

OCULOPLASTICS

Novel Approaches to Orbital Lymphangioma

BY ANNIE STUART, CONTRIBUTING WRITER

INTERVIEWING KENNETH V. CAHILL, MD, JILL A. FOSTER, MD, AND MARY O'HARA, MD

Although benign and representing only 1 to 3 percent of all orbital masses, congenital lymphangiomas are an obstinate bunch: These hamartomatous, unencapsulated tumors intertwine with surrounding normal tissue, increase in size with infections, and create proteinaceous or blood-filled cysts that can bleed spontaneously—despite the absence of an identifiable blood supply.^{1,2}

Treatment options have included conservative management, systemic steroids, partial surgical resection, and interventional radiology procedures.² But lymphangiomas are diverse and unpredictable; even with treatment, long-term visual and cosmetic outcomes are often unsatisfactory. In recent years, clinicians have searched for—or come across—new approaches that may help in some cases.

Possible Presentations

Also called lymphatic malformations, lymphangiomas may be isolated or multiple, located in just one area, such as the eye, or also other areas of the body. Consisting of dilated sacs of lymphovascular tissue, periocular tumors may affect the conjunctiva, the eyelids, and the orbit, often leading to problems such as proptosis, globe displacement, optic neuropathy, and physical disfigurement. Some are deep, while others are superficial and clearly visible to the naked eye, sometimes discoloring the skin and thickening the conjunctiva.^{1,2} (See Fig. 1A.)

Orbital lymphangiomas can make their first appearance anytime from infancy up to the teen years, said Kenneth V. Cahill, MD, an oculoplastic surgeon.

“The orbital cyst can enlarge rapidly over hours or a day or two,” said Dr. Cahill, “often presenting with a sudden onset of eyelid swelling or proptosis. That rapid increase in volume can cause pressure and pain, and it can put the eye at risk as well. Multiple acute episodes of cyst enlargement are a hallmark of the disorder.”

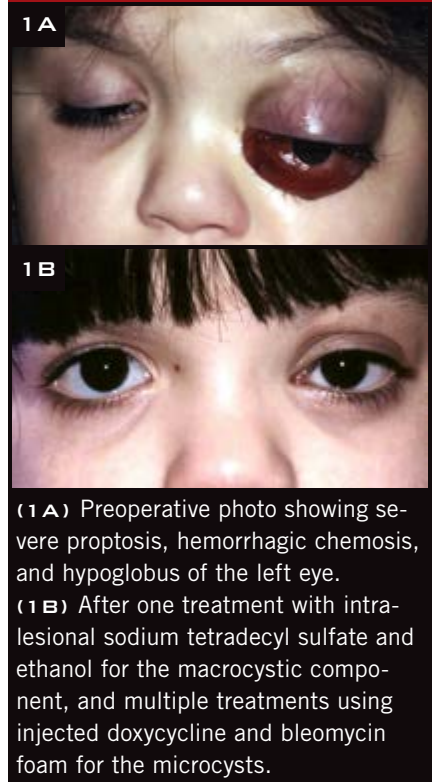
Approaches to Treatment

In treating lymphangiomas, there is no “one size fits all,” said Mary O’Hara, MD, a pediatric ophthalmologist. “It really depends upon what you find.”

When to treat. “If the lymphatic proliferation is not extreme and the bulk of the lesion and the cysts are not threatening vision or causing physical distortion, you can usually wait them out,” said Dr. O’Hara. “Some lymphangiomas never require treatment. But bleeding or lymphatic proliferation that causes cyst expansion and compromises the optic nerve or causes severe proptosis usually forces your hand,” said Dr. O’Hara. “In children, the effect on vision is always paramount.”

Even when vision is not immediately threatened, said Jill A. Foster, MD, an oculoplastic surgeon, treatment may be considered when most of the lymphangioma’s volume consists of fluid-filled cysts. “With the suc-

Before and After



(1A) Preoperative photo showing severe proptosis, hemorrhagic chemosis, and hypoglobus of the left eye.

(1B) After one treatment with intralesional sodium tetradecyl sulfate and ethanol for the macrocystic component, and multiple treatments using injected doxycycline and bleomycin foam for the microcysts.

cesses seen in percutaneous draining and ablation of visually threatening lymphangiomas, we are optimistic that earlier treatment will decrease subsequent enlargement, visual threats, and chronic fibrosis.”

The treatment team. Lymphangiomas require a team approach with clear lines of communication, said Dr. O’Hara. “Consult with subspecialty colleagues, such as the ophthalmic plastic surgeon and the pediatric ophthalmologist. Don’t forget to include

the pediatrician in the treatment plan.”

Dr. Foster relies on the input of pediatric ophthalmologists in treating these patients. “For example, if the lymphangioma is causing deprivation [amblyopia] or refractive amblyopia, pediatric ophthalmologists provide input about the speed with which we should do treatment,” she said. During interventional radiology procedures, she added, the ophthalmologist is on site in case there is an increase in orbital pressure or any concerns raised by the radiologist.

Depending on the location of the lymphangioma, other specialists may also need to be involved, said Dr. O’Hara. “If it’s located in a sinus cavity, for example, an otolaryngologist may try to marsupialize the cyst to keep it from re-forming. The neurologist became a very important part of our treatment team when one of our patients had a seizure disorder from several lymphangiomas intracranially.”

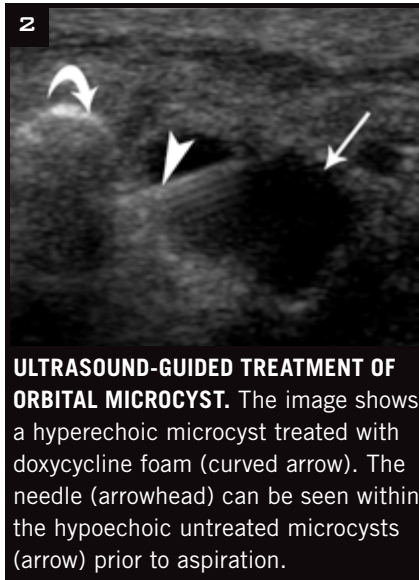
Novel Approaches to Sclerotherapy

In the past, said Dr. Foster, we were never particularly satisfied with our treatment interventions for lymphangiomas. But the field is changing.

Past challenges. “For acute bleeds, we drained the cyst percutaneously to relieve pressure,” said Dr. Foster, “but this only managed the acute problem without addressing the underlying condition.” Surgical excision has also been challenging historically, she said, causing postoperative transudate or exudate and swelling. “And after debulking, residual material remains, which continues to cause problems.”

Newer techniques. Over the past decade, Drs. Cahill and Foster have worked closely with interventional radiologist William E. Shiels II, DO, to modify techniques of drainage and sclerotherapy for the periocular area. They’ve achieved rapid resolution of lymphangiomas with either a primary treatment or after attempted surgical resections.¹

Plan treatment protocol. Planning is particularly important because of the variability of these tumors, said Dr. Foster. “For example, sometimes you



need to approach cysts in layers,” she said, “treating the anterior cysts and then, a month later, treating the cysts in a more posterior position.”

Real-time imaging. A combination of fluoroscopy and B-scan ultrasonography is critical to the safe and accurate performance of these treatments, said Dr. Cahill. “You need real-time imaging to monitor where you are and ensure there is no leakage. Ultrasound is better for some of the smaller cysts where fluoroscopy is not an option.”

Treating macrocysts. The key with macrocysts, said Dr. Cahill, is to create a closed system by inserting a soft, stable catheter into the cyst. After complete drainage of the macrocysts, he and Dr. Foster recommend dual-drug chemoablation with intracystic infusions of sodium tetradecyl sulfate 3 percent—followed by aspiration—and then infusion of ethanol 98 percent solution, which is also removed. Working synergistically to destroy the cysts’ linings, this dual-drug treatment with the indwelling catheter can be used only for macrocysts, she said, which occur in a minority of cases.

After treatment, the catheter is left in place for a few days to evacuate intracystic transudate and minimize postoperative swelling. “We also think the catheter may help make treatment more effective because it enables the collapsed cyst to remain collapsed and to scar closed,” said Dr. Cahill. “If it

fills up with fluid, there’s a chance it may re-epithelialize and remain inflated.”

Treating microcysts. It isn’t possible to drain microcysts in the same way, said Dr. Foster, so there will still be a significant amount of postoperative edema after treatment. However, other techniques can address some of the unique characteristics of microcysts. Dr. Foster and Cahill recommend treating cysts smaller than 1 cm with needle puncture, individual cyst drainage, and injection of bleomycin or doxycycline foam.

Foam. For microcysts, foam offers several advantages over solutions, said Dr. Cahill. It is less likely to extravasate and damage adjacent tissues. “The foam’s bubbles also enable you to fill the cysts and cover endothelial walls with a much smaller amount of medicine,” he said, adding that this is especially important when using more toxic medications such as bleomycin, where you need to limit the total dose. Finally, the foam—along with the needle—shows up on ultrasound, allowing you to monitor treatment without the use of radiation. (See Fig. 2.)

Multiple treatments. At an average follow-up period of 43 months, Drs. Foster and Cahill have reported no recurrences in patients who completed treatment using these approaches to cyst ablation.¹

When multiple treatments are required, they are most often aimed at eliminating multiple cysts, which can’t always be treated in a single episode, said Dr. Cahill. However, sometimes a single cyst requires more than one treatment. “These tend to be lesions receiving a microscopic delivery of blood,” said Dr. Cahill. These blood-filled lesions on average require nearly twice the number of treatments as cysts filled with serosanguineous fluid.¹

Surgery still a risk? Even after sclerotherapy, Drs. Cahill and Foster consider resection a risk. “There may be an occasional lymphangioma you can resect,” said Dr. Foster, noting that in some cases, you might relieve an acute compressive problem surgically

Variations on a Theme

Lymphangiomas can be challenging to manage, given their varied presentations. Our lymphangioma experts provide the following as a starting point for treatment considerations.

- **For small lesions that are asymptomatic**, take a conservative approach and follow the patient closely.
- **For functional compromise from bleeding**, evacuate the cyst and place a sclerosing agent within the body of the cyst to collapse it.
- **For increased tumor volume due to macrocystic-type lymphangioma tissue**, consider sildenafil or percutaneous drainage and ablation to collapse the walls of the cyst.
- **For a lymphangioma with a large vascular component**, consider experimental treatment with propranolol. It is now an established treatment to decrease the size of capillary hemangiomas. “So my suspicion is that its successful treatment of lymphangioma involved lesions with a large vascular component,” said Dr. O’Hara.
- **For microcystic lesions**, try multiple treatments with ultrasound-guided placement of intralesional sclerosing foam.
- **For a lymphoproliferative response**, consider systemic steroids. Dr. O’Hara has seen several children with upper respiratory tract infections and significant proptosis from proliferation of intraorbital lymphatic tissues. She’s had “fairly good results” treating them with systemic steroids.

with cyst drainage or address cosmesis by removing fibrous tissue left over from an inflammatory reaction. “But I’m not sure debulking surgery actually improves the clinical picture,” she said.

In fact, it may make things worse, said Dr. Cahill. Surgery may aggravate the lymphangioma and cause it to become more leaky. He noted that he hopes these newer ablation methods may lessen fibrotic tissue proliferation and the necessity of subsequent surgery.

Sildenafil

Sildenafil is a newcomer on the lymphangioma scene. It was found serendipitously, said Dr. O’Hara, when doctors treating pulmonary arterial hypertension found it led to regression in some children with intrathoracic lymphatic malformations. This finding subsequently prompted a double-blind, placebo-controlled trial at Stanford University, which is ongoing.³

Mechanism of action? Best known for its treatment of erectile dysfunction, sildenafil is a selective vasodilator. With lymphangioma, it may help collapse cystic channels by decreasing the contractility of vascular smooth muscle, said Dr. O’Hara.

Case studies. Dr. O’Hara and

colleagues tried sildenafil with two particularly intransigent cases. A 12-month-old had undergone multiple interventional radiology procedures without success for recurrent cysts that were causing proptosis, threatening the health of his optic nerve, and predisposing him to deprivation amblyopia, said Dr. O’Hara. The other patient, a 12-year-old, was being considered for enucleation despite multiple sclerosing procedures throughout infancy and childhood. With sildenafil treatment, both achieved remission for more than one year.

Dosing. “We used the dosing guidelines of the Stanford study, since none exist in the literature,” said Dr. O’Hara. The toddler was started on 1 mg/kg per day and increased to 3 mg/kg per day over about a month and continuing for about five months. “It was really quite dramatic how much swelling went down in the first month. There was continuing improvement in swelling over the next few months of treatment. While he was on sildenafil, our ENT colleagues did two more drainage procedures and a marsupialization of one of the large cysts. After that, we tapered him off the medicine over a two- to four-week period.”

For the 12-year-old, they used close

to an adult dose of 20 mg three times daily. “The results were so good with sildenafil,” said Dr. O’Hara, “that our oculoplastic colleagues elected not to go forward with debulking and enucleation.”

Possible side effects. Side effects of sildenafil include headache; stuffy nose; erythema of the neck, face, and chest; swelling in hands, ankles, and feet; irregular heartbeat; and tinnitus and hearing loss, said Dr. O’Hara. Vision changes have been associated with long-term sildenafil use. Dr. O’Hara cautioned about the possibility of intermittent erections in the postpubertal child.

She also warned against using this medication in combination with other medicines that lower blood pressure, such as beta-blockers. “You shouldn’t consider using propranolol and sildenafil at the same time,” she said.

Long-term results? Questions remain about the ideal length of treatment, long-term results, and tolerability of the medication in infants and children who require more than one treatment.

Another question, said Dr. Cahill, is whether a combination of sildenafil and percutaneous ablation might have a synergistic effect and achieve even better results. “Time will tell which approach is better,” he said. “It may become a question of whether some patients will have their best outcome with the use of both modalities.” ■

1 Hill RH et al. *Ophthalm Plast Reconstr Surg*. 2012;28(2):119-125.

2 Gandhi NG et al. *JAMA Ophthalmol*. 2013;13(9):1228-1230.

3 Swetman GL et al. *N Engl J Med*. 2012;366(4):384-386.

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