Implementation of new endovenous treatments in therapy for lateral embryonic veins

Ulrike Huegel, MD, *and* Iris Baumgartner, MD, *Bern, Switzerland*

ABSTRACT

Klippel-Trénaunay syndrome is characterized by a persistent lateral embryonic vein. This so-called marginal vein has a large diameter causing venous stasis and venous hypertension because of the absence of valves along its entire length. The extensive diameter of the vein impedes successful treatment by sclerotherapy. Surgical removal is considered technically challenging for potential severe intraoperative blood loss due to the large perforators to the deep veins. Here we show that endovenous treatments (laser ablation, cyanoacrylate adhesive) might be feasible options in therapy for lateral embryonic veins. (J Vasc Surg Cases and Innovative Techniques 2019;5:243-7.)

Keywords: Klippel-Trénaunay syndrome; Marginal vein; Endovenous laser; Cyanoacrylate

The Klippel-Trénaunay syndrome (KTS) was first described in 1900 by the French physicians Maurice Klippel and Paul Trénaunay.[1] More than a century later, the eponym has been attached to a rare, complex malformation characterized by the clinical triad of capillary malformations, soft tissue and bone hypertrophy, and atypical, mostly lateral varicosity. As concomitant phenomena, deep infiltrating venous malformations, deep vein anomalies, and lymphedema have also been described. The etiology of KTS is unknown; it is likely due to a mesodermal abnormality that occurs during early fetal development.[2] At the beginning of the first embryonic phase, the venous outflow from the primitive lower limb occurs through a lateral fibular vein into the posterior cardinal vein. In the second stage, an anterior medial tibial vein appears, which becomes the main draining vein of the calf, whereas the lateral fibular vein moves posteriorly. With a defect at this stage, the lateral fibular vein will persist and become the marginal vein.[3] The marginal vein is usually thick walled; it is located immediately under the skin, and it is incompetent along its entire length because of the absence of valves. Drainage is either into a lateral branch of the profunda femoris vein or into the internal iliac vein. The vein sometimes crosses anterior in the thigh and joins the femoral vein next to the great saphenous vein.[2]

Indications for treatment of a marginal vein include hemorrhage, infections, thromboembolism, pain, heaviness, swelling, and ulcers due to chronic venous insufficiency. In the case of limb length discrepancy in childhood, treatment is also recommended to achieve length discrepancy correction.[2,4] The management of the marginal vein has been largely conservative, and compression therapy was the mainstay.[2]

In the case of symptomatic marginal veins, surgery was the classic therapy in the past. The marginal veins may have large perforators to the deep veins; therefore, closed stripping should be avoided because of the risk of excessive bleeding and hematomas.[5] The surgical excision is technically demanding. Because of intradermal extension, the veins could tear easily and provoke serious bleeding. Sclerotherapy with ethanol, sodium tetradecyl sulfate, and polidocanol foam has also been used. These agents cause endothelial damage, inflammation, thrombosis, and fibrosis that ultimately obliterate the vascular channels. At last, all sclerosants become diluted by blood and are rendered ineffective.[6] Herein we see the main limitation of sclerotherapy in the treatment of marginal veins because their great volumes cause quick dilution of the sclerosant and therefore impede effective destruction of the vessel endothelium. Another limitation of sclerotherapy is the risk of causing deep venous thrombosis by extension of the sclerosant into the deep venous system over the numerous perforators.

Thermoablative techniques such as laser and radiofrequency have demonstrated efficacy in the treatment of varicose veins since the late 1990s.[7] Their use in therapy for marginal veins is viewed critically because of their wide lumen and the location immediately under the skin.[2] A few case reports on endothermal ablation of the marginal vein in children have already been published.[8-10] Using large quantities of tumescent anesthesia with ultrasound verification of skin separation, endovenous laser might be an efficient treatment option. In the case of tortuous marginal veins with great numbers of tributaries, *n*-butyl cyanoacrylate embolotherapy might be a feasible alternative.

The patients provided written informed consent to the publication.

From the Department of Angiology, Swiss Cardiovascular Center, Inselspital, Bern University Hospital, University of Bern.

Author conflict of interest: none.

Correspondence: Ulrike Huegel, MD, Department of Angiology, Swiss Cardiovascular Center, Inselspital, Bern University Hospital, Freiburgstrasse, 3010 Bern, University of Bern, Switzerland (e-mail: ulrike.huegel@insel.ch).

The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2468-4287

https://doi.org/10.1016/j.jvscit.2018.12.016

Fig 1. Case 1. Magnetic resonance imaging showing the ectatic marginal vein (*arrows*) in the lateral aspect of the lower limb before endovenous laser ablation.

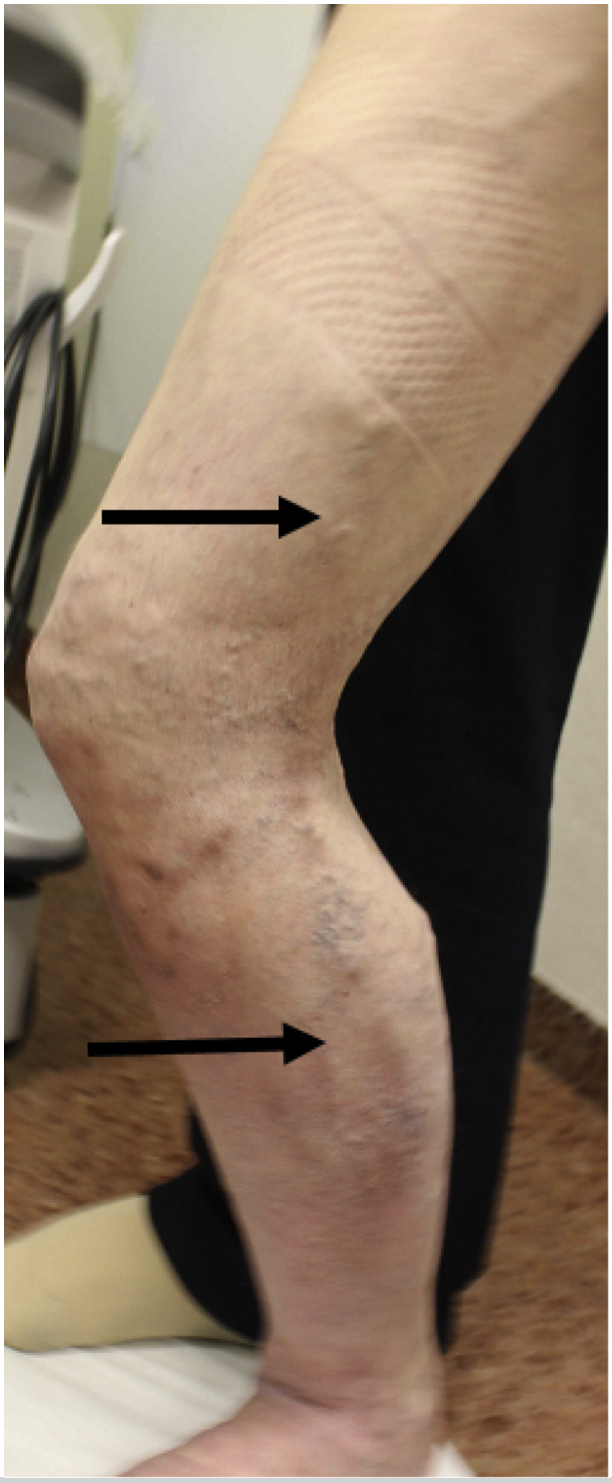

Fig 2. Case 1. Clinical aspect 20 months after endovenous laser ablation indicating a discrete brown stain at the former course of the marginal vein (*arrows*).

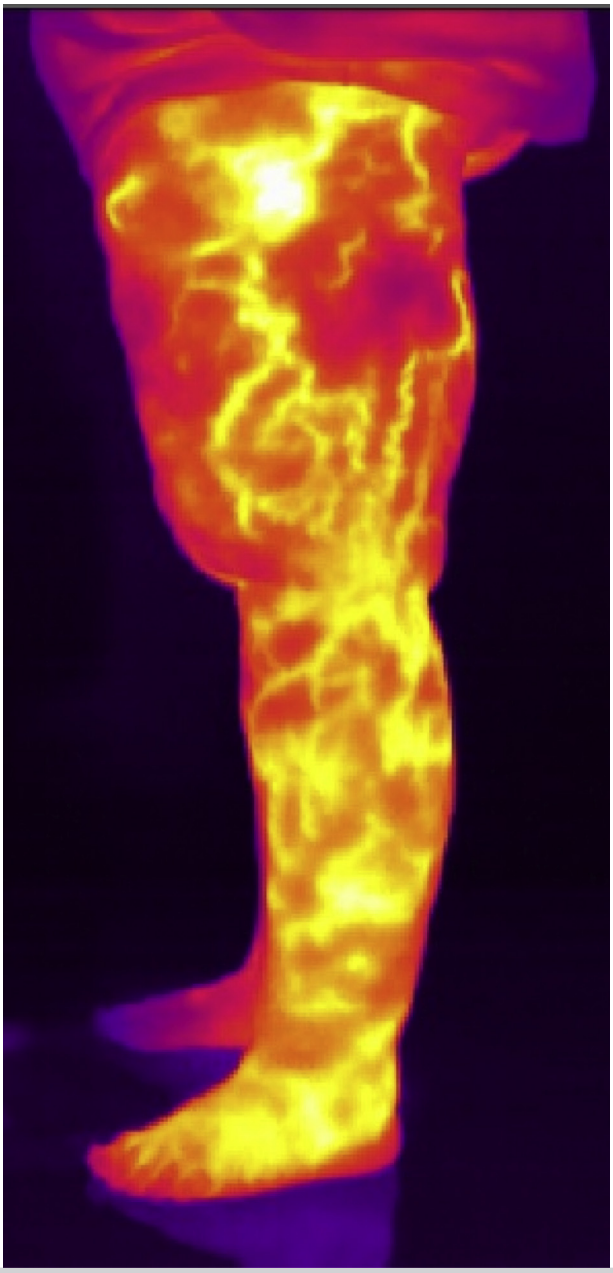

Fig 3. Case 2. Thermography of the lower limb depicting tortuous marginal vein with multiple tributaries.

CASE REPORT

Case 1. We report the case of a 31-year-old woman with KTS and a protruding large lateral embryonic vein on the left leg with a maximal diameter of 1.4 cm (Fig 1) and discomfort due to venous stasis with limb swelling while standing. Because of a localized intravascular coagulopathy, the patient was treated with an oral anticoagulant in prophylactic dosage. Besides swelling, no other clinical signs of chronic venous insufficiency were apparent. On the right leg, lymphedema and a capillary malformation were present. In the past, the patient had been treated unsuccessfully with repeated ethanol injections. Because of the high venous volume, the ethanol was quickly diluted and did not cause effective cellular damage to the endothelial layer to induce thrombosis and vascular occlusion. To occlude the vein, we used a diode laser with a wavelength of 1470 nm at a setting of 10 W (VenaCure Laser 1470; AngioDynamics, Latham, NY) with a total of 13,900 J over 76 cm (180 J/cm). Puncture of the vein was realized under ultrasound guidance using a 14-gauge peripheral intravenous catheter. The nearest distance between the skin surface and vein was 3.5 mm. The laser fiber (NeverTouch Direct; AngioDynamics) was advanced over the complete subcutaneous length of the vein from the ankle to the hip. After tumescent anesthesia was applied, the laser was activated and pulled back continuously with a velocity of 1 cm per 8 seconds. Each segment was passed by the laser fiber repetitively until the fiber could no longer be advanced, so indicating closure of the vein. An ultrasound control after 20 months revealed continued success with complete closure of the treated vein segments. At clinical examination, only a discrete brown stain indicated the former course of the vein (Fig 2). The patient reported a reduction of swelling and heaviness.

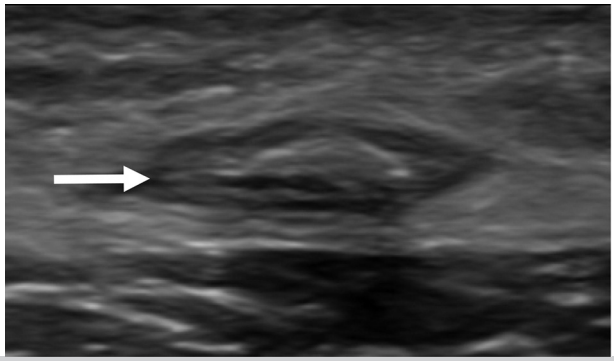

Fig 4. Case 3. Ultrasound of occluded marginal vein 3 weeks after treatment with *n*-butyl cyanoacrylate.

Case 2. A 47-year-old woman with a painful lateral embryonic vein of 8 mm in maximal diameter and multiple subcutaneous tributaries (Fig 3), soft tissue hypertrophy, leg length difference, and extended capillary malformation of the left leg was treated with *n*-butyl cyanoacrylate (VenaSeal; Medtronic, Minneapolis, Minn). The medical adhesive was injected through a 5F catheter for the straight parts of the vein and through an 18- or 20-gauge peripheral intravenous catheter in the tributaries. A total quantity of 9 mL of *n*-butyl cyanoacrylate was injected in two treatment sessions. Because of an antiphospholipid syndrome, the patient is receiving oral anticoagulation, which did not have to be stopped for the procedure. The ultrasound control after 26 months indicated therapeutic success with complete closure of the treated vein segments. A reduction of swelling and pain was achieved.

Case 3. A 16-year-old boy with incomplete KTS was suffering from swelling of the left leg and was disturbed by a large marginal vein with a diameter of 10 mm and multiple protruding tributaries. No other signs of chronic venous insufficiency were present.

Two treatment sessions were necessary; in each session, 4.5 mL was applied. The procedures were performed under sterile conditions. The adhesive was injected through an 18- or 20-gauge peripheral intravenous catheter. No anticoagulation was used during the procedure or in the follow-up. The ultrasound control after 26 months indicated therapeutic success with complete closure of the treated vein segments (Fig 4). Besides reduction of swelling, the patient profited from the decrease of the cosmetically disturbing veins.

DISCUSSION

The literature to date has demonstrated that endovenous laser ablation is effective and safe in the treatment of great saphenous veins.[11] There is a paucity of reports using endovenous laser ablation for treatment of the marginal vein in KTS. Three reports with a total of 13 patients demonstrated good results.[8-10] Some authors do not recommend laser closure of the vein because of the risk of skin burns and uncomfortable scarring.[5] In our experience, these side effects can often be avoided with a correctly applied and large enough volume of tumescent anesthesia. In contrast to the great saphenous vein, embryonic marginal veins are not surrounded by a fascial envelope; when fluid is injected around the vein, there is a quick dispersion, so that the fluid has to be reinjected to maintain a sufficient "isolating sheath." Nevertheless, the current thermoablative techniques will not be applicable to the management of all marginal veins because of their extremely superficial location right beneath the skin. This anatomic peculiarity in combination with a thin dermis bears a high risk of heat damage of the skin.[12]

For those tortuous marginal veins with intradermal extension that were not suitable for thermoablative techniques or ethanol because of the risk of skin necrosis, we introduced *n*-butyl cyanoacrylate. We chose this sclerosant because in our experience, sclerosants like polidocanol and sodium tetradecyl sulfate are not effective enough to destroy the vessel endothelium of these embryonic veins.

In our two cases, we used *n*-butyl cyanoacrylate after a surgical intervention was not considered the optimal treatment because of high bleeding risk due to the intradermal extension and to avoid scarring of these young patients. Sclerotherapy with ethanol was also declined because of the risk of skin necrosis. In the treatment of truncal varicosity, *n*-butyl cyanoacrylate has already proved its efficiency and safety.[13,14] On intravenous administration, it elicits a granulomatous foreign body reaction and a concomitant inflammatory vein wall reaction, leading to subsequent fibrotic degradation.[15] No tumescent anesthesia is necessary for this procedure.

Using endovenous laser ablation in the case of a marginal vein with large diameter, straight course, and sufficient distance to the skin and *n*-butyl cyanoacrylate in two cases with marginal veins of small caliber, tortuous courses, multiple subcutaneous tributaries, and intradermal extension, we reached good results with complete closure of the marginal vein confirmed by ultrasound. We defined a complete closure as no discrete segment of patency >5 cm. The procedures were not mixed with phlebectomies or foam sclerotherapy. All patients had a subjective reduction of swelling and heaviness of the treated legs. Whereas we saw skin staining after our laser procedure, no discoloration appeared after *n*-butyl cyanoacrylate, but the adhesive remained palpable. No thrombosis or pulmonary embolism occurred.

CONCLUSIONS

Endovenous laser ablation and the medical adhesive *n*-butyl cyanoacrylate (VenaSeal) seem to be effective in treatment of the marginal vein in KTS during short-term follow-up. Our findings so far are encouraging, but more experience is needed to recommend these new treatment modalities in congenital vascular malformations such as KTS.

REFERENCES

1. Klippel M, Trénaunay P. Du naevus variqueux osteo-hypertrophique. Arch Gen Med 1900;3:641-72.
2. Gloviczki P, Driscoll DJ. Klippel-Trénaunay syndrome: current management. Phlebology 2007;22:291-8.
3. Lewis FT. Development of the veins in the limbs of rabbit embryos. Am J Anat 1906;5:113-20.
4. Belov S. Correction of lower limbs length discrepancy in congenital vascular-bone diseases by vascular surgery performed during childhood. Semin Vasc Surg 1993;6:245-51.
5. Matassi R, Vaghi M. Management of the marginal vein: current issues. Phlebology 2007;22:283-6.
6. Rosenblatt M. Endovascular management of venous malformations. Phlebology 2007;22:264-75.
7. Lawaetz M, Serup J, Lawaetz B, Bjoern L, Blemings A, Eklof B, et al. Comparison of endovenous ablation techniques, foam sclerotherapy and surgical stripping for great saphenous varicose veins. Extended 5-year follow-up of a RCT. Int Angiol 2017;36:281-8.
8. King K, Landrigan-Ossar M, Clemens R, Chaudry G, Alomari AI. The use of endovenous laser treatment in toddlers. J Vasc Interv Radiol 2013;24:855-8.
9. Wales L, Nasr H, Bohm N, Howard A, Loftus I, Thompson M. Paediatric venous malformation: treatment with endovenous laser and foam sclerotherapy. EJVES Extra 2007;14:6-7.
10. Patel PA, Barnacle AM, Stuart S, Amaral JG, John PR. Endovenous laser ablation therapy in children: applications and outcomes. Pediatr Radiol 2017;47:1353-63.
11. Van den Bos R, Arends L, Kockaert M, Neumann M, Nijsten T. Endovenous therapies of lower extremity varicosities: a meta-analysis. J Vasc Surg 2009;49:230-9.
12. Lee BB, Baumgartner I, Berlien P, Bianchini G, Burrows P, Gloviczki P, et al. Diagnosis and treatment of venous malformations. Consensus document of the International Union of Phlebology (IUP): updated 2013. Int Angiol 2015;34:97-149.
13. Morrison N, Gibson K, Vasquez M, Weiss R, Cher D, Madsen M, et al. VeClose trial 12-month outcomes of cyanoacrylate closure versus radiofrequency ablation for

incompetent great saphenous veins. J Vasc Surg Venous Lymphat Disord 2017;5:321-30.
14. Proebstle TM, Alm J, Dimitri S, Rasmussen L, Whiteley M, Lawson J, et al. The European multicenter cohort study on cyanoacrylate embolization of refluxing great saphenous veins. J Vasc Surg Venous Lymphat Disord 2015;3:2-7.
15. Almeida JI, Min RJ, Raabe R, McLean DJ, Madsen M. Cyanoacrylate adhesive for the closure of truncal veins: 60-day swine model results. Vasc Endovascular Surg 2011;45:631-5.

Submitted Oct 2, 2018; accepted Dec 2, 2018.