Microcystic Lymphatic Malformations of the Tongue
Diagnosis, Classification, and Treatment

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Objective: To describe a classification of microcystic lymphatic malformations of the tongue and to investigate different treatment methods.

Design: Retrospective review of patients treated for microcystic lymphatic malformations of the tongue. Lymphatic malformations were classified into the following 4 groups according to their extent: isolated superficial microcystic lymphatic malformations of the tongue (stage I); isolated lymphatic malformations of the tongue with muscle involvement (stage II; stage IIA, involving a part of the tongue; stage IIB, involving the entire tongue); microcystic lymphatic malformations of the tongue and the floor of mouth (stage III); and extensive microcystic lymphatic malformations involving the tongue, floor of mouth, and further cervical structures (stage IV).

Patients: Twenty patients with microcystic lymphatic malformation of the tongue.

Main Outcome Measures: Medical records were reviewed for demographic data and extent and treatment of the lymphatic malformations.

Results: Three patients had stage I disease; 5 patients, stage II; 3 patients, stage III; and 9 patients, stage IV. In 6 patients, the lymphatic malformations could be completely removed by carbon dioxide laser surgery; the remaining 13 patients had persistent disease.

Conclusions: The initial stage seems to predict outcome. Carbon dioxide laser therapy provides good results primarily in stages I and IIA lymphatic malformations. In advanced lymphatic malformations (stages IIB, III, and IV), an interdisciplinary approach is necessary, because complete surgical excision is often impossible owing to the diffuse growth behavior, and therefore recurrence and persistence are common.


Lymphatic malformations are rare malformations of the lymphatic system that occur most frequently in the first decade of life. Fifty percent of all lymphatic malformations are already obvious at the time of birth, and as many as 90% are diagnosed by the end of the second year of life owing to clinical symptoms. Both sexes are equally affected, and there is no predilection for any race. The precise pathogenesis of lymphatic malformations is still unknown. Increasingly, the possible influence of molecular markers on the development and growth of lymphatic malformations has been analyzed to define new approaches for the treatment of these lesions. Traditionally, these lesions are classified according to their histologic appearance into capillary, cavernous, and cystic lymphatic malformations. This classification, however, was replaced by a distinct category based on the radiographic morphology into microcystic, macrocystic, and combined lymphatic malformations. About 60% of all lymphatic malformations are found in the head and neck region. Regarding the mouth, the tongue is most commonly affected. Lymphatic malformations involving the tongue tend to be microcystic, poorly defined, diffuse lesions. They typically occur in the anterior two-thirds of the tongue and involve the lingual dorsum. The characteristic macroscopic aspect is a granular appearance of the lingual surface owing to multiple lymph-filled cysts with a color ranging from transparent to purple, in the case of occasional rupture of capillaries into lymphatic spaces. The main histologic features of lymphatic malformations are the same regardless of their anatomic location. They are composed of thin-walled, cystically dilated vascular channels lined by inconspicuous endothelial cells and filled with proteinaceous lymph fluid. Lingual lymphatic malformations often grow slowly, and in many cases they are qui...
escent for some time. Recurrent upper respiratory tract infections or accidental trauma commonly enlarge the lymphatic malformation or worsen the swelling. Macroglossia secondary to lymphatic malformation of the tongue can cause airway obstruction, swallowing difficulty, malocclusion, and speech problems.10

Various treatment modalities with varying success have been reported for lymphatic malformations. Complete excision of lymphatic malformations is the treatment of choice,12 but other methods like cryotherapy, electrocautery, sclerotherapy, corticosteroid administration, and embolization have also been investigated.13,14 Despite the variety of possible treatment modalities, lymphatic malformations of the tongue still represent functional and aesthetic problems for the patients. Therefore, the aim of the present study was to describe a classification of microcystic lymphatic malformations of the tongue and to investigate different treatment methods.

METHODS

We reviewed and analyzed the medical records of all patients with microcystic lymphatic malformations of the tongue seen in the Department of Otorhinolaryngology—Head and Neck Surgery of Philipps-Universität Marburg from January 1, 1998, through December 31, 2008, with respect to age and sex distribution, symptoms, clinical presentation, management, treatment outcome, and follow-up. Lymphatic malformations were classified into the following 4 groups according to their extent (Figure 1): 1. Isolated superficial microcystic lymphatic malformations of the tongue (stage I); 2. Isolated lymphatic malformations of the tongue with muscle involvement (stage II; stage IIA, involving a part of the tongue; stage IIB, involving the entire tongue); 3. Microcystic lymphatic malformations of the tongue and the floor of mouth (stage III); and 4. Extensive microcystic lymphatic malformations involving the tongue, floor of mouth, and further cervical structures (stage IV).

RESULTS

Twenty patients (13 male and 7 female) with microcystic lymphatic malformations of the tongue were included in the evaluation. Their ages at initial presentation ranged from newborn to 20 years (mean age, 7.4 years). Thirteen of them had been treated at another hospital before the initial presentation at our department. The treatment methods included surgical reduction, laser therapy, corticosteroid therapy, and OK-432 (Picibanil; Chugai Pharmaceutical Co, Ltd, Tokyo, Japan) injections. Patient characteristics are given in Table 1.

The lymphatic malformations were reported to be apparent at birth in 11 cases and after birth in 7 cases. In the remaining 2 cases, no information was available regarding the time of onset. Eight patients had isolated lymphatic malformations of the tongue and therefore could be classified as having stages I and II disease according to our classification. In 3 patients, lymphatic malformations of the tongue extended to the floor of mouth (stage III). The remaining 9 patients were classified as having stage IV disease owing to the extent of the lymphatic malformations.

STAGE I

Three patients presented with superficial microcystic lymphatic malformations of the tongue (patients 1, 9, and 15) (Figure 2). The symptoms at the initial presentation were swelling, hemorrhage, pain, and difficulties in chewing. Complete excision of the lymphatic malformations with a carbon dioxide (CO2) laser was performed in all 3 patients. In patient 15, 2 treatment steps were necessary. All patients remained without significant complications during the treatment period. The cosmetic aspect and function improved after CO2 laser therapy. The average follow-up time was 12 months. In this period, no clinical signs of recurrence became obvious.

STAGE II

Five patients presented with microcystic lymphatic malformations of the tongue with muscle involvement, classified as stage IIA in 3 patients and stage IIB in 2 patients. They had symptoms such as bleeding, speech disturbances, dysphagia, pain, and recurrent enlargement during upper aerodigestive tract infections. Complete excision of the lymphatic malformation with a CO2 laser was performed in the 3 patients with stage
IIA disease (patients 4, 7, and 16). In 2 of them, 2 treatment steps were necessary. The average follow-up was 39 (range, 2-108) months. In this period, no signs of recurrence were seen in 2 patients, whereas 1 patient returned 9 years after laser therapy with swelling and pain of the tongue after an upper respiratory tract infection. Results of an ear, nose, and throat–specific examination revealed a recurrence of the lymphatic malformation, which was again resected by means of laser surgery.

Partial excision was performed in 1 patient with stage IIB disease (patient 2, Figure 3). This patient initially received laser treatment. The first laser treatment was performed at 9 years of age. The patient was treated with intravenous antibiotics and corticosteroids several times because of recurrent infection leading to swelling and bleeding. Because this conservative treatment also led to a good functional result, indication for further laser treatment was restricted.

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The wait-and-see policy was indicated in an 8-year-old girl (patient 5) with a stage IIB lymphatic malformation of the tongue. A biopsy was performed at 3 years of age at another hospital to obtain a histologic diagnosis. Owing to severe arterial bleeding after biopsy, a tracheotomy was performed that was surgically closed a few weeks later. Laser therapy had been planned but, owing to the absence of severe symptoms, the parents did not want to have any surgical treatment. Recurrent swelling episodes were treated with oral antibiotics.

STAGE III

Three patients presented with stage III disease. Symptoms included swelling, pain, bleeding, difficulties in chewing and swallowing, and cosmetic deformity. Two of them (patients 3 and 13) were treated with an open approach (Figure 4). An anterior wedge resection was performed in both patients to reduce macroglossia, and, in patient 3, the part of the lymphatic malformation involving the floor of mouth was surgically resected. Both patients had undergone surgery at other hospitals and are currently under observation because they have persistent disease.

Treatment of the tongue with the Nd:YAG laser only (bare fiber, 0.6 mm; laser power, 10-20 W; interstitial mode; irradiation time, 0.5-2.0 seconds) was performed twice in patient 8, who had a microcystic lymphatic malformation of the tongue and the floor of mouth. This therapy option was chosen owing to recurrent bleeding episodes leading to anemia. Afterward, there were no clinical signs of a residual lymphatic malformation of the tongue. Owing to the absence of symptoms, the parents did not want to have therapy of the residual lymphatic malformation of the floor of mouth. This patient was unavailable for follow-up after 3 months.
StAGE IV

Nine patients presented with stage IV disease (patients 6, 10-12, 14, and 17-20) (Figure 5 and Table 2). Symptoms at initial presentation were swelling, dysphagia, pain, speech disturbances, recurrent bleeding, cosmetic deformity, and airway obstruction. In patients 12 and 19, the prenatal diagnosis of airway compromise owing to a huge lymphatic malformation of the upper aerodigestive tract led to the ex-utero intrapartum treatment procedure.16 Although maternal-fetal circulation was maintained by delaying placental separation, laryngoscopy and intubation were performed to secure the airways in the newborns. Patient 19 died at 17 months of age due to a massive lymphatic malformation of the neck and thorax after several surgical attempts to reduce the mass of the lymphatic malformation. Patient 12 was surgically treated for lymphatic malformation of the neck, and the lingual lymphatic malformation has so far been managed by close observation owing to the absence of severe symptoms. Patients 11 and 20 were also observed in narrow intervals, because the patients had huge lymphatic malformations of the tongue, floor of mouth, and neck with a massive mandibular hypertrophy. Both patients have had multiple previous treatments at other hospitals without much success. Complete resection of the lymphatic malformation is currently not possible in either patient. Therefore, the correction of the mandibular deformity and the reduction of the lymphatic malformation are planned at 16 years of age. Meanwhile, the patients are being treated by orthodontists to achieve a good preoperative result.

The other 5 patients with stage IV lymphatic malformations of the tongue underwent surgery or laser surgery. In one patient (patient 14) with a lymphatic malformation of the tongue and the submandibular region, complete excision of the lingual lymphatic malformation was performed with a CO2 laser, whereas the submandibular lymphatic malformation was treated by conventional surgery. There were no clinical signs of residual disease. Partial excision with a CO2 laser was performed in patients 10 and 18. Complete resection was not possible in these patients owing to the large dimension of the lymphatic malformation. In patient 10, the submandibular mass was resected using an open approach, whereas in patient 18, the cervical parts of the lymphatic malformation were resected by means of conventional surgery. The other 2 patients were treated with an open approach (patients 6 and 17). Macroglossia was reduced by means of an anterior wedge resection. Both patients had previously undergone CO2 laser and tracheotomy at other hospitals. All patients with persistent disease are currently under observation.

COMMENT

Lymphatic malformations are vascular malformations with an unknown cause.3 They are estimated to make up 6% of all benign soft-tissue tumors in children.17 When the malformations occur in the tongue, the symptoms may include hemorrhage, excessive salivation, speech disturbances, difficulties chewing and swallowing, airway obstruction, and orthodontic abnormalities such as mandibular prognathism and malocclusion. Functional impairment and cosmetic deformity significantly affect the quality of life of patients with lymphatic malformations of the tongue.

The history and results of the physical examination usually suggest the diagnosis of lymphatic malformation of the tongue. The history of microcystic lymphatic malformations of the tongue is typically one of recurrent enlargement secondary to infection and trauma. Results of the physical examination usually reveal multiple small vesicles of varying size covering the surface of the involved parts of the tongue. Localized growth often forms an exophytic lesion with a nodular surface due to the presence of vesicles. These vesicles may be translucent or blood filled if there has been rupture of the capillary tufts, which can happen subsequent to infection and trauma or spontaneously. A superficial, localized appearance was found in 3 patients in this se-
ries, whereas the other patients had infiltrating lymphatic malformations.

Imaging is always recommended if therapeutic consequences can be expected. The only exception is a small, obviously superficial lymphatic malformation. If the lymphatic malformation does not seem to be superficial and the extent of the lesion has to be determined, magnetic resonance imaging is the method of choice. Lymphatic malformations display highly increased signal intensity on T2-weighted images, whereas in T1-weighted images, their signal intensity is usually similar or slightly less than that of muscles.

It is important for physicians to recognize unusual lesions such as lymphatic malformations because early recognition and, if possible, surgical excision are essential for optimal outcome. The diagnosis is made by characteristic surface lesions. For inexperienced physicians, or in cases where lesions with atypical clinical features are encountered, a definite diagnosis is difficult. In one of our patients, a biopsy was performed to obtain a diagnosis at the hospital where the patient had been treated before. Performing a biopsy always bears the risk of severe bleeding, as described herein. The patient required a tracheotomy owing to massive bleeding after the biopsy. This example shows the necessity of referring patients with suspected lymphatic malformations to centers that are specialized for the diagnosis and treatment of lymphatic malformations.

The management of microcystic lymphatic malformations of the tongue is especially challenging because of the potential for recurrent infection, hemorrhage, airway compromise, feeding difficulties, and interference with the development of normal speech, as well as concerns for aesthetics. Although it is desirable to treat lingual lymphatic malformations by total excision if possible, the extent of lymphatic malformations may force the surgeon to perform a partial resection.

In the present series of patients with microcystic lymphatic malformations of the tongue, it was possible to perform complete excision with a CO2 laser in all patients with stage I disease and in 3 patients with stage IIA disease. The excision of lymphatic malformations was performed with a small laser focus of less than 0.3 mm (laser power, 2-4 W). The use of the CO2 laser has been reported to be effective in the treatment of lymphatic malformations.
forms for debulking or complete excision. The advantages of the CO\textsubscript{2} laser compared with conventional surgery include less postoperative edema, tissue trauma, and blood loss. The laser ablation of lymphatic malformation vesicles may avoid partial resection of the tongue in certain cases and prevent bleeding. Vaporization of bleeding areas is performed with the CO\textsubscript{2} laser in a defocused mode with a laser power of 8 to 15 W. Because of the diffuse nature of microcystic lymphatic malformations of the tongue, it is often hard to distinguish between involved tissue and healthy tissue, which makes complete extirpation difficult. Because in stage II disease the superficial lymph cysts are connected with deeper cysts in the underlying muscle, CO\textsubscript{2} laser ablation should be continued to a sufficient depth to ensure the destruction of the deeper cysts. Reepithelialization after CO\textsubscript{2} laser ablation is usually complete after a few weeks, and scarring is usually minimal. For stages I and IIA microcystic lymphatic malformations of the tongue, CO\textsubscript{2} laser surgery seems to be an excellent curative treatment option. In stages IIB, III, and IV disease, CO\textsubscript{2} laser surgery seems to be useful as a part of a combined or staged approach.

Different surgical techniques have been described to treat extensive lymphatic malformations of the tongue, including wedge resection, bilateral marginal resection, U-shaped resection, and Jian or Dingman glossectomy. Because an anterior wedge resection was performed in 4 patients with stages III and IV lymphatic malformations in the present series, the residual lymphatic malformations were followed up regularly but were not treated owing to the absence of severe symptoms.

In general, the decision to perform surgical or laser surgical treatment should be made after careful reflection. Surgeons and patients must be aware of the fact that laser surgical ablation often leads to a reduction of symptoms but only very rarely achieves permanent curative results. However, this must be distinguished from the local laser surgical excision of superficial lymphatic malformations (stages I and IIA) that can be curative. When conventional surgery is indicated, we generally pursue a more radical approach because of the awareness that after repeated, less-invasive surgical approaches, significant scarring can be observed in deeper tissue layers, which makes function-preserving surgical interventions more difficult and often leads to more functional damage than a primarily more-invasive surgical approach.

In addition to these treatment strategies, radiofrequency ablation and sclerotherapy are therapeutic options in the treatment of lymphatic malformations. Radiofrequency ablation offers a relatively new minimal invasive therapy option primarily in stages I and II lesions, because it can be used to reach precise areas of tissue involvement. However, radiofrequency ablation was not used in our series.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Treatment (Age)</th>
<th>Previous Treatments (Age)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Anterior wedge resection and reduction of the parts of the LM in the floor of mouth (3 y); close observation</td>
<td>Surgical reduction (1 mo); laser treatment of the tongue (2 mo); several OK-432 injections (2-4 mo); tracheostomy and gastrostomy tube placement (4 mo) OK-432 injection into floor of mouth (3 y)</td>
</tr>
<tr>
<td>10</td>
<td>CO\textsubscript{2} laser treatment of the tongue (4.5 y); resection of the submandibular mass (4.75 y); CO\textsubscript{2} laser treatment of the tongue (5.25 y); close observation</td>
<td>Surgical reduction of the cervical mass (twice) (2 and 4 wk); laser treatment of the tongue (3 times) (2, 4, and 5 y); partial tongue reduction (7 y)</td>
</tr>
<tr>
<td>11</td>
<td>Close observation</td>
<td>Surgical reduction (1 y)</td>
</tr>
<tr>
<td>12</td>
<td>EXIT procedure (birth); resection of the cervical mass (2 wk); close observation</td>
<td>None</td>
</tr>
<tr>
<td>14</td>
<td>Resection of the submandibular part of the LM and CO\textsubscript{2} laser treatment of the tongue (13 y)</td>
<td>Surgical reduction (1 y)</td>
</tr>
<tr>
<td>17</td>
<td>Surgical reduction of the facial mass (twice) (1.75 and 2.5 y); anterior wedge resection, reduction of the LM of the floor of mouth (5.25 y); close observation</td>
<td>Tracheostomy (2 wk); partial resection (4 wk); several OK-432 injections (4-12 mo); laser treatment</td>
</tr>
<tr>
<td>18</td>
<td>Tracheostomy; reduction of the cervical mass (21 y); CO\textsubscript{2} laser reduction of the laryngeal parts (21.5 y); CO\textsubscript{2} laser treatment of the supraglottic parts (21.75 y); Nd:YAG laser treatment of the tongue and the floor of mouth (22 y); tracheotomy closure (22.5 y); CO\textsubscript{2} laser treatment of the tongue (23 y); close observation</td>
<td>Laser therapy of the tongue, larynx, and pharynx (39 times) (3-20 y)</td>
</tr>
<tr>
<td>19</td>
<td>EXIT procedure (birth); reduction of the cervical mass (2 wk); CO\textsubscript{2} laser treatment of the hypopharyngeal mass (5 wk); CO\textsubscript{2} laser treatment of the laryngeal mass (6 wk); tracheostomy (8 wk); reduction of the cervical mass (8 wk); thoracoscopy and Nd:YAG laser of the tongue (5 mo); close observation, died at 17 mo</td>
<td>None</td>
</tr>
<tr>
<td>20</td>
<td>Close observation</td>
<td>Reduction of the cervical mass and tracheostomy (2 wk); tongue reduction and reduction of the cervical mass (2 y); angioembolization (4 y)</td>
</tr>
</tbody>
</table>

Abbreviations: CO\textsubscript{2}, carbon dioxide; EXIT, ex-utero intrapartum treatment; LM, lymphatic malformation.
The use of sclerotherapy, like OK-432 injections, should be limited to macrocystic lesions because the sclerosing solution cannot diffuse from lumen to lumen in microcystic lesions. Because of the microcystic appearance of the presented lingual lymphatic malformations, sclerotherapy was not considered in these patients.

The option of conservative management with solitary observation should only be considered in asymptomatic patients before a definite treatment is performed. The potential risk of an acute enlargement of the lymphatic malformation secondary to upper respiratory tract infection or spontaneous or traumatic hemorrhage always has to be kept in mind. In particular, an increase in size, hemorrhage into the cysts, and infection of the cysts may render surgery at a later date more difficult.

With the watchful waiting attitude, the appearance of first symptoms should be followed by a course of antibiotics. The present concept is to provide patients with all stages of lymphatic malformation with a prescription for an oral antibiotic to be used immediately in case of an alteration like a size progression or swelling caused by a suspected infection of the lymphatic malformation. Treatment with an oral cephalosporin (eg, cefuroxime axetil, 500 mg twice daily) for 7 to 10 days is recommended in these cases. If oral therapy is insufficient, antibiotics have to be administered intravenously. Patients receive a 5- to 7-day treatment with cefuroxime, 1.5 g 3 times daily or 80 mg/kg body weight daily (maximum daily dose, 4.5 g) in 3 doses by the intravenous route. Although antibiotics should be administered to prevent the occurrence or the spread of infection, in case of acute swelling of the lymphatic malformation, corticosteroids may be prescribed to reduce edema. Corticosteroids were administered for 3 days in a dosage adapted according to the body weight (5 mg/kg body weight; maximum daily dose, 250 mg).

The combination of antibiotics and short-duration systemic corticosteroids usually leads to a reduction of symptoms and a decrease of swelling and inflammation as described in patient 2. This was previously shown by other study groups. Therefore, this concept is currently used in all patients with lingual lymphatic malformations before definite treatment. Khurana et al also reported a good functional result after multiple intralesional corticosteroid injections into lymphatic malformations of the tongue. Systemic corticosteroids probably alter lymphatic malformations by reducing lymphoid hypertrophy, stabilizing vasculature to decrease hemorrhage and fluid osmosis into the tissues, and causing lymphatic malformation channels to involute.

Management of huge lymphatic malformations is complex and requires an interdisciplinary approach involving different specialties. Macroglossia of the lymphangiomatous tongue may lead to skeletal and dental problems like mandibular prognathism and malocclusion. Therefore, maxillofacial surgeons and orthodontists should be involved at an early stage of treatment. In case of speech problems, the patients should be introduced to personnel in the Department of Phoniatrics. In the present case series, 13 patients had lymphatic malformations that could only be partially resected owing to their great dimension or because the lingual lesions were intricately interwoven into muscle fibers, which made complete excision impossible. In one patient, repeated laser reductions of the lymphatic malformation were performed because recurrent infection led to swelling of the residual lymphatic malformation.

All patients with microcystic lymphatic malformations of the tongue should be followed up regularly. In one of our patients, recurrence of lymphatic malformation occurred after 9 years without any symptoms or clinically obvious disease. This case shows that the infiltrating growth pattern of microcystic lymphatic malformations always includes the risk of postsurgical recurrence, even in rather small lymphatic malformations.

Because of their infiltrative nature and their location, microcystic lymphatic malformations of the tongue continue to pose a therapeutic challenge. Recent studies of lymphatic endothelium have shed light on how the lymphatic system is formed and grows, but the pathogenesis of lymphatic malformations is still unclear. Understanding the pathogenesis at the molecular level may generate new options for the treatment of microcystic lymphatic malformations of the tongue.

Our staging system seems to be useful to assess the outcome of patients with microcystic lymphatic malformations of the tongue. It seems to distinguish curable lingual lymphatic malformations from incurable lesions more precisely than the classification by de Serres et al. Lingual lymphatic malformations of stages I, IIA, IIB, and III, which belong to stage II according to de Serres et al (Table 1), differ regarding the possible treatment modalities and outcome. In contrast to patients with stages IIB and III lingual lymphatic malformations, patients with stages I and IIA lingual lymphatic malformations are easier to treat, and the lymphatic malformations can be completely resected in most cases. Patients with more advanced stages often have persistent disease after treatment owing to the diffuse infiltration of the involved structures. This result affirms that the stage of the lesions has a major effect on the outcome. However, in patients with lymphatic malformations of all stages, the therapeutic goal should be to counter functional restrictions, avoid complications by internal hemorrhage or superinfections, and to achieve an optimal aesthetic result.
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REFERENCES