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CLINICAL INVESTIGATION

Sclerosing Therapy for Orbital Lymphangioma Using Sodium Tetradecyl Sulfate

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Abstract

Purpose: To describe the results of intralesional injection of the sclerosing agent sodium tetradecyl sulfate in patients with orbital lymphangioma.

Methods: Four young patients with a history of orbital lymphangioma were treated on one or more occasions with percutaneous puncture and injection of sodium tetradecyl sulfate under computed tomography guidance. Resolution of the signs and symptoms, complications resulting from surgery, and recurrence of bleeding were studied.

Results: Three patients with a long-standing history of unilateral proptosis and one patient with progressive unilateral visual loss from multiple recurrent orbital hemorrhages were studied. Treatment ranged from one to three sodium tetradecyl sulfate injections. All patients showed improvement of their signs and symptoms after treatment. A decrease in the size of lesions was demonstrated by orbital imaging. Visual acuity and intraocular pressure remained unchanged. Complications included transient postoperative localized inflammation in all cases and transient ophthalmoparesis in one patient. Follow-up time ranged between 15 and 36 months, during which no recurrence of bleeding was observed.

Conclusions: Our study suggests that intralesional injection of sodium tetradecyl sulfate under computed tomography guidance is an effective treatment for patients with orbital lymphangioma and is not associated with vision-threatening complications. **Jpn J Ophthalmol** 2008;52:298–304 © Japanese Ophthalmological Society 2008

Key words: orbital lymphangioma, sclerosing, sodium tetradecyl sulfate

Introduction

Orbital lymphangioma is a benign, slowly progressive vascular malformation that is probably congenital but which may not become clinically apparent for months or years after birth. Most patients are diagnosed during the first decade of life. Clinically, orbital lymphangioma usually presents as gradually increasing proptosis. Deep orbital lesions may be present with acute onset of proptosis resulting from spontaneous hemorrhage into what has been previously unrecognized lesions. The infiltrative tumor mass may compress the globe or optic nerve, causing refractive errors, secondary glaucoma, and optic nerve dysfunction.[1]

The management of orbital lymphangioma is challenging. Observation is the preferred method of management for many of these lesions. Surgery is almost never curative and often results in progressive loss of function with multiple surgical debulking attempts;[1–3] it has, therefore, become a treatment of last resort. Alternatives to simple surgical resection include carbon dioxide laser ablation, systemic corticosteroids, and irradiation, all of which have displayed varied degrees of success in the past.[3–5]

Sclerotherapy is not a new concept. Injection of orbital vascular malformations with various types of sclerosing solutions has been reported.[6–9] Sclerosing agents work by

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producing endothelial damage that eventuates in endofibrosis and results in thrombosis of the vessels.[10] Sodium tetradecyl sulfate is one sclerosing solution that has been successfully used for treatment of vascular lesions in various sites such as oral and facial hemangiomas and intracutaneous telangiectasia of the leg, face, and trunk.[11,12] It has also been used in treatment of lymphangioma. Preliminary results have shown that sodium tetradecyl sulfate may be a useful therapeutic option in patients with eyelid and orbital lymphangioma.[7,8] The purpose of this study was to evaluate the outcome of intralesional injection of 3% sodium tetradecyl sulfate for the treatment of orbital lymphangiomas in Thai patients. We describe the technique of percutaneous puncture under computed tomography (CT) guidance, which allowed a more precise sclerosing agent injection.

Materials and Methods

A prospective study of four patients with orbital lymphangioma at Ramathibodi Hospital was conducted from January 2003 to December 2005. Based upon clinical findings and CT and/or magnetic resonance imaging (MRI) examination, the lesions in the orbit were punctured directly under CT guidance. Each patient was given 3% sodium tetradecyl sulfate (Thrombovar; E-Z-EM, Montreal, Canada) intralesionally. The main outcome measures were lesion regression evidenced by clinical examination and radiographic studies, functional and cosmetic outcomes, and comprehensive eye examination. Signed informed consent was obtained from all study subjects. The study was approved by the local institutional review board.

Each patient received from one to three injections in total that were spaced at least 3 months apart, with each injection involving a volume of 1.5–2 ml of sodium tetradecyl sulfate. A comprehensive eye examination was performed before the first treatment and at 1 day, 1 week, 1 month, and 3 months after the first injection and every 3 months thereafter. Clinical postoperative evaluation and CT scans were obtained and evaluated for changes in the size or position of the tumor. Results of examinations conducted before 3 months after each injection were not evaluated.

Injection Technique

The procedure was performed under local anesthesia in three patients and general anesthesia in one patient. Local anesthesia was done by subcutaneous injection of 2% lidocaine HCl combined with 0.5% bupivacaine HCl into the selected location, usually the lower eyelid. A preinjection CT scan of the orbit was performed to localize the lesions. After the skin was disinfected with povidone iodine, a 20-gauge intravenous catheter with a 10-ml syringe was inserted percutaneously into the tumor. Negative pressure aspiration was done until backflow of fluid or blood into the syringe was visible. The lesion was emptied as much as possible. Thereafter, a small amount of diluted radiopaque contrast medium (0.5 ml) was injected. Another CT scan was performed to verify that the tip of the needle was in the cavity and that the contrast medium had filled the mass (Fig. 1). If the tip of the needle was in the correct position, the previously injected contrast medium was withdrawn and a suitable amount of the prepared sodium tetradecyl sulfate solution (2 ml of 3% sodium tetradecyl sulfate mixed with 0.5 ml of contrast media), usually 2–2.5 ml, was injected. A CT scan was performed at the end of each procedure to identify the drug distribution and check for evidence of leakage. The average length of each procedure was 30 min. After the injection, the patients were given intravenous dexamethasone (0.3 mg/kg) and cloxacillin (50–100 mg/kg) divided into four doses every 6 h, followed by oral prednisolone (1 mg/kg per day) and oral cloxacillin (50–100 mg/kg) for 1 week.

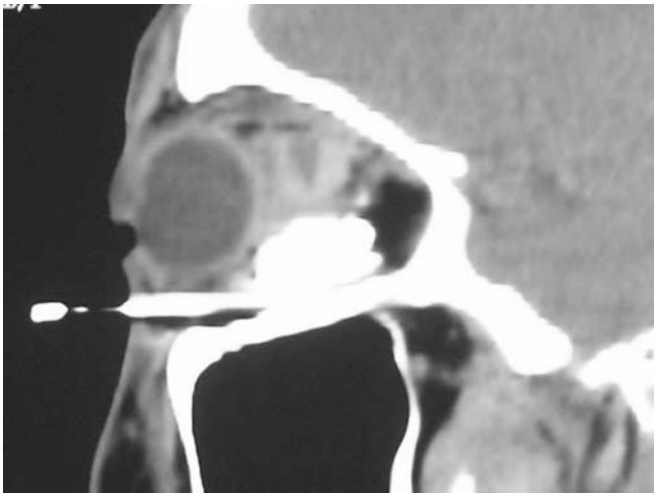

Figure 1. Computed tomography (CT) scan showing the correct position of the needle in the orbit and a good filling of contrast media in the lower part of the tumor (case 3).

Results

We studied three male patients and one girl ranging from 10 to 18 years of age. All patients presented with an orbital lesion without eyelid involvement. Patients received an average of two (range, one to three) intralesional injections of sodium tetradecyl sulfate. At the end of the follow-up period, visual acuity, visual field, and intraocular pressure remained unchanged. Complications included one case of ophthalmoparesis that resolved spontaneously over a 2-week period (case 3). Immediately after the procedure all patients experienced pain that lasted for 2–6 h, and all developed a moderate, localized inflammatory reaction, including eyelid swelling, ecchymosis, chemosis, and subconjunctival hemorrhage, that resolved over a 1-week period. None of the patients reported systemic complications. The follow-up period after the last injection ranged

Table 1. Clinical features and treatment outcome

No.	Age (years)	Sex	Clinical presentation	Initial VA	No. of injections	Outcome	Final VA	Recurrence	Follow-up period (months)
1	15	Male	Recurrent orbital hemorrhages	HM	1	No recurrent hemorrhage	HM	No	24
2	10	Male	Progressive proptosis	20/20	1	3.5 mm decrease of proptosis	20/20	No	36
3	18	Male	Progressive proptosis	20/20	3	9 mm decrease of proptosis	20/20	No	15
4	16	Female	Progressive proptosis	20/20	2	4 mm decrease of proptosis	20/20	Yes	15

VA, visual acuity; HM, hand motion.

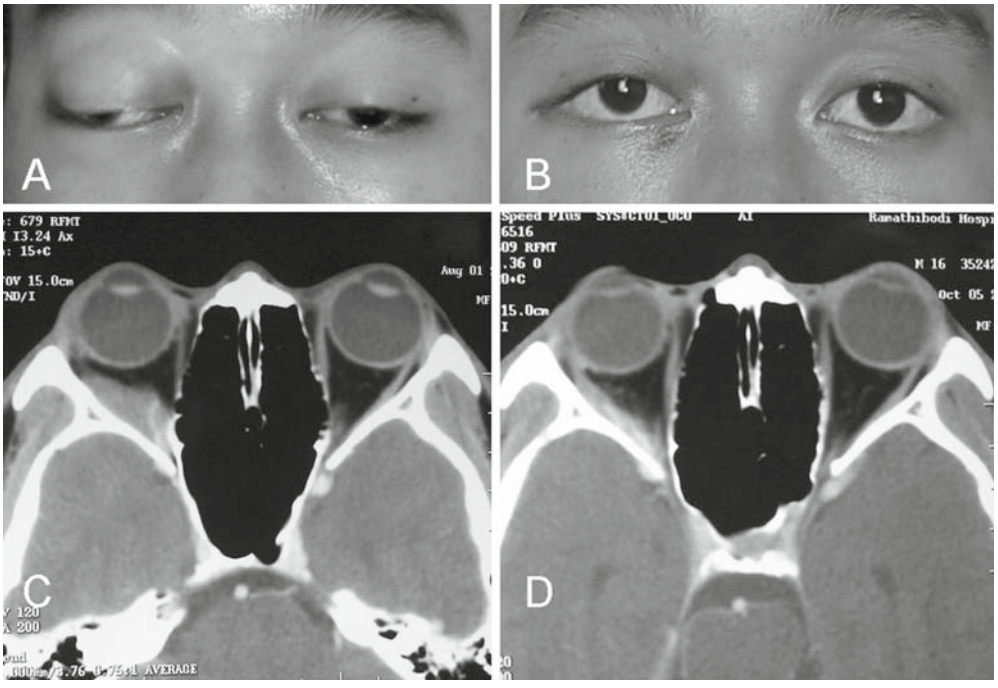

Figure 2. A A 15-year-old boy with acute severe proptosis of the right eye caused by orbital lymphangioma with spontaneous hemorrhage. **B** On the day after drainage, the orbital signs and symptoms were completely resolved. **C** CT scan of the orbit with contrast prior to injection showing an ill-defined enhancing lesion occupying the inferolateral aspect of the right orbit. **D** Three months after sclerotherapy, there is moderate shrinkage of the lesion.

from 15 to 36 months. The clinical features and outcome of each patient are summarized in Table 1.

Case 1

A 15-year-old boy presented in January 2002 with a 3-day history of acute proptosis and visual loss in the right eye. Visual acuity was no light perception in the right eye and 20/20 in the left eye. There was moderate eyelid swelling, ecchymosis, and subconjunctival hemorrhage in the right eye. He had right proptosis of 8 mm and a right afferent pupillary defect. His right extraocular movements were limited in all directions. A CT scan revealed an ill-defined heterogeneous enhancing lesion occupying the inferolateral aspect of the right orbit. A presumed diagnosis of orbital lymphangioma with spontaneous hemorrhage was made. Orbital aspiration was performed, followed by intravenous methylprednisolone 1 g/day for 3 days with improvement of orbital signs and symptoms. Visual acuity was improved to hand motion. An incisional biopsy was performed a week later and confirmed the diagnosis of lymphangioma. Over the next year, the patient had three episodes of recurrent hemorrhage and was treated by repeated drainage (Fig. 2A, B). In July 2003 the patient underwent a sclerosing injection under CT guidance. Three months after the injection, CT revealed moderate shrinkage of the lesion (Fig. 2C, D). During 2 years of follow-up after the injection, he had no recurrent hemorrhage and no further ocular symptoms.

Case 2

A 10-year-old boy had gradual progression of right eye protrusion over a 6-year period. On examination, his vision was 20/20 bilaterally, and he had 4 mm of right proptosis. MRI and CT of his orbits revealed an ill-defined, multilobulated, intra- and extraconal mass in the medial aspect of

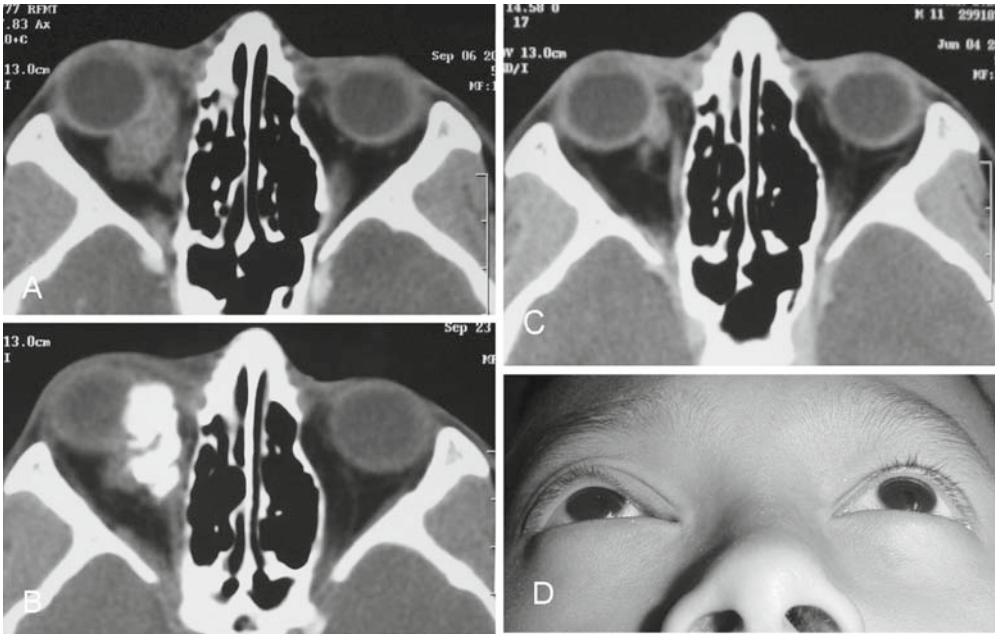

Figure 3A–D. A 10-year-old boy with moderate proptosis caused by orbital lymphangioma. **A** CT before treatment shows a right orbital mass. **B** After the procedure, there is a good filling of the sclerosing agent without leakage. **C** CT shows a small residual tumor 3 months after one injection. **D** The eye 1 year after treatment.

right orbit (Fig. 3A). In September 2003 the patient underwent direct puncture via the inferonasal portion of the right lower eyelid with sodium tetradecyl sulfate (Fig. 3B). After 3 months, the right proptosis had decreased significantly to 0.5 mm. A CT scan showed significant regression of the infiltrating mass (Fig. 3C). Three years after the injection, the right eye was completely normal with a small residual tumor detected by CT examination.

Case 3

An 18-year-old man presented with a 2-year history of slowly progressive left proptosis. The left eye had an acuity of 20/20. He had full ocular motility. Hertel's exophthalmometric measurements were 15 mm in the right eye and 25 mm in the left eye, indicating a marked proptosis. MRI scan of the orbits showed a well-defined, multiseptated, lobulated, intraconal mass of the left orbit. The mass appeared heterogeneous in T1-weighted images and demonstrated a bright signal in T2-weighted images, consistent with either a lymphatic or vascular abnormality. A diagnosis of orbital lymphangioma was made, and the first sclerosing injection was started in September 2003 via the inferomedial part of the left eyelid. An immediate postinjection CT scan revealed filling of the sclerosing agent in the lower part of the mass (Fig. 1). By the 3-month follow-up, the left proptosis had decreased to 8 mm, which was confirmed by imaging. Sclerotherapy was repeated in January 2004 at the same site. By 3 months after the second injection, the left proptosis had decreased to 4 mm. A third injection was done in January 2005 with direct puncture of the medial left upper lid. Postinjection examination revealed good filling of the sclerosing agent in the upper part of left eyelid. Three months later, the patient had only 1 mm of proptosis. He had been asymptomatic for 15 months, with stable mild proptosis. The last CT image showed a small residual tumor in the medial portion of the left orbit (Fig. 4B).

Case 4

A 16-year-old girl presented with a 10-year history of left proptosis and biopsy-proven left orbital lymphangioma. She had undergone three previous intralesional triamcinolone injections with minimal improvement of symptoms. Visual acuity was 20/20 bilaterally and Hertel exophthalmometer measurements revealed 8 mm of proptosis in the left eye (Fig. 5D). Direct puncture and instillation of sodium tetradecyl sulfate was done twice at an interval of 3 months. By 3 months after the second injection, there was 2 mm of residual proptosis with a remarkable decrease in tumor size (Fig. 5C). The patient was satisfied with her cosmetic appearance (Fig. 5E). This improvement remained stable for 15 months, after which the lymphangioma began to increase in size with 4 mm of proptosis.

Discussion

Management of orbital lymphatic malformation is controversial. Many authors believe that lymphangioma of the orbit is best managed conservatively.[1,2] Symptom exacerbation tends to occur during upper respiratory tract infections and may be managed with short-course systemic corticosteroids. Repeat drainage may be required to manage acute orbital symptoms and compressive optic neuropathy in

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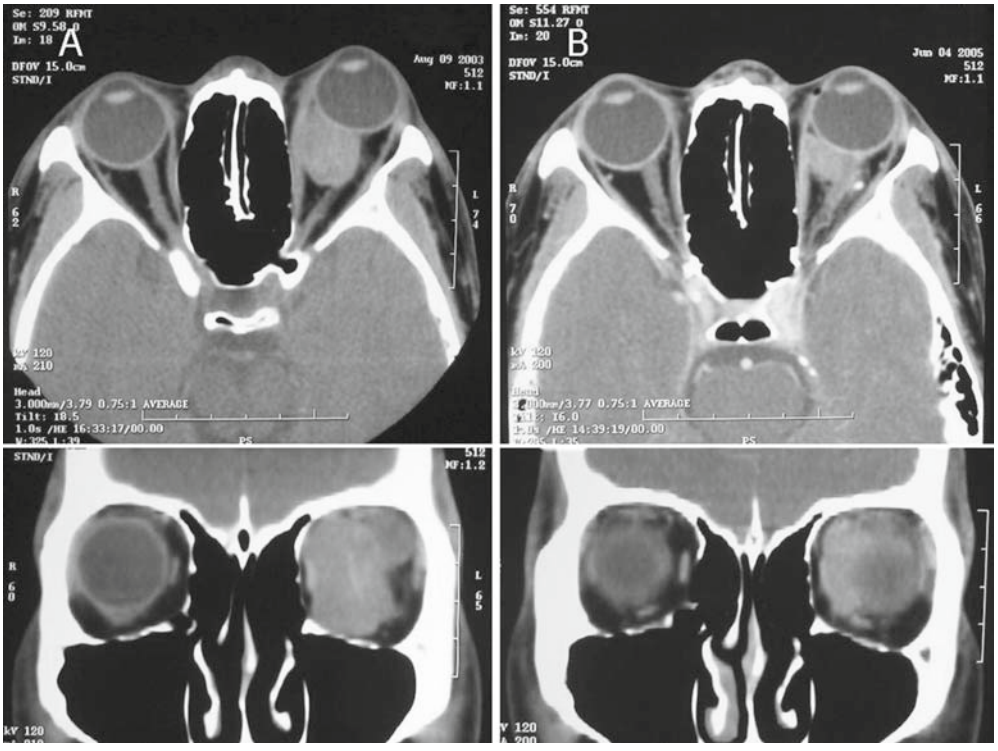

Figure 4A, B. CT scan of an 18-year-old man with left orbital lymphangioma. **A** Before injection and **B** 3 months after the last injection with a sclerosing agent.

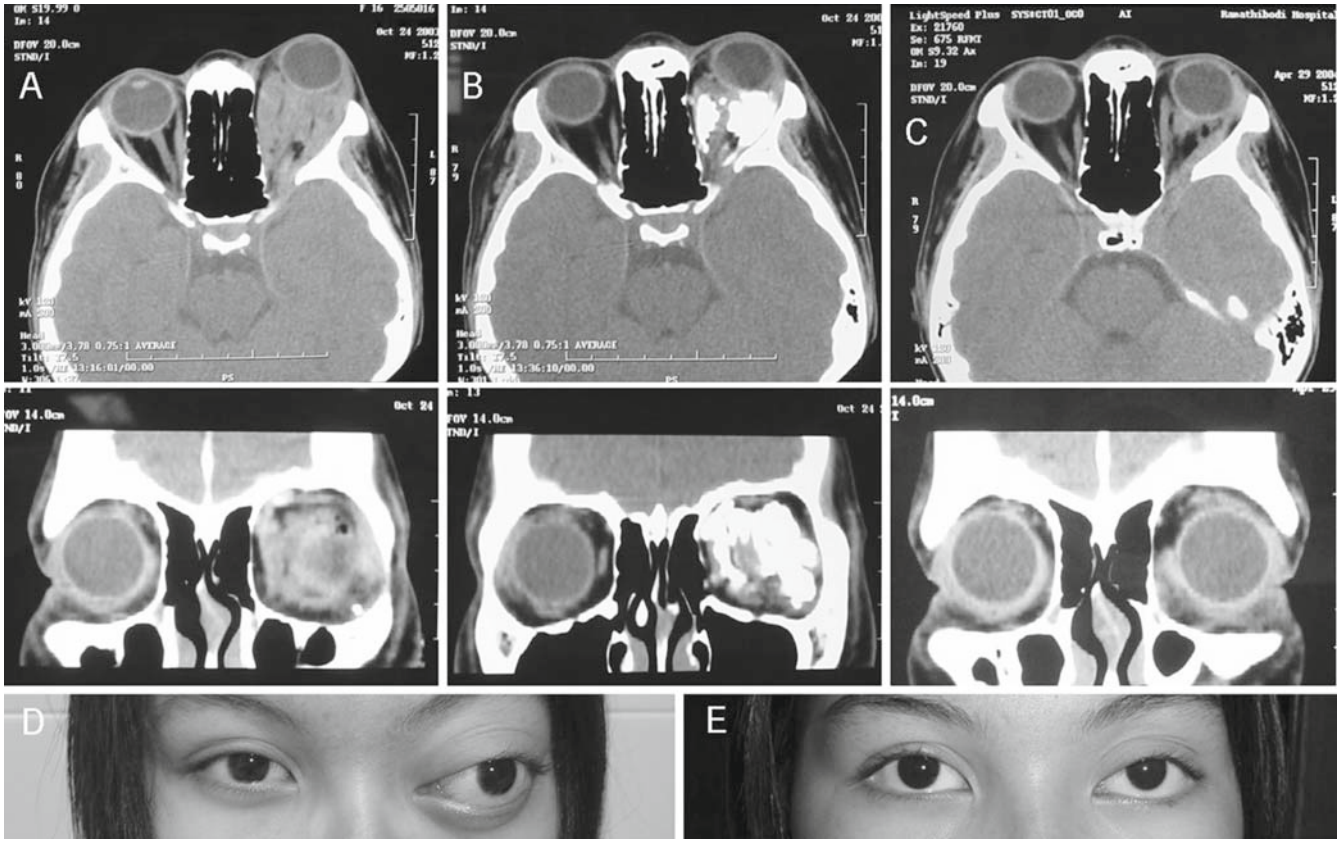

Figure 5A–E. A 16-year-old girl with left orbital lymphangioma. **A** CT scan prior to injection showing an infiltrating left intraconal mass. **B** Filling of the sclerosing agent after injection. **C** Six months after injection, there was a remarkable regression of the tumor. Appearance prior to (**D**) and after (**E**) the sclerosing injection.

cases of intralesional hemorrhage. Because of the infiltrative character of this malformation, complete removal is considered impossible. Complications of surgical excision include damage to surrounding structures, particularly nerves and muscle tissues, scarring, and recurrence. Recently, intralesional injection of a liquid polymer has been reported to facilitate surgery.[13] Some authors recommend bony orbital decompression to treat progressive proptosis.[14]

Sclerotherapy refers to the introduction of a foreign substance into the lumen of a vessel, causing thrombosis and subsequent fibrosis. A wide variety of sclerosing solutions have been shown to be a safe and effective for treating varicose and telangiectatic veins. The use of sclerosing agents, including picibanil (OK-432), sodium tetradecyl sulfate, and sodium morrhuate, for the treatment of lymphangiomas has been discussed in the literature.[6–9]

An intralesional injection of OK-432, a streptococcus-derived sclerosing agent, was given to one patient with improvement of proptosis and shrinkage of the lesion.[6] However, complications such as increased intraocular pressure as a result of local inflammation were noted, and the optimal dose of this drug still needs to be determined. In another study,[9] 5% sodium morrhuate was effective in tumor debulking in six patients with orbital lymphangioma. The proptosis decreased by an average of 1.5 mm, and lesions decreased in size by an average of 50%. Complications included one case of orbital hemorrhage that resolved spontaneously and transient keratopathy in all patients with anterior orbital lesions.

Sodium tetradecyl sulfate is a clear, colorless, surface-active substance composed of sodium 1-isobutyl-4-ethyloctyl sulfate plus 2% benzyl alcohol; it is supplied in 2-ml ampules of 1% and 3% solution.[10] It is one of the most widely used, safest, and most effective solutions for destroying unwanted veins. In 1999 Wojno[7] published his experience of injecting sodium tetradecyl sulfate into three patients with orbital lymphangiomas that involved the eyelid. The size of the lymphangioma decreased in one patient, but the other two patients showed minimal results. The puncture was performed with a different technique in each case, including fluoroscope-guided, CT-guided, and direct visualization. A subsequent study by Svendsen[8] demonstrated promising results of percutaneous puncture and injection of sodium tetradecyl sulfate under radiological fluoroscopic guidance (road map technique) in six patients with orbital lymphatic malformation. These two case series suggest the efficacy of sclerosing therapy with sodium tetradecyl sulfate, and they show an acceptable side-effect profile.

We have been using this treatment modality for patients with orbital lymphangioma since 2003. None of our patients have undergone major debulking surgery except for intralesional steroid injection or aspiration drainage. We are using a direct puncture under CT guidance that is safe, convenient, and easy to perform. This technique reduces the risk of the sclerosing solution penetrating undesirable spaces, which might lead to morbidities. All patients in our study tolerated the procedures well, and no irreversible complications were noted. The treatment has been successful in three of the four patients so far, although it is too early to judge the long-term outcomes. Only one patient (case 4) developed regrowth of lymphangioma 15 months after two previous successful injections. The multilobulated characteristics of the mass in this patient suggest that this regrowth might have been due to inadequate injections. Previous multiple intralesional steroid injections might also have resulted in a relatively higher content of scar tissue within the lymphangioma, which in turn affected the distribution of sclerosing solution within the mass. One patient developed transient ophthalmoparesis after the third injection, probably caused by minor leakage of the sclerosing substance into the orbit.

Ophthalmologists should not puncture the orbital lesion directly if they are not sure the lesion is a lymphangioma, and before the procedure, ophthalmologists must be prepared for possible unfavorable complications such as orbital hemorrhage.

In conclusion, our study shows that intralesional injections of sodium tetradecyl sulfate is a useful treatment for orbital lymphangiomas. The satisfactory results and low complication rate of sclerotherapy make it a good alternative to surgical intervention in selected cases.

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