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Extensive muscle necrosis and infection following treatment of a lower extremity vascular malformation with Sotradecol and absolute ethanol

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Venous malformations are a subset of low-flow vascular malformations. These are usually present at birth and grow commensurate with the child. The treatment of low-flow vascular malformations has been studied extensively. Many interventions have been devised to benefit this patient population in regard to the pain, ulcerations, infections, cosmetic concerns, and overall bulk associated with these malformations. Treatment can begin with compression garments. Another treatment is sclerotherapy. This can be done as a stand-alone treatment or as an adjunct to surgical excision. Percutaneous sclerosis of venous malformations has an efficacy of between 74 and 90% in relieving symptoms. We present a case of percutaneous sclerotherapy with Sotradecol and ethanol into an extensive lower extremity venous malformation in the setting of orthopedic megaprosthesis. We feel that this led to extensive soft tissue necrosis and infection of the limb and created a precipitous situation. ***Blood Coagul Fibrinolysis*** **21:480–486 © 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

Blood Coagulation and Fibrinolysis 2010, 21:480–486

Keywords: clotting disorder, ethanol, muscle necrosis, Sotradecol, vascular malformation

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Received 17 November 2009 **Revised** 27 January 2010
Accepted 9 February 2010

Introduction

Venous malformations are a subset of low-flow vascular malformations as categorized by Mulliken in 1982 [1]. These are usually present at birth and grow commensurate with the child and may show exuberant expansion in adulthood [1–3]. The treatments of low-flow vascular malformations have been studied extensively. Many interventions have been devised to benefit this patient population in regard to the pain, ulcerations, infections, cosmetic concerns, and overall bulk associated with these malformations. Studies have demonstrated that intramuscular or intraosseous venous malformations, which are often misdiagnosed as hemangiomas, may also lead to pathologic fractures [4]. Plain radiographs may demonstrate these associated osseous deformities, soft-tissue swelling, and pathognomonic phleboliths [4]. A tailored compression garment is often the first-line treatment for symptomatic venous malformations in the extremities. The next level of treatment is sclerotherapy. This can be done as a stand-alone treatment or as an adjunct to surgical excision. Some of the agents investigated for sclerotherapy in venous malformations are Sotradecol (1% sodium tetradecyl sulfate; Bioniche Pharma, Bogart, Georgia, USA), 5% sodium morrhuate, ethanolamine oleate, Picibanil (OK432; Chugai Pharmaceutical Co. Ltd., Tokyo, Japan), bleomycin, ethanol, and hypertonic saline. These are used individually or in conjunction with one another. Percutaneous sclerosis of venous malformations has an efficacy of between 74 and 90% in relieving symptoms [3,5].

We present a case of percutaneous sclerotherapy with Sotradecol and ethanol into an extensive lower extremity venous malformation in the setting of orthopedic hardware. We feel that this led to extensive soft tissue necrosis and infection of the limb and created a precipitous situation.

Case report

A 39-year-old white woman presented to us with a diagnosis of an extensive venous malformation of her left lower extremity, including the buttock, groin, and ipsilateral labia majora. This diagnosis had been made clinically and based on a magnetic resonance imaging (MRI) scan. She had been followed closely for decades by a hematologist-oncologist for a consumptive coagulopathy. Baseline laboratories for the patient recorded a prothrombin time of 16.7 s, which corrected to 11.6 s on mixing, and a partial thromboplastin time (PTT) of 34 s, which corrected to 32 s upon mixing. Factor analysis showed that the factor V level was 59%, factor VII level 78%, factor VIII level 69%, and factor X level 64%. These are all lower than normal. The fibrinogen level was 65 mg/dl with a D-dimer of 8–16 mg/l. The antithrombin level was 71%, which is below the lower cutoff of 80–120%. The baseline platelet count was approximately 150 000 platelets per microliter. This picture is most consistent with a chronic disseminated intravascular coagulopathy, and the low antithrombin level suggests that there is ongoing consumption of this inhibitor.

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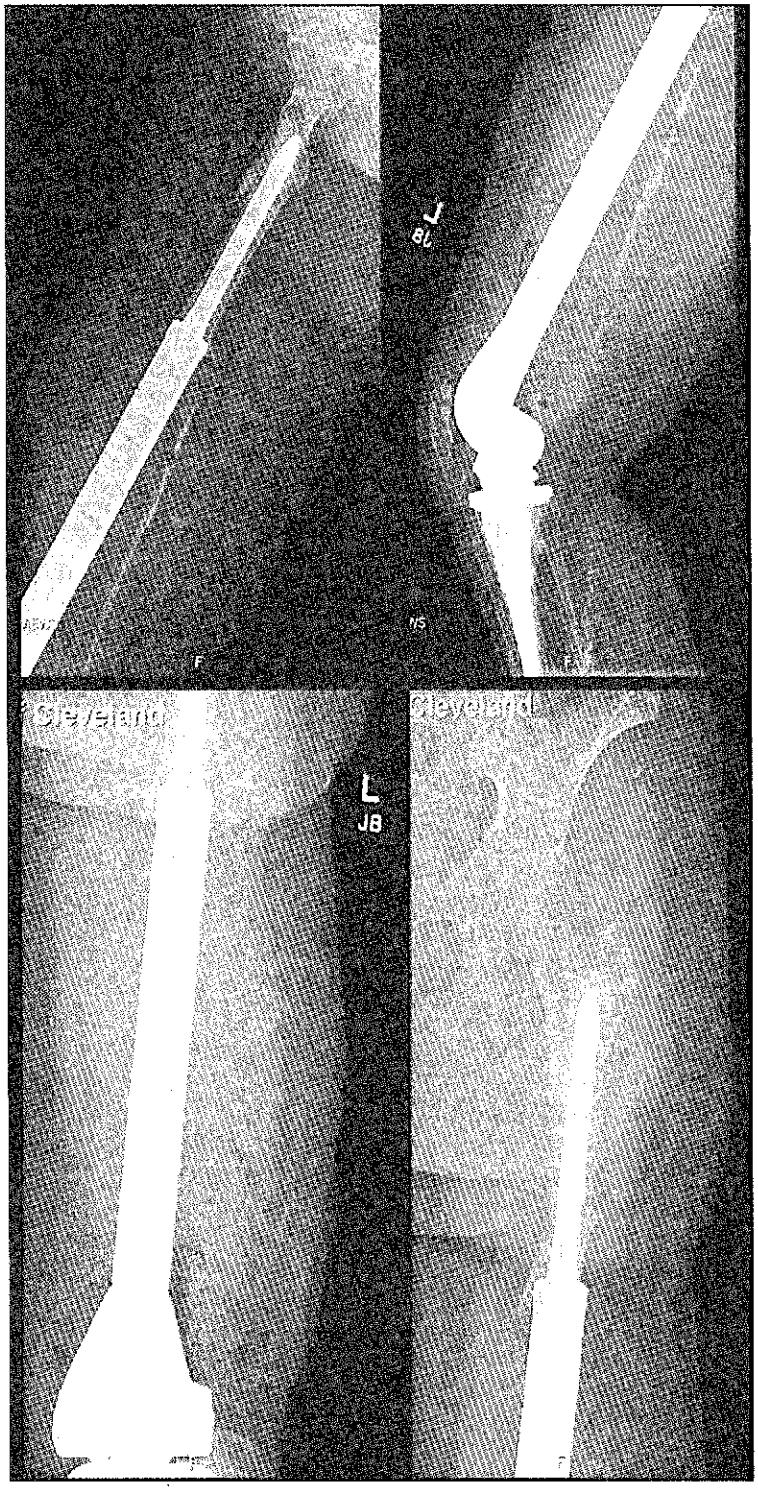
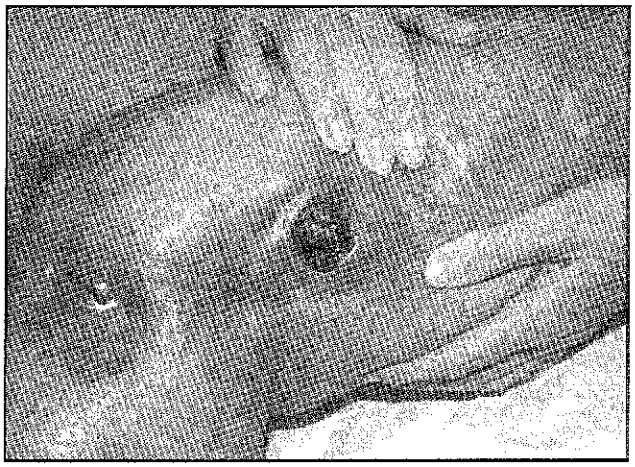
Fig. 1



Radiographs demonstrating the orthopedic hardware.

Fig. 2

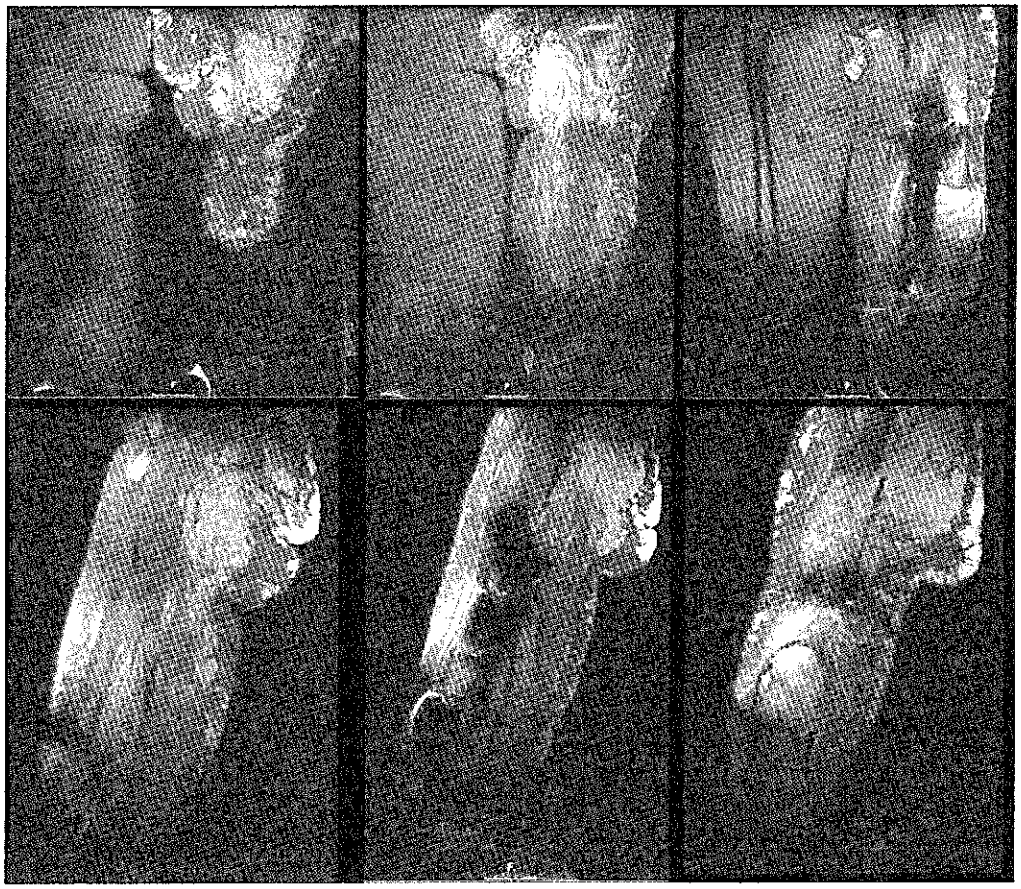


The patient demonstrates the ability to express fluid and necrotic tissue from lateral thigh wound.

The patient had been seen by several clinics specializing in vascular anomalies. She had been prescribed continuous use of a pressure garment. The patient had undergone a left total knee replacement due to pathologic involvement. She had sustained a periprosthetic fracture and due to overall thinning of the femur necessitated a reconstruction with a distal femoral megaprosthesis total knee replacement (Fig. 1).

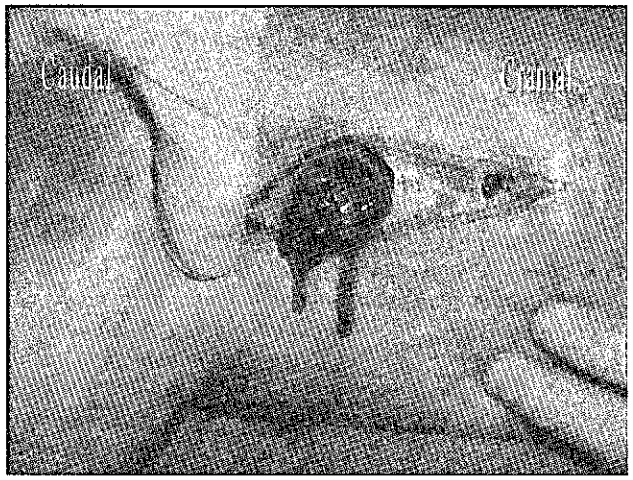
The patient elected to have sclerotherapy by an interventional radiologist who was out of network with her other subspecialists. Intralesional sclerotherapy of the left knee region with 15 mg absolute alcohol and 5 mg Sotradecol, mixed with Ethiodol contrast agent (10:2 ratio; ethiodized oil; Savage Laboratories, Mellville, New York, USA) was performed under ultrasound and fluoroscopic guidance. Large, aberrant venous channels around the knee were targeted, as these were most symptomatic in regard to bleeding and pain. Within 4 weeks, the patient presented with persistent febrile episodes to 39°C. Clinically, the lateral wound from her orthopedic incisional scar from a procedure approximately 2 years prior broke

Fig. 3



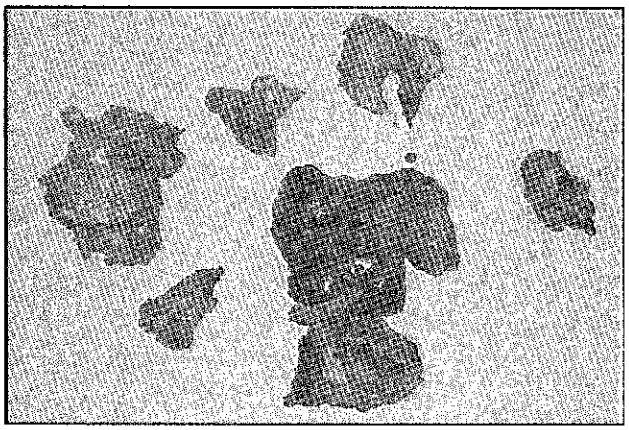
Magnetic resonance short-tau inversion recovery images demonstrating the extent of the vascular malformation and necrotic collection in the mid-thigh.

Fig. 4



Intraoperative findings. With gentle pressure, necrotic muscle was expressed from the wound.

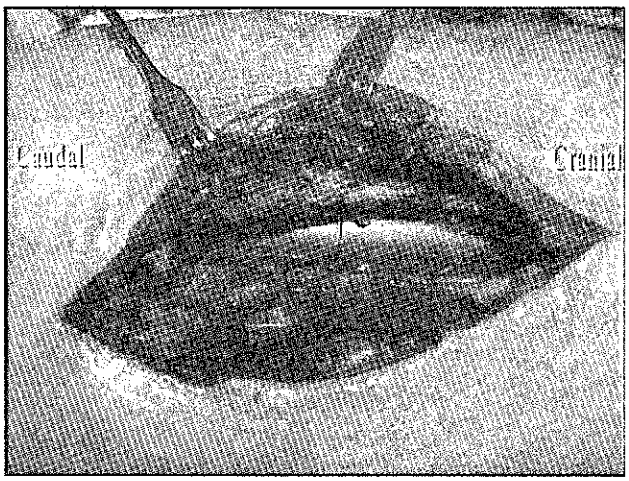
Fig. 6



The specimen after completion of the first debridement.

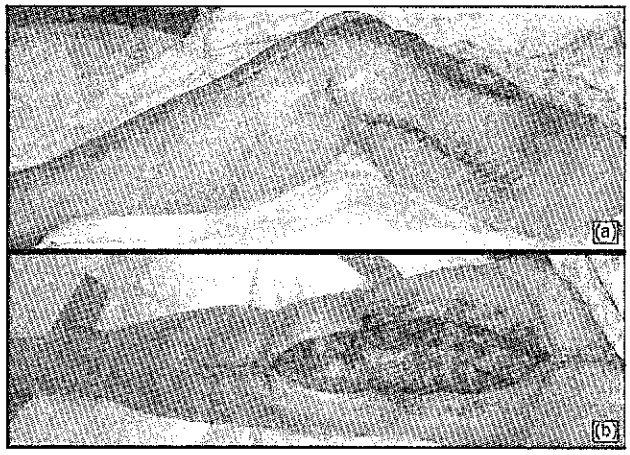
down demonstrating extensive muscle necrosis and purulent drainage (Fig. 2). This area was one of the targeted areas of prior sclerosing. The culture from this purulent drainage grew *Streptococcus viridans*. An MRI demonstrated a large necrotic area in the region that was injected with the sclerosing agents (Fig. 3). The patient was taken to the operating room for debridement and irrigation. The infected portion of the scar was excised along with large portions of necrotic muscle, which extruded from her incision with gentle pressure. Extensive areas of muscle were ultimately removed involving the lateral and anterior thigh (Figs 4–6). Pathologic analysis revealed skin and subcutaneous tissue demonstrating ulceration, organizing abscesses with areas of fibrosis, calcifications, and evidence of remote hemorrhage. Due to the patient's consumptive coagulopathy, she was transfused with packed red blood cells, cryoprecipitate, and fresh frozen plasma on multiple occasions. The patient was taken to the operating room 2 days after the first debridement for a secondary examination and washout. The lateral thigh defect was covered by de-epithelializing a bi-pedicle skin flap and closing this in a 'vest-over-pants' fashion (Fig. 7). The patient was followed closely by the infectious disease team and had vancomycin, fluconazole, and piperacillin/tazobactam administered by a peripherally inserted central catheter

Fig. 5



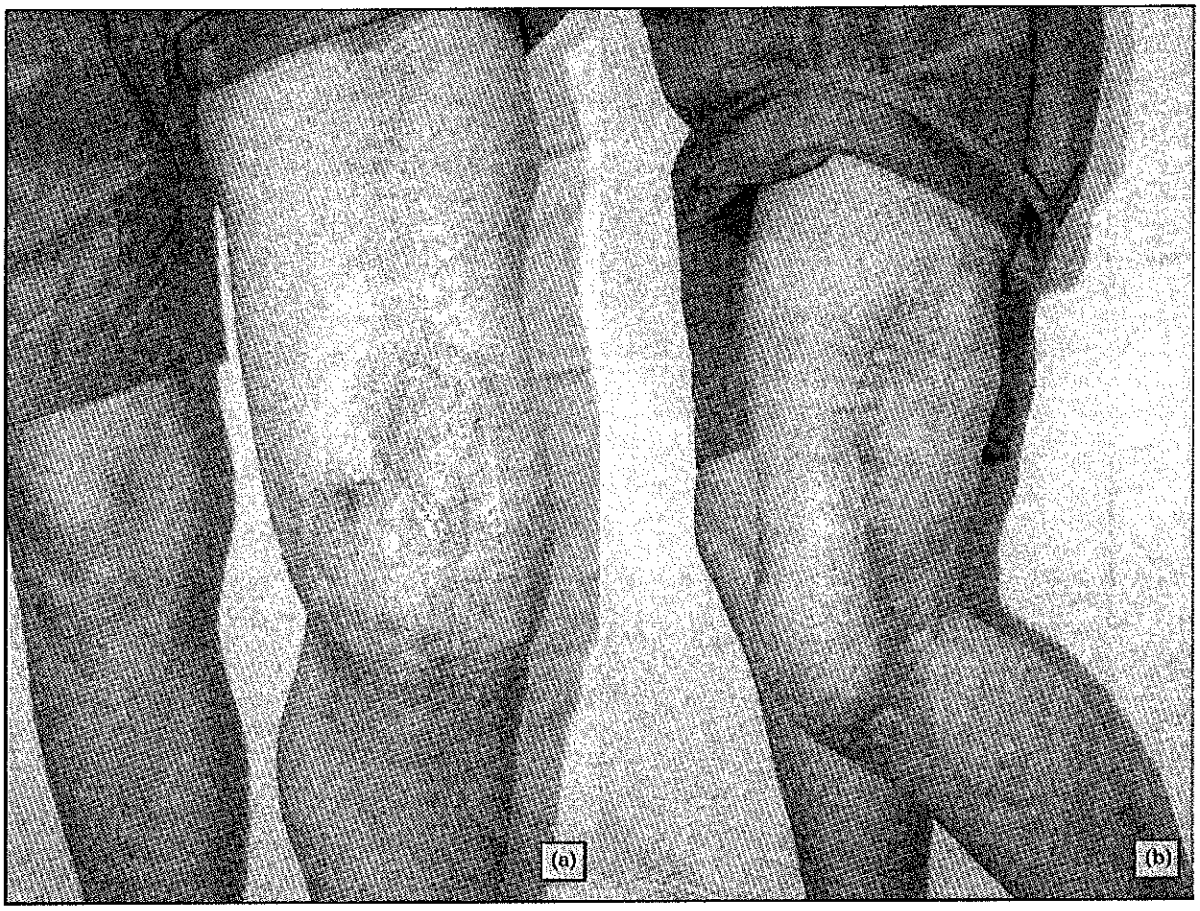
The femoral component of the megaprosthesis was exposed after the removal of necrotic muscle.

Fig. 7



(a) and (b) Vastus muscle group was plicated over the femoral implant and the lateral site was closed after deepithelialization of a bi-pedicle skin flap.

Fig. 8



(a) and (b) No signs of overt infection noted at 4 months postoperatively by clinical examination and laboratory data.

(PICC) line. This antibiotic regimen was tailored to include only tigycycline. She was on intravenous antibiotics for a total of 6 weeks from the last operation. Ultimately, the clinical infection abated and the wounds healed well. There were no signs of overt infection noted at 4 months postoperatively by clinical examination and laboratory data (Fig. 8a and b).

Discussion

Sotradecol and ethanol have been described and used widely as sclerosing agents for many low-flow vascular malformations. In the patient presented here, these agents were utilized in the treatment of a large venous malformation of the lower extremity in the setting of extensive orthopedic hardware. The main indication for this patient's treatment was to relieve pain and decrease bleeding episodes. There were no plans during the time of injection of surgical excision concomitantly.

Sotradecol is a nonpyrogenic sclerosing agent [6]. The agent is Food and Drug Administration (FDA) approved for use in the clinical setting of small, uncomplicated varicose veins of the lower extremity [6,7]. Its mechanism of action is the inflammation of the vessel intima and ultimate thrombus formation [6]. The effect of the sclerosant is proportional to the concentration and inversely proportional to the blood velocity [8].

The uses of this agent for sclerotherapy have been well documented in many low-flow states, including venous malformations [5,7–14], lymphatic malformations [9], varicose veins of the extremity [6,7], and digestive tract varices. Additionally, a number of case reports have demonstrated an expanded range of clinical uses such as the treatment of venous malformations of the glans penis [15] and even the injection of the soft palate for snoring [16]. This body of knowledge of Sotradecol in low flow states is in stark contrast to that of the use in high flow states. The use of Sotradecol has been described in high flow states in the treatment of hemangiomas and arteriovenous malformations [17–20]. Another report cites the successful

use in an acquired digital arteriovenous malformation [21].

Even though the off-label use of Sotradecol has been expanding, this agent has been shown to have several possible untoward effects. There are reported cases of anaphylaxis spanning the decades of its use [22–24]. In addition, many authors have cited extensive soft tissue necrosis after the use in the approved setting of varicosities [25]. Some authors have postulated that the intra-arterial injection of the agent may be a potential cause of extensive tissue necrosis in varicose cases. Furthermore, the incidence of skin necrosis with sclerotherapy of venous malformations with ethanol is significant. Many authors feel that this outcome is manageable with reconstructive surgery and is, thus, acceptable.

Absolute ethanol has also been used as a sclerosing agent for venous malformations. It is the most often used agent in this clinical setting due to its cost-effectiveness and low recurrence rate. Ethanol sclerotherapy is painful and requires general anesthetic. The mechanism of action is thrombosis by denaturation of blood proteins, denudation of vascular endothelium, and fracture of the vascular wall to the level of the internal elastic lamina [26,27]. There have been many cited complications with the use of ethanol for venous malformations. These include severe pain, swelling, acute blistering, damage of sensory nerves and major motor nerves, muscle atrophy, skin and soft tissue necrosis, hemolysis, and even airway compromise and tracheotomy after injection into a venous malformation of the tongue [27]. Another series demonstrates a case of pulmonary hypertension and cardiovascular collapse due to a high plasma concentration after percutaneous sclerotherapy with ethanol [26]. The skin necrosis with ethanol has been reported to be as high as 20% and is postulated to occur from reflux from superficial veins to capillary beds. Another postulate is that the alcohol inadvertently is injected into the subcutum proper. To combat this outcome, manual compression, rubber banding, or mechanical occlusion of the draining vein is used [28].

The patient cited was not a candidate for curative amputation, given the involvement deep into the pelvis of the malformation. The patient had multiple procedures for orthopedic stabilization of her lower extremity and many complications related to bleeding postoperatively. She had one prior episode of bleeding from a lateral wound 1 year prior to sclerotherapy. She had sought outside consultation for sclerotherapy of the affected limb with no plans of surgical intervention afterwards.

We postulate that the injection led to extensive necrosis of muscle and ultimate infection in a limb with a prosthetic implant. The infection was the first in this patient's history. There was no evidence of infection in that lower extremity prior to the injection of these sclerosing agents. It is a possible hypothesis that the procedure may have introduced bacteria into the area via the needle itself. However, this is a rarer complication as cited in the literature when done under aseptic technique.

In conclusion, the use of sclerosing agents in venous malformations is widely accepted as an effective treatment. Some authors are attempting to expand the use to selective high flow states, but these indications need to be studied in carefully controlled trials in order to be validated. For now, embolization followed by surgery is still the standard of care. The case presented highlights that the risks associated with the use of sclerotherapy in some low flow states, and in particular, in the setting of previous hardware need to be cautiously approached in a tertiary care center with a multimodality team.

Acknowledgement

The present study was supported by the Department of Plastic Surgery, University Hospitals Cleveland, Case Western Reserve University, Cleveland, OH 44106, USA.

The authors have no conflicts of interest or financial matters to disclose regarding this article.

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