Venous Malformations of Klippel-Trenaunay Syndrome — Treatment by Steam Sclerotherapy

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Abstract

Background: Klippel-Trenaunay syndrome (KTS) is characterized by capillary malformation, varicosities and bony or soft tissue hypertrophy. Conservative treatment is indicated in all cases. Surgery is reserved only for complications. Minimal invasive treatments such as thermal ablation and ultrasound-guided foam sclerotherapy (USGS) for venous insufficiency are currently preferred over surgery.

Objectives: To present our treatment experience with KTS patients comparing the results of steam vein sclerosis (SVS) and foam to US-guided foam sclerotherapy (USGS) alone.

Methods: Sixteen patients were treated with USGS alone or with SVS+USGS between 2003 and 2016. Assessment of signs, symptoms, results and overall patient satisfaction was performed before, during and after the treatments.

Follow up visits (mean 39 months, range 24-60) were scheduled once a month for the first three months and once every three months thereafter.

Results: Patients mean age was 28 years (range 15-56). The CEAP clinical classification was C4 in 11 patients (69%), 4 in C5 (25%) and one patient in C6 (6%). The average number of sessions was 14 (range 9-21) for USGS alone and 5 (range 3-7) after SVS.

No major complications were encountered. All patients reported improvement in signs and symptoms. 75% were very satisfied with the cosmetic result.

Conclusion: SVS and USGS are valid and effective minimal invasive ambulatory procedures for the treatment of KTS patients. Procedures are essentially pain-free with excellent results, albeit the treatment period is long. SVS first, followed by foam considerably and significantly shortens the treatment period. Long-term results and larger study groups are warranted.

ABBREVIATIONS


INTRODUCTION

Klippel-Trenaunay Syndrome (KTS) is a rare complex congenital vascular malformation described by the two French physicians [1]. This syndrome of unknown etiology is benign and usually affects only one extremity. It is characterized by capillary malformation, giant varicosities and bony or soft tissue hypertrophy. In sharp contrast to Klippel-Trenaunay-Weber (KTW) there are no arterio-venous connections in KTS.

Since the basic pathology cannot be corrected, treatment is directed to alleviate and control the symptoms. Treatments are mostly conservative and non-invasive unless symptoms result in severely impaired quality of life. Severe limb length discrepancies (more than 2 cm) at a young age are usually treated by epiphysiodesis or osteotomy.

Varicosities usually appear on the lateral aspect of the leg with large "venous lakes" resulting from persisting embryonic veins. Patients complain of swelling, pain and more advanced symptoms and complications of chronic venous insufficiency [2-5].

Stripping of the saphenous vein and debulking of varicosities failed to alleviate symptoms in most of the patients. New minimally invasive treatment methods for venous insufficiency were introduced among which thermal ablation and foam-sclerotherapy are popular.
This report presents our experience utilizing steam vein sclerosis (SVS) followed by ultrasound-guided foam sclerotherapy (USGS) to treat patients with KTS.

**PATIENTS AND METHODS**

A total of sixteen patients were diagnosed with KTS and treated from October 2003 to September 2016. They consist of two groups; the first included nine patients treated by ultrasound-guided foam sclerotherapy alone (USGS). The second group included seven patients treated by steam vein sclerosis (SVS) followed by sclerotherapy (USGS).

The diagnosis in our patients was made by history of port-wine stain from birth and large varicosities as well as by clinical assessment. A thrill or murmurs were sought for to rule out Klippel-Trenaunay-Weber or Parkes-Weber syndrome, which was however not found in any of the patients. The presence of a thrill or murmur may represent an arteriovenous malformation resulting in a high-flow anomaly. Large varicosities and their location along the leg were noted. Measurements of the length and circumferences of both legs were taken. A duplex scan was performed to demonstrate the existence of an intact deep venous system, to rule out arteriovenous connection and to show venous insufficiency. Patients with arteriovenous malformation, aplasia of the deep venous system or those with evidence of deep venous thrombosis (DVT) were excluded.

Comparative limb X-ray were undertaken to demonstrate length difference. Some patients had magnetic resonance imaging (MRI) to determine the infiltration and extent of the lesion.

Patients were treated by USGS as described by Cabrera [6], namely direct percutaneous injections of foam into insufficient veins. The foam greatly increased the volume and surface area of the liquid sclerosant and should be considered as a new treatment modality. Polidocanol (Sclerovein, Resiang, Switzerland) at concentrations 2%-4% was used as the sclerosing agent. Foam was prepared at a ratio of 3:1 air to sclerosant by Tessari's method [7] utilizing two syringes; one filled with air the other with the sclerosant, attached to a three-way stopcock.

In each treatment session, 10-25 ml of foam was injected under continuous duplex imaging (Logic 400 Pro series GE, M7 Series Mindray), after which the leg was elevated and wrapped by elastic bandages. During the injection as the foam filled the treated vein a typical impressive vasospasm was noted immediately. At the beginning of the next session the treated vein was reevaluated and if partially compressible and still with flow another injection was added.

Treatments were performed once a month, starting with the main axis and then all refluxing tributaries. The number of necessary sessions was judged by US findings. Every patient was seen once a month after a treatment session or after three months if no treatment was indicated.

Thermal ablation was performed by steam vein sclerosis (SVS) as introduced by Milleret [8]. Treatment was performed in the operation room under local tumescence anesthesia and sedation. Tumescence anesthesia is used to isolate the treated vein and prevent thermal injury to the surrounding tissues as well to shrink venous size and allow a better thermal effect. After a month at the follow up visit duplex assessment revealed still active venous tributaries that were treated by USGS.

A follow up examination including physical examination, duplex assessment and satisfaction questionnaire, was done once a month until treatment was completed and every three months thereafter.

Treatment was completed after two consecutive visits with an intact duplex scan.

Patients’ satisfaction was evaluated by the treating physician. Patients were asked to grade their opinion on the results on a scale of 1 to 5 where 1 is totally unsatisfied and 5 is completely happy. Different scores were given to pain control, limb function and cosmetic overlook.

**RESULTS**

There were 9 females and 7 males with a mean age of 28 years (range 15-56 years). There were five females and four males in group I; four females and three males in group II (Table 1). The average follow-up was 39 months (range 24-60). In all sixteen patients the main complaint was limb disfiguration by the giant varicosities and the port-wine stains combined with functional impairment from swelling and heaviness of the legs. In eleven patients (69%) pain in the affected leg was disabling. Asymmetric bulging of the toes was noted in 6 (37%). Five patients (31%) have had superficial thrombophlebitis and three reported of occasional minor bleeding. In one patient embolization with alcohol injections has been tried in the past, but without significant improvement.

On physical examination, port-wine stains, representing capillary malformations, were encountered in all patients. Stains were irregular, violaceous-to-erythematous patch, which usually covered an extensive portion of the lateral aspect of the leg (Figure 1). Varicosities were present in the affected leg and especially lateral large venous lakes (lateral embryonic vein). In one male patient both legs were affected. One patient presented with an ulcer. Involvement of the ipsilateral lower buttock and labia majora were encountered in two patients (Figure 2). In addition, gigantism of toes in one patient and syndactyly in another were observed (Figure 3). There was only a small difference in the length of the affected limb (less than 1 cm) when compared to the unaffected limb in one patient. In some patients the difference in circumference of the affected leg was severe (Figure 4). The veins, although containing large quantity of blood, easily collapsed under low pressure. They typically expanded during standing and partially collapsed in supine position.

The CEAP (clinical class, etiology, anatomic distribution and pathophysiology), (9) clinical classification (C1-C6) was C4 in 11 patients (69%), C5 in 4 patients (25%) and C6 in one (6%).

Improvement in the functional ability and in the disfiguration was noted in all patients. Pain was ameliorated in 13 patients, and at last follow up 88% (14 out of 16) had no residual pain. Shrinkage in varices size and of a paler color of the skin lesion compared to the appearance prior to the treatment was noted in all patients (Figure 5).

Twelve patients (75%) were very satisfied with the final
Figure 1 Typical findings in a patient with KTS: port-wine, irregular, erythematous patch, stain representing capillary malformation. Large varicosities along the lateral aspect of the leg.

Figure 2 Capillary malformation involvement of the ipsilateral buttock.

Figure 3 A less common appearance demonstrating gigantism of toes and involvement of both lower extremities and trunk.

Figure 4 Large discrepancy in the circumference of the affected lower extremity.

Figure 5 Varicosities around the knee and in the anterolateral aspect of the calf before treatment (right side) showing improved appearance after treatment (left side).

cosmetic result. Three young females and one male expected a better cosmetic result. There was no bleeding from the lesion during or after treatment in any patient. The small ulcer, in one patient, completely healed within 7 weeks.

We have encountered no major complication such as DVT, pulmonary emboli, severe nerve injury or prolonged superficial thrombophlebitis, and all patients tolerated the procedures well and returned immediately to normal daily activities.

In three patients the foam filling a large blood lake (Figure 6) resulted in a painful coagulum that necessitated evacuation by a large caliber needle (16G).

On the long-term follow up four patients developed skin pigmentation that spontaneously disappeared within 10-15 months (Figure 7).

There was no statistical significance when compared
the demographics and CEAP classification between the two treatment groups, namely treatment with USGS alone compared to treatment with SVS+USGS (Table 1).

Group I: treatment by USGS alone - The average number of sessions needed for the treatment, as judged by US finding, in 9 patients was 14 (range 9-21).

Group II: treatment by SVS followed by USGS – The average number of sessions needed in the 7 patients was merely 5 (range 3-7).

DISCUSSION

In 1900, the two French physicians Klippel and Trenaunay described a rare congenital syndrome characterized by capillary malformation, giant varicosities and bony or soft tissue hypertrophy, usually affecting one extremity [1]. The capillary malformation is a large cutaneous nevus (osteohypertrophic varicose nevus), port-wine stain, invariably present on the affected limb. Capillary malformations were detected in the vast majority of patients with KTS, approximating 100% [2-5].

Varicose veins arising, on the affected limb, in childhood, often contain a persistent lateral embryonic vein (persistent sciatic vein). Hypertrophy of soft and bony tissues may result in limb elongation and thickening [1,4,5,10].

In most cases (80%), only one leg is involved. Both legs may be affected in 2%-20% of the cases; and all four extremities account for merely 2%-3%. A single upper limb may be involved in 11%-13% and ipsilateral upper and lower limb account for 5%-18% of the cases [4,5,10]. In our group of patients, fourteen out of sixteen (88%) had a single lower extremity involvement and two had involvement of both legs.

Klippel-Trenaunay syndrome (KTS) is of unknown etiology and has no gender preponderance. There is no true pathognomonic test. Several theories were suggested over the years: Servelle [10] believes that deep venous system abnormalities such as agenesis, hypoplasia or external compression by a fibrous band lead to obstruction and hypertension, which resulted in varices and limb hypertrophy. Others contend that a mesodermal defect

| Table 1: comparison of presentation and results in the two treatment groups. |
|-----------------------------|-----------------------------|
| **Number of patients**      | 9                          | 7                          |
| **Gender**                  | 5 females, 4 males          | 4 females, 3 males          |
| **CEAP**                    | C4-6 (67%); C5-3 (33%)      | C4-5 (71%); C5&C6-2 (29%)  |
| **Number of sclerotherapy** | 14 (range 7-21)             | 5 (range 3-7)               |
| **Skin burn**               | 0                          | 1 (14%)                    |
| **Long-term pigmentation**  | 3 (33%)                    | 1 (14%)                    |
| **Painful coagulum**        | 3 (33%)                    | 1 (14%)                    |
| **Improvement in function** | 9 (100%)                   | 7 (100%)                   |
| **Decreased pain**          | 7 (78%)                    | 6 (86%)                    |
| **Satisfied with cosmetics**| 6 (67%)                    | 6 (86%)                    |

Figure 6 Ultrasound scan demonstrating large venous "lakes".

Figure 7 Large varicosities in the lower buttock and posterolateral aspect of the leg before (in the right side) and after (in the left side) treatment. Pigmentation and a healing skin burn due to the steam are present.
with unimpeded and normal venous flow [11,12] or a mixed mesodermal and ectodermal dysplasia [12,13] is responsible for KTS. There are no obvious large arterio-venous fistulae in KTS. Venous and lymphatic malformations such as KTS, or CLVM according to the new classification, are characterized by slow-flow. In sharp contrast, Klöppel-Trenaunay-Weber syndrome (more correctly Parke-Weber syndrome or CLAVM) containing arterio-venous malformations with considerable shunts are a fast-flow anomaly.

Associated abnormalities in other systems, such as lymphedema or involvement of abdominal and pelvic organs may also occur in KTS.

The diagnosis is made by history of capillary malformation at birth with varicosities appearing in early childhood, physical examination and duplex scanning. Duplex has a high sensitivity and specificity for extremity venous anatomy and function [14].

Additional imaging studies can be obtained. CT may demonstrate the anatomical extent of the lesion as well as the surrounding tissues. CT, however, incurs radiation and contrast media is necessary to demonstrate the venous system. MRI is therefore considered a better assessment imaging modality. Its utilization, in children due to technical demands will require anesthesia. Ascending venography which is more invasive allows for embolization if necessary [5].

Complications of KTS may include bleeding in up to 25% of the patients, which may be local at the site of capillary malformation or varicosities or systemic such as vaginal, urinary and gastrointestinal (mainly rectal) tract bleeding. Cellulites, superficial and/or deep venous thrombosis as well as pulmonary embolism have been reported too, in up to 22% of the patients [2,5,15,16].

As in all congenital malformations, treatment is aimed at the complications and their prevention, relief of functional impairment, pain control and cosmetic improvement. The mainstay is a conservative treatment with graduated compression and leg activation and elevation.

Some non-vascular surgical procedures (like epiphysiodesis) were suggested in childhood to prevent elongation of the involved limb [17]. The indication is a leg discrepancy exceeding 2 cm in a growing child. Other possible procedures include amputation of a grossly hypertrophied and malfunctioning toes or digits.

Removal of symptomatic varicosities either by stripping and ligation or by debulking can be performed only in the presence of an intact deep venous system. Complete excision, in KTS, is seldom possible and operation should not be done to improve cosmetics at the expense of function. Surgery can damage venous and lymphatic structures. Following stripping and ligation of varicose veins symptoms improved in approximately 40% of the patients but 25% reported of a worse condition [2,3,5,15,16,18]. Some patients did poorly after surgical procedures and developed pain, a larger edema and a non-healing wound. Even when all patients reported initial improvement following surgery, in an experienced center, varicosities recurred in 50% of the patients [18]. Others have reported on persistent symptoms in 90% of the patients after surgery [15,16]. Thus, surgery should be reserved for selected symptomatic patients to achieve good results. In most patients with KTS the management should be non-operative [2,3,5,9,15,16,18]. The use of garments, especially in young patients, often fails due to poor patients’ compliance. When intervention is required minimal invasive treatment should be offered over open surgery although it is not well established in patients with KTS.

In 2003, Cabrera et al. were the first to report on the treatment of venous malformations by USGS. The initial results, utilizing Polidocanol mixed with CO2, were beneficial in 92% of the patients [6]. Similar to our results, a recently published paper, treating patients with venous malformations (including KTS) by USGS, have reported similar results. Some of their patients, as one of our patients, underwent embolization, prior to USGS, with scant results [19,20].

Because KTS patients have usually more complex varicosities, a larger number of treatment sessions are required. Our average number of sessions with USGS alone is similar to that reported in a previous study [19].

Thermal ablation was introduced for the treatment of venous insufficiency in the beginning of the millennium. Different wave length lasers and radiofrequency ablation were employed [21-23] with successful ablation of part of the insufficient veins. A long and rather non-tortuous vein segment is required for a successful treatment utilizing a laser fiber or a radiofrequency catheter.

SVS with its steam energy supplied via a tube rather than through a catheter enables utilizing a very short catheter or even the connection of a needle for treatment [8] thus, allowing treatment of a larger amount of refluxing venous “lakes” and/or tortuous veins that are typically found in patients with KTS.

This was the rational for our choice of SVS, rather than laser or radiofrequency, for ablation treatment in patients with KTS. We report, herein, on a group of patients with classical KTS treated by either USGS alone or by SVS followed by USGS with excellent short and mid-term results. Functional integrity, cosmetic results and patient’s satisfaction were used as end points. Severe complications of USGS are uncommon. The formation of cutaneous ulcer following injection, described for one patient only in each of previous studies [19,20] was not (yet) encountered in our patients.

In our modest experience USGS is an effective minimally invasive ambulatory procedure that offers a valid alternative in the treatment of giant varicosities in patients with KTS. This group of patients requires more treatment sessions compared to patients with chronic venous insufficiency.

Moreover, utilizing a thermal ablation procedure first and then follow with USGS seems more effective. SVS treatment first followed by USGS can considerably shorten the number of treatment sessions and thus seems to offer the best choice for patients with KTS.

Treatments are essentially pain-free and have excellent short and mid-term results. Long-term results and larger study groups are warranted.
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