Lymphangiomatosis is a rare, multisystem congenital disorder that results from the proliferation and infiltration of lymphatic channels into visceral organs, the skeletal system, and soft tissues. The accompanying symptoms depend on the extent and location of these lesions, although patients with multifocal disease often have a worse prognosis. Lesions of the skeletal system are often diagnosed by pathological fractures, progressive spinal deformity, and bone pain. Published case reports have shown that patients with progressive axial skeletal involvement suffer significant morbidities, including chronic pain, myelopathy, weakness, paralysis, and respiratory problems, and have high rates of mortality. There are currently no treatment guidelines for lymphangiomatosis with bony involvement. Procedures attempted for skeletal involvement include resection, sclerotherapy, radiotherapy, and kyphoplasty. To our knowledge, this is the first report of a percutaneous transoral clivoplasty and C-1 and C-2 vertebroplasties performed for the treatment of severe pain due to lymphangiomatosis of the clivus and upper cervical spine.

Case Report

History and Neurological Examination

An 18-year-old woman with a history of lymphangiomatosis presented to the Center for the Relief of Pain (W.S.R.) with medically refractory occipital headaches. She was diagnosed at the age of 3 years with a chest lymphangioma, and thereafter numerous soft-tissue lesions were discovered, which were biopsied; the results confirmed diffuse hereditary lymphangiomatosis. She had undergone numerous sclerotherapies for her disease, with resolution of pain thereafter. The patient described the headaches as dull, aching, nonradicular, and severe, interfering with her normal daily activities and her overall quality of life. Her visual analog scale (VAS) score was 8 of 10, and her Pain Disability Index (PDI) score was 39 of 60. Conservative medical management including physical therapy, neurology and pain anesthesia evaluations, and occipital and cervical injections provided minimal relief of symptoms. Her medications included clonidine, pregabalin, amitriptyline, and 120–180 mg of morphine equivalents daily. The
patient was neurologically intact without evidence of myelopathy or weakness.

Neuroimaging Findings

Admission CT and MRI studies of the brain and cervical spine demonstrated 5 bony lytic lesions that were consistent with her diagnosis of lymphangiomatosis. These involved the clivus, the anterior arch of C-1, the lateral masses of C-1 bilaterally, and the odontoid process of C-2 (Fig. 1A and B). These lesions were confined to the bony elements, without invasion into the intracranial space, spinal canal, or other surrounding neural or vascular structures. Flexion/extension radiographs of the cervical spine showed no evidence of instability.

Surgical Technique

The patient underwent a percutaneous transoral CT-guided vertebroplasty of these 5 lesions. General anesthesia with orotracheal intubation was induced, and the patient received preoperative cefazolin. A CT scan was performed to assist with visualization of the spinal cord and brainstem intraprocedurally. The patient remained supine on the CT scanner throughout the procedure. Under direct visualization, local anesthetic was administered and a small stab incision was made in the posterior oropharynx. A small bone cannula (Jamshidi needle) was then carefully passed, using CT guidance, through the pharyngeal musculature into the junction of the anterior and middle third of the clivus (Fig. 2). When the stylet was removed, a low-pressure flow of clear fluid was observed, consistent with lymph. Polymethylmethacrylate cement containing barium for radiopacity was injected, again under CT guidance, to ensure that the lytic region was reconstructed without breaching the bony margins. The above steps were then repeated, with new trajectories to target the lateral masses of C-1 bilaterally as well as the anterior arch of C-1 and the odontoid process of C-2 (Fig. 3). There were no complications. Following the intervention, the patient was extubated and recovered in the recovery unit. She received no postoperative or long-term antibiotics. She was discharged home the same day.

Postoperative Course

Immediately postoperatively, the patient experienced complete resolution of her pain, with a VAS score of 0 of 10, and her findings on neurological examination remained intact. The patient was soon weaned off of all pain medications, and she remained medication free at her 6-month follow-up, having returned to full activity shortly after the procedure. Her VAS score was also maintained at 0, as was her PDI. A repeat CT scan was performed at the 6-month follow-up and demonstrated that the cement was unchanged in position, with no progression of deformity or instability (Fig. 4). At her 2-year follow-up the patient was pain free with a VAS score of 0, was taking no pain medications, and had resumed all of her normal college activities. Given the patient’s young age and child-bearing status, the decision was made to refrain from further imaging as long as she remained asymptomatic.

Discussion

Lymphangiomatosis is an exceptionally rare disorder that results in lymphatic proliferation and infiltration into surrounding tissues. The condition is not known to have any gender predilection and often is diagnosed before the age of 20 years. Diffuse lymphangiomatosis is believed to be closely related to Gorham-Stout syndrome, a condition in which the lymphangiomata are limited to the skeletal system. Lesions can infiltrate any organ, and symptom-
atology is highly dependent on the affected organ system. Patients may present with chylous pleural or pericardial effusions. Patients with skeletal involvement may present with pathological fractures, deformity, and bone pain. Patients with multifocal disease often have a poor prognosis, and the combination of pulmonary and spinal involvement appears to be associated with high rates of morbidity and mortality.

Currently, there are no set treatment protocols for diffuse lymphangiomatosis. Treatment tends to be palliative for symptomatic control, which is dependent on the location of the lesions, and frequently involves surgery and/or radiation. This may be combined with systemic therapies such as bisphosphonates, vitamin D, interferon alpha, bevacizumab, or tyrosine kinase inhibitors for bony disease. However, well-designed studies to evaluate the efficacy of such interventions are lacking. Radiotherapy has been most consistently used to prevent disease progression, with several promising case reports pertaining to Gorham-Stout syndrome.

The largest radiation study was a national survey of 230 German radiation institutions amounting to only 10 total cases, including 6 patients treated primarily with radiation and 4 treated with surgery, followed by postoperative radiation. Eight of these 10 cases were progression free in the tissue that received radiation, with a median follow-up of 42 months. A literature analysis by Heyd et al. reported similar percentages (77.3%) of stable or regressing disease in 44 patients who received radiation. Case reports have demonstrated positive responses to a range of therapeutic strategies, but a true treatment algorithm has yet to be formulated.

With respect to surgical interventions for bony disease, reports ranging from sclerotherapy to various fusion constructs have been published. However, the osteolytic nature of lymphangiomatosis is a treatment challenge because autologous or cadaveric grafts are also susceptible to lymphangioma invasion. According to the literature, surgical interventions have had mixed results (Table 1). One of the earliest case reports is of an 8-year-old boy described by Canady and Chou in 1980. On initial evaluation, the patient reported a chronic suboccipital headache but was neurologically intact, with imaging revealing multiple lytic lesions of the skull base, C-1, and C-2, with posterior fossa enlargement. In 1971 the patient underwent a suboccipital craniotomy, C-1 posterior arch removal, and a C-2 laminectomy, with relief of headaches. Four years later he presented with progressive cranial nerve deficits from basilar impression and extensive cervical bone resorption. He was treated with an occiput–T1 fusion with iliac crest grafts and halo brace placement. One year later, he presented with severe myelopathy and cerebellar signs. Further excision of C5–7 vertebral bodies with fibular strut grafts resulted in recovery of some function; however, the patient ultimately progressed to quadriparesis and died of respiratory failure.

Jea et al. discuss treatment of a 4-year-old girl with lymphangiomatous lesions throughout the skull base and upper cervical vertebrae. She presented with headaches and ear pain, and demonstrated widespread lytic lesions as well as an acquired Chiari I malformation. The team performed a decompressive suboccipital craniectomy and C-1 laminectomy, with improvement in head and neck pain and no signs of craniovertebral instability. Long-term follow-up was not discussed in the paper.

Watkins et al. presented 2 surgical cases also managed...
with open surgical intervention. The first case, a 15-year-old girl with multifocal disease, experienced worsening radiculopathy and myelopathy and a progressive cervical kyphosis—from 29° to 48° over 13 months. She underwent an anterolateral corpectomy with decompression and anterior fusion from C-4 to T-2 with a fibular allograft and halo placement, with plans for posterior stabilization. Her hospital course was complicated by persistent chylothorax and chylopericardium, and she died of cardiopulmonary arrest 12 days after surgery. The second case was a 13-year-old boy with pain, weakness, and myelopathy who demonstrated 125° of cervicothoracic kyphosis from C-7 to T-3 and severe cord compression. He required numerous procedures for fluctuating results on neurological examination and instability. He underwent C6–T4 anterior discectomies and fusion with posterior facetectomies and halo placement. He then underwent C6–T4 vertebrectomies with graft and plate fixation. A third procedure was performed via an anterior supraclavicular approach, in which plating and graft were removed and more extensive posterolateral C6–T2 corpectomies were performed. Eventual posterior stabilization was performed, with C2–T7 instrumentation. He was hospitalized for a total of 2 months with a chylothorax and transient mesenteric artery syndrome. Interferon therapy was started 3 months postoperatively. At his 1-year follow-up he was neurologically intact.

To date, there have been only a few cases of lymphangiomatosis treated with osteoplasty. Mifsut et al. described a patient who underwent multiple failed surgical interventions for lower-limb discrepancy before she was correctly diagnosed with lymphangiomatosis affecting the bones of the lower extremities. She was then treated with percutaneous osteoplasty of her femur and tibia, after which there were no longer any signs of disease progression for at least 2 years. Wallace and Ross presented a patient with continued hip, back, and sacral pain. Despite surgical debulking, the patient ultimately underwent a sacral osteoplasty and experienced complete relief of his pain 4 months postoperatively. Similarly, Carbó et al. also describe an osteoplasty performed for axial skeletal lymphangiomatosis in a 10-year-old boy with Gorham-Stout syndrome. The patient underwent an L-3 and L-4 kyphoplasty with improvement of his preoperative VAS score from 8 to 2. His disease was stable with no progression at 4 years after surgery.

Due to the rarity of this disease as well as its multifocal nature resulting in a wide range of reported treatment modalities, there is a paucity of literature to direct a practitioner’s management of bony lymphangiomatosis. Moreover, not only is there a high morbidity and mortality rate associated with the disease itself, but many of the available treatment options, particularly open surgical fusion techniques, carry substantial risk. In contrast, results of osteoplastic interventions are promising, although few of these cases involve the axial spine. In the case we present, the patient suffered from long-standing pain and headaches that were refractory to medical management and was found to have lesions in a difficult-to-treat location. Surgical fusion would most likely require an occipital-cervical fusion via a posterior approach for prophylactic stabilization, thus not even addressing the anterior pathology. Alternatively, a more morbidity-producing far-lateral approach could be considered, yet this would probably still require stabilization from behind.

The option of a percutaneous clivoplasty with C-1 and C-2 vertebroplasties eliminated the need for fusion, treated the anterior pathology, and avoided the morbidity associated with an extensive surgical fusion. Vertebroplasty is a well-established procedure for pain management for vertebral pathological entities such as metastatic tumors, hemangiomas, osteoporotic fractures, and multiple myeloma. Our patient was experiencing upper cervical pain and headaches, and after thorough workup to exclude other causes including intracranial pathology, it was believed that her pain was probably related to her lymphangiomatosis. The transoral approach provided the most direct and
least morbid avenue for achieving treatment goals. In addition, our patient experienced complete resolution of her pain immediately following the procedure, and she was discharged home the same day. Her imaging showed no disease progression, and her symptoms remained well controlled at the 6-month follow-up. She continued to be pain free at the 2 years follow-up visit.

**Conclusions**

To our knowledge, this is the first report of multifocal skeletal lymphangiomatosis of the clivus and upper cervical spine that was successfully treated with percutaneous clivoplasty and vertebroplasty, resulting in complete resolution of pain. Percutaneous transoral osteoplasty may represent an important treatment option for patients with skeletal lymphangiomatosis of the clivus, C-1, and C-2. This case report may serve as a building block for further studies of minimally invasive treatment for axial and subaxial cervical lytic spine lesions. Obtaining a series of patients is difficult given the rarity of the disease, but it would aid in evaluating this procedure for any perioperative or long-term complications. Long-term follow-up will prove beneficial in ensuring the permanency of the treatment.

**References**


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**TABLE 1. Summary of patients who have undergone surgical procedures for management of skeletal lymphangiomatosis**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Locations &amp; Symptoms</th>
<th>Technique</th>
<th>Results</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jea et al., 2003</td>
<td>Diffuse cervical &amp; skull base lesions; Chiari &amp; basilar invagination Symptoms: headache</td>
<td>Chiari decompression w/ C-1 laminectomy for progressive headaches</td>
<td>Improved headaches, no postop clinical or radiological cervical instability; no long-term follow-up documentation</td>
<td></td>
</tr>
<tr>
<td>Watkins et al., 2003 (Case 1)</td>
<td>Cervical spine, skull base, &amp; pulmonary lesions; 48° cervical kyphosis Signs/symptoms: limited cervical ROM due to kyphosis &amp; w/ myelopathy &amp; weakness</td>
<td>Anterolat C4–T2 corpectomy &amp; structural allograft</td>
<td>Fluctuating results on neuro exam secondary to cardiopulmonary instability</td>
<td>Chylothorax &amp; chylopericardium resulting in cardiopulmonary arrest on postop Day 12</td>
</tr>
<tr>
<td>Watkins et al., 2003 (Case 2)</td>
<td>Cervicothoracic spine, 125° cervicothoracic kyphosis Signs/symptoms: myelopathy, neck pain, leg weakness, falling</td>
<td>C6–T4 ant discectomies, autograft fusion, &amp; pst facetectomies &amp; halo traction; C6–T4 vertebrectomies w/ auto- &amp; allograft &amp; plate fixation Removal of plate &amp; allograft &amp; C6–T2 corpectomies w/ allograft &amp; plate fixation &amp; halo traction C2–T7 pst instrumentation</td>
<td>Postop weakness demonstrated after his 1st &amp; 2nd ops required revision &amp; more extensive corpectomies &amp; decompression Interferon therapy initiated 3 mos postop; motor function improved &amp; he was neurologically intact at 1-yr follow-up</td>
<td>Postop weakness &amp; cord edema requiring revision surgeries &amp; steroid treatments Chylothorax &amp; transient mesenteric artery syndrome</td>
</tr>
<tr>
<td>Wallace &amp; Ross, 2005</td>
<td>Multifocal Symptom: sacral pain</td>
<td>Percutaneous cementoplasty to sacrum</td>
<td>Resolution w/in 1 hr of procedure, 1/5 at 1-wk follow-up, 0/5 at 4-mo follow-up</td>
<td></td>
</tr>
<tr>
<td>Mifsut et al., 2013</td>
<td>Femur &amp; tibia Symptom: pain</td>
<td>Curettage &amp; bone graft unsuccessful; percutaneous osteoplasty to femur &amp;ibia</td>
<td>2-yr follow-up w/o disease progression or resorption</td>
<td>Curettage &amp; bone graft resulted in resorption</td>
</tr>
<tr>
<td>Carbó et al., 2015</td>
<td>Gorham-Stout syndrome: 10-yr-old child w/ pain &amp; w/ osteolysis of L-3 &amp; L-4 vertebrae</td>
<td>Vertebroplasty w/ PMMA</td>
<td>Preop VAS 8–10; postop VAS 2–3; progression free for 4 yrs</td>
<td></td>
</tr>
</tbody>
</table>

Ant = anterior; CN = cranial nerve; neuro exam = neurological examination; Oc = occiput; PMMA = polymethylmethacrylate; pst = posterior; ROM = range of motion.

**Disclosures**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**Author Contributions**

Conception and design: all authors. Acquisition of data: Sweet. Drafting the article: Wright, Kusyk. Critically revising the article: all authors. Reviewed submitted version of manuscript: Wright. Administrative/technical/material support: Rosenberg, Sweet.

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