Intralesional Endoscopy of Advanced Lymphatic Malformations of the Head and Neck

A New Diagnostic Approach and a Potential Therapeutic Tool

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**Objectives:** To evaluate the morphologic properties of advanced lymphatic malformations of the head and neck and to investigate possible therapeutic interventions by intralesional endoscopy.

**Design:** This case study analyzes the outcome of intralesional endoscopy of lymphatic malformations of the head and neck and discusses the results of this approach.

**Setting:** Academic medical center.

**Patients:** Endoscopy was performed on 4 patients with cervicofacial lymphatic malformations.

**Interventions:** Endoscopy of lymphatic malformations.

**Results:** The endoscopic inspection and assessment of the lesions revealed detailed information about morphologic aspects like the structure of intralesional septa, internal vascularization, and intercystic correspondence and channel networks. Anatomic landmarks could be followed on their intralesional courses.

**Conclusions:** Intralesional endoscopy of lymphatic malformations provides insight into the morphologic properties of the lesion and is a useful supplementary tool during conventional surgical intervention and for sclerosing therapy. The technique allows a detailed assessment of these lesions and opens a broad spectrum of therapeutic options.


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**TREATMENT OF ADVANCED CERVICOFAcial LYMPHATIC MALFORMATIONS**

The treatment of advanced cervicofacial lymphatic malformations is challenging. Our knowledge about the exact morphologic characteristics and the nature of this disease and our ability to make detailed predictions about the clinical course are still limited. Increasing efforts are under way to establish endoscopic methods in soft-tissue surgery, including thyroid and parathyroid surgery,1–2 surgery of branchiogenic cysts,3 transoral extirpation of submandibular glands,4 sialendoscopy5 and sentinel lymphadenectomy.6–7 Herein, we describe another innovative technique: the endoscopic approach to advanced lymphatic malformations of the head and neck. To our knowledge, this is the first description of intralesional endoscopy of cervicofacial lymphatic malformations. Through further field work, this technique, which is still at a very early stage, has the potential to improve our knowledge of the nature of this disease and so contribute to achieving better therapeutic results and reducing surgical complications. It is already becoming a practical supplementary tool for diagnosis and therapeutic intervention in the clinical routine.

**METHODS**

Herein, we describe the cases of 4 children with lymphatic malformations of the head and neck who were admitted to the Angioma Center and who were eligible for an intralesional endoscopic approach to the malformations. The procedures were performed between November 2008 and June 2009. All parents were fully informed about the new and alternative nature of the interventions, which were performed after obtaining written informed consent in all cases. Data analysis was carried out in accordance with the requirements of and after approval by the institutional ethics commission.

**POPULATION AND PATIENT HISTORY**

Endoscopy was performed on 4 pediatric patients, ages 11 days (patient 1), 13 months (patient 2), 27 months (patient 3), and 14 years (patient 4). Three patients had extensive bilateral cervicofacial multicystic lymphatic malformations, and 1 had a solitary lesion in the left submandibular region.

Two patients had been treated in multiple settings at other institutions prior to their admission. Patient 2, a 13-month-old with a massive cervicofacial lesion, had been previously treated elsewhere several times through sclero-
therapy with picibanil (OK 432). Patient 3, a 27-month-old, had been treated elsewhere with bleomycin. Patient data, medical history, and predominant clinical symptoms are summarized in Table 1.

PRETREATMENT ASSESSMENT AND FOLLOW-UP

In addition to undergoing clinical examination by an otolaryngologist and a pediatrician, all patients were evaluated by B-mode and Doppler ultrasonography of the neck and magnetic resonance imaging (MRI) of the head, neck, and thorax prior to surgery. Follow-up was performed by routine clinical examination with photographic series and ultrasonography.

ENDOSCOPIC APPROACH

The interventions were performed while the patient was under general anesthesia in the operating theater. A rigid pediatric neuro-endoscope (OI Handy Pro, Karl Storz GmbH & Co KG, Tuttingen, Germany) was used to perform the endoscopy. Inspection was performed with a 0° optic device. The endoscope contained 2 working channels for drainage and instillation of fluids and for insertion of surgical instruments (eg, microscissors, biopsy clamps, coagulation electrodes). A skin incision was made on the 3 patients with advanced cervicofacial lymphatic malformations as for conventional access for open surgery. In these cases, a routine histologic examination was performed after surgery. Intralesional biopsy specimens were taken by biopsy clamps through the endoscope in 1 case. A transcutanous approach was chosen for patient 4, a 14-year-old, through a cervical skin incision approximately 2 cm long.

Table 1. Patient Data and Predominant Clinical Features

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Prior Treatments</th>
<th>Predominant Clinical Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11 d</td>
<td>Thoracocervicofacial lymphatic malformation</td>
<td>None</td>
<td>Acute respiratory distress</td>
</tr>
<tr>
<td>2</td>
<td>13 mo</td>
<td>Cervicofacial lymphatic malformation</td>
<td>Multiple treatments with picibanil (OK 432)</td>
<td>Dysphagia, disfigurement, and facial and skeletal asymmetry</td>
</tr>
<tr>
<td>3</td>
<td>27 mo</td>
<td>Thoracocervicofacial lymphatic malformation</td>
<td>Multiple treatments with bleomycin</td>
<td>Acute respiratory distress</td>
</tr>
<tr>
<td>4</td>
<td>14 y</td>
<td>Macrocytic submandibular lymphatic malformation</td>
<td>None</td>
<td>Submandibular swelling</td>
</tr>
</tbody>
</table>

Table 2. Findings of Ultrasonography and MRI

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sonographic Features of the Lesion</th>
<th>Sonographic Relation to Cervical Structures</th>
<th>Features on MRI</th>
<th>Relation to Cervical Structures on MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bilateral hypoechoic and anechoic multicystic mass, few septa, precipitation phenomenon</td>
<td>Major cervical vessels and muscles embedded in the mass</td>
<td>Multiple, different-sized cysts up to 35 mm, hyperintensity in T2 around the septa after contrast medium application</td>
<td>Posterior displacement of the carotid artery; internal jugular vein on both sides sheathed by tumor</td>
</tr>
<tr>
<td>2</td>
<td>Large hypoechoic lesions beside small and diffuse hyperechoic lesions</td>
<td>Lack of gross delineation of the tumor</td>
<td>Multiple, different-sized cysts, extension from sternum to temporal bone</td>
<td>Displacement of the right carotid artery and the trachea</td>
</tr>
<tr>
<td>3</td>
<td>Multiple cystic lesions, wide variation of echogenicity and diameter</td>
<td>Cysts attached to carotid artery and internal jugular vein</td>
<td>Multiple, different-sized cysts up to 50 mm, heterogeneous signal intensity</td>
<td>Mediastinal involvement with displacement of the trachea and atelectasis of the upper lobe of the right lung</td>
</tr>
<tr>
<td>4</td>
<td>Anechoic homogeneous mass</td>
<td>Clear delineation from surrounding tissue</td>
<td>Homogeneous mass, no evidence of vascularization or septation</td>
<td>Location, dorsal and medial to submandibular gland</td>
</tr>
</tbody>
</table>

Abbreviation: MRI, magnetic resonance imaging.

RESULTS

PRETREATMENT IMAGING

Both the ultrasonography and MRI of the treated patients showed heterogeneous features of the lymphatic malformations. Multiple cystic lesions with a wide variation in size, echogenicity, and signal intensity on the MRI were evident in all 3 advanced cases. Major cervical vessels such as the carotid artery and the internal jugular vein were displaced or sheathed by the mass. An exact delineation was possible only on patient 4, who had a solitary lesion. The findings of the imaging procedures are summarized in Table 2.

INTRAOPERATIVE ENDOSCOPIC FINDINGS

In all 4 cases, endoscopy provided an internal view of the lymphatic malformations and enabled the surgeon to gain further impressions about the structure of the lesions. Furthermore, endoscopy enabled identification of the major cervical vessels and facilitated the safe resection of the tumor. Herein, we report intraoperative findings and results of the endoscopic intralesional procedures for each case (Table 3).

Case 1

The intralesional endoscopic inspection in case 1 revealed multiple corresponding fluid-filled cysts sep-
rated by thin-walled membranes. The cystic subunits were chambered and segmented by multiple septa. Microcystic and macrocystic regions corresponded through multiple channels. Major cervical vessels had an intraleisonal course and were also identified by endoscopy (Figure 1).

Case 2

The intralesional endoscopic view in case 2 revealed a mixed microcystic and macrocystic mass with a heterogeneous tissue consistency. Cystic regions with smooth linings and signs of vascularization were present (Figure 2A) beside fibrotic and "hypovital" areas resembling tissue of endocardium (Figure 2B). The surprising predominance of microcystic components revealed during the intervention did not appear preoperatively in the MRI findings (Figure 2C). The endoscopic findings were concordant with the histologic examination of the biopsy specimens that were taken during endoscopy. Smooth and thin-walled cysts (Figure 2A and D) existed beside fibrotic scar tissue and components with rough internal linings (Figure 2B and E).

### Table 3. Intraoperative Findings and Endoscopic Intralesional Procedures

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Approach</th>
<th>Intraoperative Finding</th>
<th>Procedure During Endoscopy</th>
<th>Benefit of Endoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Combined conventional surgical resection with intralesional endoscopy</td>
<td>Common carotid artery and internal jugular vein not safely detected by macroscopic approach</td>
<td>Identification of major cervical vessels in their complete course</td>
<td>Protection of major cervical vessels and nerves, safe preparation and tumor dissection</td>
</tr>
<tr>
<td>2</td>
<td>Combined conventional surgical resection with intralesional endoscopy, lavage with doxycycline</td>
<td>Adhesions to carotid sheath, scar tissue, irregular morphologic traits, predominant microcystic components</td>
<td>Dissection of intracystic and intercystic septa, creation of a macrocystic cavity</td>
<td>Enabling therapeutic lavage and sclerosing with doxycycline</td>
</tr>
<tr>
<td>3</td>
<td>Conventional surgical resection combined with intralesional endoscopy</td>
<td>Multicystic cervical mass corresponding with thoracic parts</td>
<td>Identification of the border to thoracic cysts, ligation of corresponding channels</td>
<td>Prevention of thoracic chylus fistula</td>
</tr>
<tr>
<td>4</td>
<td>Intralesional endoscopic evaluation, sclerosing with picibanil (OK 432)</td>
<td>Macrocytic lesion with few septa</td>
<td>Controlled instillation of picibanil</td>
<td>Prevention of leakage of sclerosing agent, smaller surgical scar</td>
</tr>
</tbody>
</table>

In case 3, the endoscope was placed inside the caudally located cervical cysts to gain an impression about the thoracic extension of the lesion that was already evident on the MRI (Figure 3A). Endoscopy revealed that some cysts contained material of both mucous and solid consistency (Figure 3B) and that cervical and thoracic components were directly communicating.

### Case 4

The lesion in patient 4, a 14-year-old, located dorsally and medially of the submandibular gland (Figure 4A), was identified after mobilization of the gland under endoscopic view. Intralesional inspection after incision of the cysts showed a smooth inner lining of the cyst and different degrees of intralesional vascularization within the cyst (Figure 4B) without evidence of septa or channels.

#### THERAPEUTIC INTERVENTIONS DURING INTRALESIONAL ENDOSCOPY

In 3 cases, a conventional surgical resection was performed after endoscopic examination. In addition, in 1 case, the intercystic septa were partially dissected, and an artificial macrocystic cavity was created to insert a drain for lavage and sclerosing therapy with doxycycline.

### Case 1

After exposing the lymphatic malformation of the 11-day-old infant, we electively incised cysts and placed the endoscope inside the lesion. The endoscope facilitated identification of the common carotid artery and the internal jugular vein on their intralesional courses (Figure 1) and served as a navigating tool during surgery.

### Case 2

Massive perivascular fibrosis of the carotid sheath in case 2 was evident beside infiltration of the soft tissue by mi-
crocystic components. We could not completely resect the fibrotic and adherent portions without risking damage to major cervical vessels and nerves and the consequent serious functional deficits. The tumor was partially resected. Intralesional biopsy specimens were taken via biopsy clamps through the endoscope. Furthermore, the intracystic and intercystic membranes were dissected by microscissors through the endoscope to create an artificial macrocystic lesion.
cavity. We then placed a drain inside this cavity for fluid outlet and lavaged the area with doxycycline.

Case 3

The cervical parts of the right-sided cervicothoracic lymphangioma of the 27-month-old were dissected after identification of the thoracic portion. The border between the cervical and thoracic portions of the multilocular lymphatic malformation was identified from the gross macroscopic observation in addition to the intralesional view with the supplementary use of the endoscope (Figure 3A). The theoretical risk of an accidental opening of the thoracic cysts during the neck surgery and the development of a chylothorax by leakage of lymphatic fluid was therefore further minimized.

Case 4

In patient 4, we drained the cystic fluid and administered picibanil (dose, 0.5 KE [Klinische Einheit]) through the working channel of the endoscope. Since the procedure was performed under endoscopic view, a possible leakage of the sclerosing medium to the surrounding tissue was reliably prevented.

COMMENT

The head and neck area is the most common site of lymphatic malformations. The pathogenesis of these lesions is still not exactly understood. An abnormal budding of lymphatic tissue from the cardinal vein or failures to connect with or separate from the venous system during embryogenesis have been proposed as potential causes for the development of lymphatic malformations. Morphologically, the malformations contain thin-walled, cystically dilated lymphovascular channels lined by inconspicuous endothelial cells, and they are filled with lymphatic fluid. Further differentiation for the histologic diagnosis is performed by immunohistochemical analysis. According to the current clinical classification, these lesions are classified as macrocystic, microcystic, or combined lesions.

Routine imaging study methods for lymphatic malformations are ultrasonography, MRI, and computed tomography. None of the 3 established imaging methods can be used to determine the exact morphologic properties in all cases, especially in regard to internal structures like septations, intercystic and intracystic channels, and detailed relationships with surrounding tissue. Furthermore, microcystic components can be confused with solid soft-tissue masses. Hemorrhages and infections can change the imaging characteristics of lymphatic malformations. Thus, these imaging studies have limitations for use in detailed preoperative assessment, especially in cases of advanced lesions, repeatedly treated cases, and lesions with substantial microcystic components.

Endoscopic inspection and assessment lymphatic malformations can reveal more detailed information than is otherwise available about morphologic aspects like structure of intralesional septa, internal vascularization, intercystic correspondences, and channel networks. It may contribute to a better analysis and complement our understanding of this disease. Common clinical observations like hemorrhage within the cystic lesions can be correlated with endoscopic findings. In the present cases, a heterogeneous pattern of vascular architecture within the lymphatic malformation was evident during our intralesional examinations. This fact might explain why some lesions have a greater tendency toward spontaneous hemorrhagic events.

In addition, a detailed understanding of the exact intralesional course of major cervical vessels cannot be gained through routine imaging in many advanced cases. Such situations occur when and if major vessels are covered and sheathed by a massive lymphatic mass. The surgical treatment of these patients involves a high risk of damage to these structures, as was evident in the present treated cases. As a further potential benefit, endoscopic examination has proven to be a useful tool to localize anatomic landmarks on their intralesional courses during the surgery.
Advanced lymphatic malformations of the head and neck are still a surgical and therapeutic challenge. Typically, multiple sessions of surgical or therapeutic interventions are performed to correct or reduce functional and aesthetic compromises. The frequent hospitalizations and multiple, partly failed therapy efforts aggravate the social and psychological sequelae of the disease itself.

Up to now, accepted therapy techniques have consisted of conventional surgery, sclerosing therapy, and laser therapy in selected cases. All treatment techniques have limitations, especially in cases of advanced disease and predominantly microcystic lymphatic malformations. Aggressive surgery can cause substantial morbidity if nerves and vessels are damaged. Sclerosing therapy is effective only in well-circumscribed, macrocystic lesions and delivers limited and unsatisfactory results in cases with microcystic lesions.

The finding of intercystic connections and multiple septations may explain why sclerosing agents may not reach a sufficient concentration to be effective in the intended regions. The finding of fibrosis within the cystic walls in cases previously treated by sclerotherapy explains why further sclerosing would likely be ineffective. Inflammatory reactions can scarcely be elicited if the vital endothelial layer is already replaced by fibrotic scar tissue.

Given all of these limitations, a constant effort is under way through combined approaches to optimize treatment and reduce the number of therapeutic interventions and hospitalizations. Endoscopy is a useful supplementary tool in this context. Endoscopic approaches have been used in various areas of head and neck surgery. For the treatment of lymphatic malformations in other areas, it has been used in the resection of abdominal lesions by laparoscopy, or by gastroscopy and colonoscopy. The endoscopic approach of lymphatic malformations will plausibly not be limited to macrocystic lesions. The creation of new cavities within a mixed lesion, as in case 2 herein, might make advanced lymphatic malformations with mixed or combined cystic structures more accessible for therapy with sclerosing agents. Procedures like coagulation of intralesional vessels, ligature of vessels by clips, dissection of membranes, and injection of sclerosing agents under endoscopic assistance are surgical interventions commonly practiced in diverse medical specialties and could potentially be performed for treatment of lymphatic malformations of the head and neck.

In conclusion, the intralesional endoscopic examinations in the present cases revealed detailed information about the morphologic aspects of lymphatic malformations of the head and neck such as intralesional septation, internal vascularization, intercystic correspondence, and channel networks. This information improves our understanding of the morphologic properties of lymphatic malformations. It proved to be a useful supplementary tool to localize anatomic landmarks on their intralesional course during a conventional surgical intervention. One can expect that intralesional endoscopic therapy will open a broad spectrum of therapeutic options in the near future. Further experiments are needed to assess the value of endoscopy for lymphatic malformations of the head and neck in the context of a multimodal approach.

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Author Contributions: Drs Eivazi and Werner had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Eivazi, Teymoortash, and Werner. Acquisition of data: Eivazi, Teymoortash, Wiegand, Roessler, Mandic, and Werner. Analysis and interpretation of data: Eivazi, Roessler, and Werner. Drafting of the manuscript: Eivazi, Teymoortash, and Werner. Critical revision of the manuscript for important intellectual content: Eivazi, Roessler, Mandic, and Werner. Administrative, technical, and material support: Eivazi, Teymoortash, Wiegand, Roessler, Mandic, and Werner. Study supervision: Eivazi and Werner.

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