Ethanol Sclerotherapy Reduces Pain in Symptomatic Musculoskeletal Hemangiomas

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Abstract Hemangiomas, benign vascular lesions, require intervention if causing pain or functional limitations. Functional deficits are common after excision, favoring minimally invasive treatments. To determine whether ethanol sclerotherapy reduces pain and lesion size and to assess complications in symptomatic musculoskeletal hemangiomas, we retrospectively reviewed 19 patients (six males, 13 females; mean age, 34 years) meeting criteria of confirmed hemangioma, treatment with ethanol sclerotherapy, and minimum of 6 weeks of followup. Fourteen were primary lesions and five were recurrent; all were painful. Thirty-eight sclerotherapy procedures were performed, with each patient undergoing a maximum of three procedures. Mean followup was 24 months (range, 2–95 months). Four patients reported full pain relief, 11 had partial relief, and four had no relief. With recurrent lesions,

one patient had full pain relief, one had partial relief, and three had no relief. For patients with lesions larger than 5 cm, two had full relief, six had partial relief, and three had no relief. Lesion shrinkage occurred in 12 patients. Temporary complications included paresthesiae (three), tendon contracture (one), skin breakdown (one), and deep vein thrombosis (one). Ethanol sclerotherapy afforded prompt pain relief in 15 of 19 patients with hemangioma, making it a reasonable option for initially avoiding surgical excision. However, the short followup of our patients requires additional long-term studies to assess the duration of the results.

Level of Evidence: Level IV, therapeutic study. See Guidelines for Authors for a complete description of levels of evidence.

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Introduction

Musculoskeletal hemangiomas are a rare form of hemangioma that typically present in young adults as an enlarging, painful mass [4, 15]. The term hemangioma is used loosely to describe various vascular tumors, and its proper use has been debated [4, 7]. Some authors strictly define hemangiomas as tumors of infancy characterized by endothelial cell proliferation and spontaneous involution during childhood [12]. They use the term “vascular malformation” for tumors of blood vessels that do not meet these criteria. Unlike cutaneous hemangiomas of infancy, musculoskeletal hemangiomas do not spontaneously regress and sometimes require treatment for symptomatic relief.

The diagnosis may be suggested by a history of increased pain and localized swelling with activity as the hemangioma becomes engorged with blood [15], but MRI

is most useful in confirming the diagnosis and ruling out malignant processes [1] (Figs. 1, 2). We use hemangioma to refer to benign-appearing vascular tumors as diagnosed by MRI, in keeping with the definition by Enzinger and Weiss of a hemangioma as “a benign but non-reactive

process in which there is an increased number of normal or abnormal-appearing vessels” [4]. When a more specific classification is needed for treatment, we perform angiography.

Surgical excision of symptomatic hemangiomas can be curative, but avoiding recurrence is largely dependent on achieving negative surgical margins [1, 9]. Hemangiomas frequently infiltrate nearby structures, making excision complicated. Surgeons often resort to performing intralesional excision rather than compromise muscle and nerve function for a benign condition; one large retrospective series reported an intralesional excision rate of 62% [1], and a smaller series reported a 30% rate of intralesional excision [3]. However, the rate of recurrence after incomplete excision is reportedly as much as 18% to 50% [1, 4, 15] and tumor remnants can grow aggressively, causing symptoms even worse than before surgery [17]. If complete excision can be achieved, the recurrence rate is reportedly as low as 0% to 9% [1, 3, 13], but complications such as fibrosis and muscle weakness are common after surgery [7].

Sclerotherapy with liquid denaturing agents has been an alternative to surgical excision of hemangiomas since the 1930s [14]. Focal hemangiomas present an ideal target for sclerotherapy owing to their low-flow state, being sequestered, or having only small, easily occluded connections to normal venous drainage, resulting in the majority of the lesion volume consisting of stagnant intraluminal fluid [2]. The number of sclerosing agents available for this procedure and sites for its application has expanded during the years. Ethanol remains a popular choice because of its high potency, availability, and ease of administration [16]. The assistance of anesthesia and ultrasound allow ethanol to be

Fig. 1A–B (A) This axial T1-weighted MR image shows an ill-defined mass hypointense to muscle located between the first and second digits of the left hand of Patient 3. (B) A corresponding T2-weighted MR image shows the mass to be extremely bright and formed of the serpiginous structures associated with a hemangioma.

Fig. 2A–C (A) This coronal T1-weighted MR image of the right thigh of Patient 19 shows an intramuscular mass isointense to the surrounding muscle but delineated by the intralesional fat often associated with a hemangioma. (B) This corresponding coronal T2-weighted MR image shows the lesion to be bright with a similar

appearance to the surrounding normal vessels. (C) A corresponding contrast-enhanced fat-suppressed T1-weighted MR image shows uniform bright enhancement of the lesion, another common imaging feature of hemangiomas.

used safely even for deep musculoskeletal lesions. The injected sclerosing agent causes endothelial damage and thrombosis of the vessels, which arrest growth and promote regression of the hemangioma [7, 14]. Although complete resolution of the tumor is unlikely, sclerotherapy often provides enough improvement in pain and function to forestall the morbidity of surgical excision on a long-term or even permanent basis [15].

Because hemangiomas often occur in the cutaneous or subcutaneous spaces, there is no published focused investigation of the utility of ethanol sclerotherapy for hemangiomas in only deep musculoskeletal locations. Currently, reports generally comprise deep and superficial lesions, often include those of the face and skull and intrapelvic lesions, or investigate the use of alternate sclerosing agents [6, 8, 9, 14–17]. There also is a paucity of literature concerning the utility of sclerotherapy as an analgesic treatment modality in these lesions, as numerous reports address cosmetic issues, spinal cord compression, or, in the case of massive lesions, cardiovascular compromise [6, 8, 16, 17].

We thus sought to determine (1) whether ethanol sclerotherapy provided effective immediate or short-term pain relief for patients with symptomatic musculoskeletal hemangiomas, (2) lesion characteristics that may limit the

pain relief afforded by sclerotherapy, (3) whether changes in hemangioma size would be seen after sclerotherapy, and (4) the rate and severity of complications resulting from sclerotherapy. We anticipated ethanol sclerotherapy would provide symptomatic relief and induce some decrease in lesion size with a low complication rate.

Materials and Methods

We retrospectively identified 69 patients from our records with a diagnosis of hemangioma treated with an interventional procedure from 2000 to 2007. For this study, we included patients with (1) a confirmed musculoskeletal hemangioma, based on a combination of MRI and ultrasound, angiography, and/or needle biopsy; (2) treatment with sclerotherapy; and (3) a minimum followup of 6 weeks. We excluded 40 patients because they underwent surgical excision of the hemangioma rather than sclerotherapy (Fig. 3). Reasons for proceeding to surgery without attempting sclerotherapy included (1) a need for open biopsy to obtain a definitive diagnosis, (2) functional deficits caused by the tumor, (3) the interventional radiologists did not believe sclerotherapy could be performed safely based on the location of the lesion, and (4) patient

Fig. 3 This diagram provides a treatment algorithm used for patients with hemangiomas seen at our center and also displays patients retrospectively identified for our study. The boxes with bolded type in the diagram display the treatment path used for symptomatic patients. IR = interventional radiology.

preference. Six more of the 69 patients were excluded for inadequate clinical followup and two patients for unsuccessful sclerotherapy—one because of inability to cannulate the feeding vessel and the second because of lack of adequate vascular flow. We excluded an additional two patients because angiography revealed the lesion to be an arteriovenous malformation (AVM), whose high flow rate and systemic connection prevented use of a sclerosing agent. This left 19 patients (six males, 13 females), with a mean age of 34 years (range, 15–82 years). All patients had MRI before sclerotherapy. The minimum followup was 2 months, and 13 of 19 patients had a followup greater than 12 months (mean, 24 months; range, 2–95 months). We reviewed medical records and recalled the five patients who failed to keep scheduled followup appointments. One patient remained lost to followup. We had prior Institutional Review Board approval.

From the medical records, we extracted demographic data, presclerotherapy symptoms and lesion characteristics, previous treatments, number of sclerotherapy treatments, presclerotherapy and postsclerotherapy MRI size data, postsclerotherapy symptoms, major and minor complications, and any future treatments needed. Previous treatments, preprocedural and postprocedural symptom and size data, and the number of sclerotherapy procedures had been abstracted from a clinical record-keeping patient worksheet designed specifically for use with sclerotherapy procedures. Minor complications were defined as those which were temporary and resolved without an invasive procedure. Major complications were defined as any which were permanent or required an invasive procedure to treat. Sixteen hemangiomas were located in soft tissue: six in the lower leg, three in the thigh, three in the hand, two in the forearm, and two in the foot. Three hemangiomas were located in bone: one in the tibia, one in the fibula, and one in the radius. Fourteen patients were treated for their initial tumor and five patients were treated for recurrence after prior resection. Lesion size ranged from 2 to 20 cm in largest diameter. All patients presented with pain. Fifteen patients had additional symptoms, including a palpable mass (11 patients), intermittent swelling (four), mild gait abnormality (two), and decreased range of motion secondary to pain (one).

Having reviewed any preprocedure imaging with the interventional radiology team at our multidisciplinary conference, patients with suspected hemangioma then were referred for percutaneous treatment of a painful vascular lesion by our center's interventional radiologists. At the time of the procedure, the patient was administered conscious sedation and local anesthetic. Ultrasound evaluation of the lesion was performed to rule out the presence of a high flow lesion with substantial systemic connection, such as an AVM or arteriovenous fistula (AVF). Patients in

whom ultrasound analysis was inadequate for ruling out high flow AVM or AVF then underwent angiography (10 patients). If an AVM or AVF was identified, these lesions were scheduled for a more appropriate bead or coil embolization procedure. As we did not consider angiography necessary for diagnosis [2], the remaining nine patients proceeded directly with the sclerotherapy procedure based on clinical suspicion and ultrasound evaluation alone. After the angiography or ultrasound evaluation, a tourniquet was placed proximally to all limb lesions if possible and inflated to a pressure less than the systolic arterial pressure to limit the escape of ethanol into arterial circulation and prevent subsequent complications. An intravenous cannula system then was introduced percutaneously into the lesion under sonographic guidance. A preliminary injection of contrast medium was performed under fluoroscopic guidance to ensure appropriate placement of the catheter, exclude arterial connection (AVM or AVF), show the vascularity and volume of the lesion, and ensure the lesion was sequestered or outflow could be limited by the tourniquet. Next, absolute ethanol (100% dehydrated alcohol) was injected into the hemangioma in a quantity determined by the volume of contrast that the hemangioma held before the filling of any minor draining veins. The ethanol was left in place for 5 to 10 minutes, depending on radiologist preference, before being aspirated. Contrast then was injected a second time to ensure diminished filling of the lesion. If used, the tourniquet remained inflated for 20 to 30 minutes after completion of the injections to allow bodily absorption of any remaining ethanol and to avoid accidental introduction of an ethanol bolus into the systemic circulation. The procedure was aborted if the hemangioma could not be cannulated or the outflow could not be controlled and was identical for soft tissue and bone lesions. Patients then were transferred to the recovery area and monitored closely for signs of hypoxia or bradycardia, which can signal the rare cardiovascular collapse associated with a systemic ethanol bolus. Patients with large hemangiomas or in whom the majority of the lesion could not be reached with one cannulation usually were scheduled for multiple sclerotherapy treatments several weeks apart to achieve optimal symptomatic relief. Some patients elected to stop after only one procedure because they achieved full relief, satisfactory relief, or no relief. Thirty-eight sclerotherapy procedures were performed in the 19 patients. Seven patients had one procedure, five patients had two procedures, and seven patients had three procedures (Table 1).

Barring immediate complications, patients were seen for an initial followup 2 to 3 months after their sclerotherapy procedure. Treating physicians documented any change in symptoms on a standardized patient information worksheet developed for use with this procedure. MRI also was

Table 1. Patient characteristics and outcomes after sclerotherapy

Patient	Site	Largest lesion diameter* (cm)	Number of treatments	Pain relief	Complications
No prior treatment					
1	Left calf	5.5	3	Partial	Deep vein thrombosis
2	Right foot	9.8	2	Partial (temporary)	None
3	Left hand	3.0	1	Full	None
4	Right ankle	8.0	1	Full	None
5	Right calf	20.0	2	None	Tingling and pain over dorsum of foot
9	Right calf	Not reported	3	Full (temporary with first)	Tibialis anterior tendon contracture
10	Left wrist	1.3	1	Partial	Mild tingling
11	Left forearm	10.0	1	Partial	None
12	Right forearm	1.9	3	Partial (temporary)	None
14	Right foot	8.0	3	Partial	Numbness
15	Left leg	7.6	3	Partial (temporary)	None
16	Right hand	13.0	1	Partial	Skin breakdown
18	Right knee	3.3	2	Partial	None
19	Right thigh	3.0	2	Partial (temporary)	None
Prior surgical resection					
6	Left thigh	8.0	1	None	None
7	Right leg	Not reported	2	Partial	None
8	Right knee	4.4	3	None	None
13	Left hand	5.5	1	Full	None
17	Left calf	14.0	3	None	None

* Determined by presclerotherapy MRI.

performed at that time to assess change in lesion size, as determined by radiologist measurements compared with preprocedural studies. If patients received partial pain relief, the possibility of additional sclerotherapy treatments was discussed during this appointment. Further routine followup included appointments at 1 and 2 years after the procedure, but patients did not routinely have reimaging in conjunction with these appointments unless there was an increase in pain or other symptoms or an increase in the size or occurrence of a palpable mass. Patients then were released from followup but invited to contact our office for any future increase in symptoms. Followup was calculated from the date of the patient's first sclerotherapy treatment to the date of the patient's last contact with our office. An additional attempt was made via telephone to contact the five patients who did not continue to keep regularly scheduled followups before release by the treating physician.

Results

By latest followup, four patients had full relief of pain, 11 had partial relief, and four had no relief (Table 1). No

patient who experienced full pain relief had a later increase in pain or required a subsequent procedure at a mean followup of 31 months. Five of 11 patients who had partial pain relief later experienced increased pain at a mean of 22 months (range, 5–60 months). Repeat sclerotherapy treatments afforded partial or full relief for three of these patients. One patient elected to have surgery rather than repeat sclerotherapy, and the fifth patient could not be contacted for additional followup.

Of patients who had no pain relief with sclerotherapy, three of the four had surgical resection before presentation to our clinic. For two of these patients, the resection had provided initial full symptomatic relief, but the mass and pain recurred. The third patient had worsened pain after resection. Of all five patients who had prior resection, one experienced full pain relief, one had partial relief, and three had no relief. Of the 11 patients whose presclerotherapy imaging revealed a large lesion (> 5 cm), two experienced full pain relief, six had partial relief, and three had no relief.

One patient of 19 had full resolution of the lesion, 11 had a decrease in size, five had no change, and two had continued growth of the hemangioma based on postsclerotherapy MRI taken 2 to 3 months after the procedure.

Although full resolution was surprising, the one patient experiencing this had an arteriogram confirm the diagnosis of hemangioma before sclerotherapy. Three of the 11 patients who had a decrease in size of the lesion later had an increase to the original size or larger by 5 months, 1.5 years, and 2 years.

Minor complications occurred in six patients. No major complications occurred. Three patients experienced temporary paresthesiae or nerve pain at the site of sclerotherapy, which fully resolved. One patient had a tibialis anterior tendon contracture develop after sclerotherapy in the lower leg, which resolved with physical therapy. One patient returned to the office 5 days after sclerotherapy in her calf with pain in her lower leg. She had a deep vein thrombosis and was treated with warfarin. She had no further problems and proceeded to have two more sclerotherapy treatments without complications. One patient who had sclerotherapy of a finger hemangioma experienced skin breakdown at the tip of his finger. This healed spontaneously without residual pain or immobility, although the patient described occasional hypersensitivity at his fingertip.

Discussion

Clear histopathologic margins are recommended to avoid recurrence after surgical excision of musculoskeletal hemangiomas [1, 9]. Despite a substantial recurrence rate with increased symptoms after less aggressive procedures, it is difficult to justify function-altering wide resections for these benign tumors. Sclerotherapy has been recognized for decades as a less morbid treatment option, with ethanol being the most common sclerosant [14, 16]. However, most reports have focused on superficial lesions and their cosmetic consequences [6, 8, 14], with few dealing exclusively with deep musculoskeletal lesions [7, 13] and the effectiveness of sclerotherapy in pain relief [7, 9]. We sought to investigate the impact of sclerotherapy on pain relief, identify characteristics influencing its effectiveness, report size change induced by sclerotherapy, and describe observed complications.

Our study is not without limitations. Because it is retrospective, we did not have quantitative data on the degree of pain relief. We did fill out a worksheet for each patient at followup designed specifically to document the outcome of hemangioma sclerotherapy, including pain changes. Our conclusions also are limited by small sample size, precluding the use of statistical analyses in investigating patient subgroups in whom sclerotherapy may be of altered benefit. However, given the lack of reports exclusively describing the outcome of sclerotherapy in symptomatic musculoskeletal lesions, we believe our data are still useful in this patient group.

Ethanol sclerotherapy afforded some degree of pain relief in 15 of our 19 patients, consistent with studies reporting pain improvement in 72% to 86% of patients with vascular malformation undergoing sclerotherapy [7, 9]. In comparison to surgical outcomes, 62% of 89 patients in the series by Tang et al. [11] had pain resolution after hemangioma excision and 37% had residual pain (mean followup, 5 years). Surgical consequences included partial bone resection, insertion of plate fixation, and muscle flap coverage. Complications included hemarthroses, infection, and permanent nerve damage. The recurrence rate was estimated at 19% and many underwent surgical excision for recurrence [11]. Although the pain improvement rate was greater in the surgical series, 79% of our patients had pain improvement without surgical morbidity, making sclerotherapy a worthwhile initial treatment. By providing specific results regarding pain outcomes, the value of this less invasive therapy can be weighed against surgical excision, which may eradicate the tumor but has moderate risk of functional deficits and recurrence [1, 7, 11]. Regardless, sclerotherapy does not limit future treatment options. In our series, successive sclerotherapy treatments provided additional pain relief, and repeat treatments for recurrent symptoms were successful. This may allow for long-term and perhaps permanent avoidance of surgical morbidity, but excision is still feasible. Sclerotherapy may even simplify subsequent excision [8, 14].

Our small numbers preclude statistical analysis of subgroup results. However, we believe the data suggest worse outcome after previous surgical excision, a point which if true is not addressed in the literature. It did not suggest a worse outcome for patients with lesions greater than 5 cm in largest diameter, which previously was reported [2, 5, 7].

Although we counsel our patients that sclerotherapy is intended to relieve pain and prevent growth rather than shrink the tumor, 12 of our 19 patients had a decrease in lesion size after sclerotherapy, and one had complete resolution. Winter et al. [14] reported complete tumor resolution in 81% of cutaneous hemangiomas sclerosed with polidocanol, whereas Hein et al. [7] suggested hemangioma swelling also may decrease in intramuscular hemangiomas. The effect may not be permanent, however, as seen in three patients in our series who experienced hemangioma growth many months after an initial size decrease. Potential explanations for temporary response are that vascular damage is reversible or incomplete. Some authors have cited recanalization and neovascular recruitment as cause for increasing symptoms and suggest serial injections for maximal results [7, 9, 17]. If the presence of a mass is concerning to the patient and marginal excision can be achieved without sacrificing function, surgical excision then may be warranted, with a reported recurrence rate less than 10% [1, 3, 13].

The complication rate in our patients aligned with the 28% rate recognized for ethanol sclerotherapy [2]. Complications were relatively minor and resolved with conservative management. Risks of sclerotherapy are primarily a consequence of the anatomic location of the lesion with respect to nearby structures [2]. Extravasation of sclerosant outside the hemangioma can cause tissue necrosis or nerve damage [9, 10, 14]. Superficial lesions are at risk for skin necrosis [2]. Temporary postsclerotherapy swelling is normal [14, 16], but persistent swelling may indicate deep vein thrombosis in the normal circulation. Rare systemic complications occur if sclerosant, particularly ethanol, leaks into arterial circulation and can include arterial thrombosis, hypotension, or even death [9, 10, 14]. This is easily avoided with available anesthesia support, serial small volume injections, and preprocedural observation of the lesion for systemic anastomoses [7, 16]. A technique has been developed to further reduce risk by using a second needle to drain the ethanol from the hemangioma [10]. We used all of the above precautions in our patients, using serial injections when a large volume of ethanol was necessary. Because of the systemic risks of ethanol and associated precautions, alternate sclerosants, such as polidocaine, sodium tetradecyl sulfate, and ethanolamine oleate, have gained favor [6, 9, 14]. However, all agents can cause tissue necrosis and hemolysis [7]. Furthermore, the largest number of ethanol sclerotherapy procedures performed in our patients was three, whereas published studies using other sclerosants report up to 10 procedures necessary [9, 14]. Our results support the existing evidence that ethanol can be used safely with adequate precautions.

In our patients with symptomatic, exclusively deep musculoskeletal hemangiomas, ethanol sclerotherapy provided symptomatic relief in 15 of the 19 patients, a similar rate as in other studies less focused on musculoskeletal lesions [7, 9]. The majority of our patients had a decrease in lesion size, and there was a low rate of minor complications. We believe these good early results suggest sclerotherapy is a reasonable option for initial treatment of symptomatic musculoskeletal hemangiomas. A longer-term followup series is necessary to assess the durability of pain relief and the recurrence rate for this procedure.

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