently pressurized to replicate the natural effects of skeletal muscle contracting around lymphatic and blood vessels. Studies have demonstrated that utilization of Intermittent pneumatic compressions leads to decreased skin stiffness and may lower fluid pressure in tissues.[29] Still, the use of intermittent pneumatic compressions is controversial due to adverse effects such as lymphatic structure damage and recurrent edema.[30] Extracorporeal shock wave therapy has demonstrated efficacy in increasing angiogenesis, decreasing inflammation, and improving lymphangiogenesis.[31] In addition, extracorporeal shock wave therapy has shown to lead to reductions in lymphedema and improve patient quality of life, which makes the therapy a promising treatment modality,[32] Finally, taping has demonstrated to be another conservative treatment by being placed along lymphatic tracks and facilitating the absorption of interstitial fluid to less congested lymphatic pathways.[25,33] However, taping is contraindicated in patients with skin infections, renal failure, diabetes, and peripheral vascular disease, making this a supplementary treatment.[34]

For patients who have had minimal improvement in swelling with conservative management, surgical treatment

is recommended and may consist of direct resection of involved tissue, suction-assisted lipectomy, lymphaticovenous anastomosis, or vascularized lymph node transfer surgery.[16] In our patient population, both patients underwent primary iliac vein stenting and were observed over a year, in the hopes that their lymphedema would improve. However, due to failure of lymphedema to significantly improve following stenting, patients were counseled on their options for lymphedema surgery. Treatments are planned based on tissue composition and chronicity of lymphedema. Patients are graded in severity by the Cheng lymphedema grading system, LVB is performed for grades 1 and 2, and both VLNT and LVB are performed for grades 3 and 4.[21] LVA is indicated in patients who undergo aggressive physical therapy but still continue to have reductions in limb function and increased pain.[37] LVA should be done at an early stage of lymphedema to prevent the long-term deterioration of lymphatic vessels from continuous fluid overload and infections.[37,38] Although traditional LVA is not routinely performed in patients with chronic lymphedema due to difficulty in identifying functional lymphatics, studies have shown that pre-operative utilization of duplex ultrasound and magnetic resonance lymphangiography can successfully identify functioning lymphatic vessels, leading to successful LVA in patients with chronic lymphedema.[39] After LVA, patients should be encouraged to ambulate, actively elevate the extremities to promote lymphatic drainage, and take antibiotics due to potential susceptibility for infection.[40] However, some studies have posited that patients may develop worsening of lymphedema if functional lymphatics are inadvertently Compromised to perform LVA and/or the LVA becomes thrombosed/occluded.[41] Despite these concerns, the published literature represents that LVA significantly improves quality of life in patients with upper and lower extremity lymphedema with decreased episodes of cellulitis and need for manual lymphatic drainage.[42]

VLNT is another surgical technique that has gained traction for the treatment of lymphedema. There are several donor sites that have been utilized for VLNT, including the groin, appendicular, ileocecal, supraclavicular, gastroepiploic, and submental lymph nodes.[15] Evidence has shown that VLNT is able to lead to volume differences, decreased episodes of cellulitis/infection, and have a positive effect on quality of life.[43] VLNT has also shown to lead to reductions in limb volume and episodes of cellulitis in patients with cancer.[44] Other studies have determined that VLNT is an adequate surgical method for treating chronic lymphedema, although patients that have upper extremity edema tend to have superior outcomes compared with those with lower extremity edema.[45] It is important to note that VLNT is effective in controlling the progression of the disease, but it is not able to reduce fibroadipose soft tissue deposition.[42] Vascularized lymph node transfer is a promising technique that should be utilized in patients with moderate to advanced stages of lymphedema in the extremities.[46]

Liposuction is one of the most common procedures for debulking in patients who have chronic lymphedema characterized by lymphatic stasis and fibroadipose soft tissue deposition.[35] Studies have shown that liposuction is an effective technique for chronic lymphedema when adipose tissue is primarily responsible for patient swelling.[19] In addition, it has been found that liposuction of lymphedema improves both physical and mental health in patients.[36] Furthermore, liposuction should aim to target areas of residual fibroadipose disposition, most commonly located in the thighs. It is critical that after liposuction, patients continue to follow up with surgeons and physiotherapists, and maintain their conservative treatments such as compression garments to limit the re-accumulation of lymphatic fluid.[19] Even in the era of physiologic procedures, liposuction and direct excision continue to be important adjunctive procedures that should be considered and if need be, performed, at least one to two years after VLNT and LVA.

In our patient experience, both patients underwent multiple lymphovenous bypass and vascularized lymph node transfer from the supraclavicular lymph nodes. One patient chose to receive liposuction to address residual fibroadipose deposition in the thigh. Both patients demonstrated significant decreases in leg circumferences postoperatively and reported substantial improvement in pain and exercise tolerance. Furthermore, both patients were extremely pleased with their results and reported that they would be compliant with postoperative wrapping protocols with decreasing frequency of wrapping as lower extremity circumference measurements improved.

Although the true incidence of May-Thurner syndrome is not yet known, the condition has been a clinical entity for six decades.[47] Thus, it is imperative that routine studies be conducted to screen for proximal venous obstructions in patients who are presenting for lower extremity lymphedema. Our study reports the incidence of two patients with May-Thurner syndrome presenting with lower extremity lymphedema who underwent successful vascularized lymph node transfer and multiple lymphovenous bypass. Furthermore, the limited number of research studies pertaining specifically to lower extremity lymphedema in May-Thurner syndrome is dismal and additional research is required to appropriately manage patients and lead to optimal patient outcomes. Although our protocol suggests that patients wait 1 year after venous stenting before undergoing additional procedures, careful observational and prospective studies are required to elucidate the appropriate interval of time to allow between venous stenting and lymphedema microsurgical reconstruction.

CONCLUSIONS

In patients with May-Thurner syndrome with chronic lower extremity lymphedema, iliac vein stenting may be an appropriate initial technique to improve patient symptoms. However, there is the potential for minimal improvement in symptoms, and as a result, it is important to consider surgical therapy, which may consist of lymphaticovenous anastomosis, vascularized lymph node transfer surgery, or liposuction. In our case report, we had a substantial decrease in lower extremity lymphedema and both patients were satisfied with their operative result.

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