



Ultrasound-Guided Foam Sclerotherapy in Patients with Klippel-Trenaunay Syndrome

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Key words: Klippel-Trenaunay syndrome, vascular malformations, varicose veins, ultrasound-guided foam sclerotherapy

Abstract

Background: Klippel-Trenaunay syndrome, a congenital disorder, is characterized by capillary malformation, varicosities and bony or soft tissue hypertrophy. Since there is no cure for this disorder, treatment is directed towards secondary prevention of venous hypertension and preservation of functional integrity of the legs. Elastic stockings are the mainstay of treatment and are indicated in all cases. Surgery is reserved only for a few selected symptomatic patients, however the outcome is unsatisfactory in most cases, with recurrent pain, edema, poor cosmetic result and limb deformity. Ultrasound-guided foam sclerotherapy is a recently introduced minimally invasive ambulatory procedure for the treatment of chronic venous insufficiency. It was recently introduced to treat this disorder.

Objectives: To evaluate the efficacy of USFS in the treatment of patients with Klippel-Trenaunay syndrome.

Methods: Seven patients diagnosed with Klippel-Trenaunay, with massive lower extremity involvement, were treated with USFS between October 2003 and October 2005. Sclerovein® (polidocanol, Resinag, Switzerland) 2–4% was used as the sclerosant. The signs, symptoms and overall patient satisfaction were assessed before, during and after the treatment.

Results: Patients' mean age was 26 years (range 15–54). The CEAP clinical classification, with ascending severity ranging from 0 (no signs) to 6 (active venous ulcer), was C4 in five patients (71.5%) and C5 and C6 in one patient each. The average number of sessions was 14.5 (range 9–21). No major complications were encountered. All seven patients reported improvement in signs and symptoms. Five of the 7 patients (71%) were very satisfied with the cosmetic result.

Conclusion: USFS is an effective minimally invasive ambulatory technique, essentially pain-free and with excellent short-term results in patients with Klippel-Trenaunay syndrome (when the deep system is functional). Long-term results and larger study groups are warranted.

IMAJ 2007;9:72–75

malformation, varicosities, and bony or soft tissue hypertrophy. It usually affects only one extremity. This syndrome is of unknown etiology and has no gender preponderance.

Many complex vascular malformations, such as Klippel-Trenaunay syndrome, are named after the physician(s) credited with the first description of the condition. These eponymous terms are often misused and misleading and tell nothing of the pathogenesis. The new classification of vascular malformation is based on the type of vascular channels involved and flow characteristics of the malformation. Klippel-Trenaunay syndrome is a slow-flow anomaly of capillary-venous or capillary-lymphatic-venous malformation and is therefore termed CVM or CLVM [2].

Since the basic pathology cannot be corrected, treatment is directed at controlling the varicosities and their complications as well as the bony and soft tissue deformities in order to preserve both cosmetic appearance and functional integrity. Because surgical procedures were poorly tolerated by patients and had high recurrence and complication rates, the cornerstone of treatment is the use of external elastic support. Elastic garments are indicated for all Klippel-Trenaunay patients.

Ultrasound-guided foam sclerotherapy is a new minimally invasive modality for the treatment of chronic venous insufficiency of the superficial system [3]. In this report we present our experience using USFS to treat seven patients with Klippel-Trenaunay syndrome.

Patients and Methods

Seven patients diagnosed with Klippel-Trenaunay syndrome were treated with ultrasound-guided foam sclerotherapy from October 2003 through October 2005 at the Multidisciplinary Medical Center. The diagnosis in our patients was made by history (port-wine stains and varices, from birth) and clinical assessment dem-

For Editorial see page 112

Klippel-Trenaunay syndrome is a complex congenital vascular malformation that was described a hundred years ago by two French physicians [1]. The syndrome is characterized by capillary

USFS = ultrasound-guided foam sclerotherapy
CEAP = Clinical, Etiology, Anatomic, Pathophysiology
CVM = capillary-venous malformation
CLVM = capillary-lymphatic-venous malformation

onstrating port-wine stains and varicosities. In addition, a thrill or murmurs were sought for but not found in any of the patients, the presence of which may represent a possible arteriovenous shunt and thus a fast-flow anomaly (arterial involvement such as in Parkes-Weber syndrome). Large varicosities and their location were noted. Measurements of the length and circumference of both legs were taken. Various imaging studies were obtained. A duplex scan was performed to demonstrate venous insufficiency, large venous lakes along the leg and an intact deep venous system, and to rule out arteriovenous shunts. Comparative limb X-rays were undertaken to demonstrate length differences. Some patients had magnetic resonance imaging scans to determine the extent and infiltration of the lesion. Patients with arteriovenous shunts or aplasia of the deep venous system were excluded, as were patients with a history of deep vein thrombosis. All our patients were studied by duplex scan prior to treatment in order to ascertain that the deep venous system was intact.

Patients were treated by USFS as described by Cabrera et al. [3]; namely, direct percutaneous injections of foam into insufficient veins. The foam greatly increases the volume and surface area of the liquid sclerosant and therefore can treat even large caliber veins. Thus it should be viewed as a new treatment modality. Since its introduction in 1997, USFS is considered one of the possible treatments for regular varicosities.

Polidocanol (Sclerovein®, Resinag, Switzerland) at concentrations of 2–4% was used as the sclerosing agent. Foam was prepared at a ratio of 3:1 air to sclerosant by Tessari's method [4] using two syringes – one filled with air and the other with the sclerosant – attached to a three-way stopcock. In each treatment session 10–25 ml of foam were injected under continuous duplex imaging (Logic 400 Pro series, General Electric, USA), after which the leg was elevated and wrapped with 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. The number of necessary sessions was judged by ultrasonographic findings. The average number of sessions was 14.5 (range 9–21). Every patient was seen once a month after a treatment session or after 3 months if no treatment was indicated. A follow-up examination including physical examination, duplex assessment and satisfaction questionnaire was performed once a month until treatment was completed and every 3 months thereafter.

Patient's satisfaction was evaluated by the treating physician. Patients were asked to grade their opinion on the results according to a scale of 1 to 5 where 1 is totally unsatisfied and 5 is completely satisfied. Different scores were given for pain control, limb function, and cosmetic appearance.

Results

Our study group comprised four females and three males with a mean age of 26 years (range 15–54 years). The average follow-up was 16 months (range 11–24). In all seven patients the main complaint was limb disfiguration by the giant varicosities

and port-wine stains, combined with functional impairment from swelling and heaviness of the legs. In five patients (71.5%) pain in the affected leg was disabling. Asymmetric bulging of the toes was noted in three (43%). Two patients (29%) had superficial thrombophlebitis and one reported occasional minor bleeding. In one patient, embolization with alcohol injections had been tried in the past but without improvement.

Physical examination disclosed port-wine stains, representing capillary malformations, in all patients [Figure 1]. The stains were irregular violaceous-to-erythematous patches that usually covered an extensive portion of the lateral aspect of the leg. Varicosities were present in the affected leg [Figure 2] and especially lateral

large venous lakes (lateral embryologic vein). In one male patient both legs were affected. One patient presented with an ulcer. Involvement of the ipsilateral lower buttock and labia majora was noted in one patient (a 16 year old girl). Another patient had gigantism of toes and syndactyly. There was only a small difference in the length of the affected limb (0.5 cm) when compared to the unaffected limb in one patient. In all the patients, the veins, although containing a large quantity of blood, easily collapsed under low pressure; they typically expanded during standing and partially collapsed in a supine position

The CEAP classification [5] defines the **clinical class**, **etiology**, **anatomic distribution** and **pathophysiology** of venous insufficiency. The clinical class, with ascending severity, ranges from 0 (no signs) to 6 (active venous ulcer). According to the clinical classification, five of our patients (71.5%) were in C4 degree with huge varicosities, one patient was in C5 with a non-active ulcer (14%) and one in C6 with an active venous ulcer (14%).

Improvement in functional ability and lessening of the disfiguration were noted in all seven patients. Pain was ameliorated in four patients, and at last follow-up 80% (4 of 5) had no residual



Figure 1. Port-wine stains representing capillary malformations. Stains are irregular violaceous-to-erythematous patches that cover an extensive portion of both legs and abdomen. Note hypertrophy of the toes.



Figure 2. Port-wine stains and varicosities in a single affected leg. A closer view of the irregular violaceous-to-erythematous patch stains.



Figure 3. Varices on the lower front leg and knee before treatment (on the right side) and after treatment (on the left side).



pain. In all patients the size of the varices was smaller and the skin lesion was a paler color compared to the appearance before treatment [Figure 3]. Five of the seven patients (71.5%) were very satisfied with the final cosmetic result, while two young female patients expected a better cosmetic result. There was no bleeding from the lesion during or after treatment in any patient. A small ulcer in one patient completely healed.

We did not encounter any major complications such as deep vein thrombosis, pulmonary emboli, severe nerve injury or prolonged superficial thrombophlebitis, and all patients tolerated the procedure well and returned immediately to their normal daily activities. In one patient the foam filling a large blood lake resulted in a painful coagulum that necessitated evacuation by a large caliber needle (16 G). On the long-term follow-up two patients developed skin pigmentation that spontaneously disappeared within 7 months.

Discussion

In 1900, two French physicians, Maurice Klippel and Paul Trenaunay, described a 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), resembling a port-wine stain and invariably present on the affected limb. Varicose veins arising on the affected limb in childhood often contain persistent lateral embryologic veins. Hypertrophy of soft and bony tissues may result in limb elongation and thickening [1,6,7]. 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% of cases, and ipsilateral upper and lower limb account for 5–18% [6,7]. In our group of patients, six of seven (85%) had a single lower extremity involvement and one patient had involvement of both legs.

Klippel-Trenaunay syndrome is of unknown etiology and has no gender preponderance. Several theories have been suggested over the years: Servelle [6] claimed that deep venous system abnormalities, such as agenesis, hypoplasia or external compression by a fibrous band, lead to obstruction and hypertension, which results in varices and limb hypertrophy. Others contend that a mesodermal defect with unimpeded and normal venous flow [8] or a mixed mesodermal and ectodermal dysplasia [9] is responsible for the disorder. There are no obvious large arteriovenous fistulae in this syndrome. Venous and lymphatic malformations such as Klippel-Trenaunay syndrome, or CLVM according to the new classification, are characterized by slow flow. In sharp contrast, Klippel-Trenaunay-Weber syndrome (more correctly Parkes-Weber syndrome or CLAVM) containing arteriovenous 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 Klippel-Trenaunay syndrome [10].

Complications may include bleeding (in up to 25% of patients), which may be local at the site of capillary malformation

CLAVM = capillary-lymphatic-arteriovenous 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 also been reported (in up to 22% of patients) [10].

As in all congenital malformations, treatment is aimed at the complications and their prevention, at reducing functional impairment, controlling pain and improving cosmetic appearance. Some surgical procedures (like epiphysiodesis) have been suggested, in childhood, to prevent elongation of the involved limb [6]. The indication is a leg discrepancy exceeding 2 cm in a growing child [7]. Other possible procedures include amputation of 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 [7,10-12]. All our patients were studied by duplex scan prior to treatment in order to ascertain that the deep venous system was intact. Complete excision is seldom possible in Klippel-Trenaunay syndrome and surgery should not be performed to improve cosmetic appearance at the expense of function. Surgery can damage venous and lymphatic structures. In one study [7] following stripping and ligation of varicose veins, symptoms improved in approximately 40% of the patients but 25% reported that their condition was worse. Some patients did poorly after surgical procedures and developed pain, a larger edema and non-healing wound. In another study in an experienced center, even when all patients reported initial improvement following surgery, varicosities recurred in 50% [12]. Other researchers reported persistent symptoms in 90% of the patients after surgery [7,10]. Thus, surgery should be reserved for selected symptomatic patients to achieve good results. In most patients with the syndrome, management should be non-operative [7,10-12]. Compression bandages are indicated for chronic venous insufficiency, lymphedema and recurrent cellulites. The use of these bandages, especially in young patients, often fails due to patients' poor compliance.

In 2003, Cabrera et al. [13] were the first to report on the use of USFS to treat venous malformations. The initial results, utilizing polidocanol, were beneficial in 92% of the patients [13]. A recent article on the use of USFS to treat patients with venous malformations (including the syndrome) reported similar results. Some of their patients, like one of ours, underwent embolization prior to USFS, with poor results [14].

Conclusions

Our experience using ultrasound-guided foam sclerotherapy to treat seven patients with classical Klippel-Trenaunay syndrome yielded excellent short-term results. Functional integrity, cosmetic results and patient's satisfaction were used as endpoints. Severe complications of USFS are uncommon. The formation of cutane-

ous ulcer following injection, reported for one patient each in previous studies [13,14], was not (yet) encountered in our patients. In our modest experience, USFS is an effective minimally invasive ambulatory procedure that offers a valid alternative in the treatment of giant varicosities in patients with this disorder. It is essentially pain-free and has excellent short-term results. Long-term results and larger study groups are warranted.

Acknowledgment. We thank Mrs. Olga Ischakov for her skillful technical help.

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Creativity is allowing yourself to make mistakes. Art is knowing which ones to keep

Scott Adams (1957-), U.S. cartoonist