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Lymphangioma circumscriptum of the tongue in paediatric patients: a clinic-pathological and immunohistochemical study with high-tech protocol and comprehensive literature analysis

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ABSTRACT

Purpose: Vascular anomalies (VAs) are a heterogeneous group of congenital disorders characterized by variable clinical presentation, biological behaviour, and therapeutic response. The classification system developed by the International Society for the Study of Vascular Anomalies (ISSVA) is currently the global standard, categorizing VAs based on histopathological features, hemodynamic, and clinical progression. Lymphatic malformations (LMs), including Lymphangioma Circumscriptum (LC)—a localized and often superficial variant—are stratified into macrocystic, microcystic, or mixed subtypes. Despite the system's widespread adoption, the absence of standardized dimensional criteria and consistent diagnostic protocols limits its applicability. The rarity of oral LC, especially in paediatric patients alongw with its clinical overlap with other vascular or neoplastic lesions, further complicates diagnosis and management. This study introduces an integrated High-Tech protocol combining High-Definition Intraoral Ultrasonography (IHDUS) and Diode Laser for the management of LC occuring in the tongue of paediatric patients. A comprehensive literature review further contextualizes the clinic-pathological significance of the herein reported approach within contemporary frameworks for vascular anomaly management.

Methods: All patients underwent a structured three-step protocol: IHDUS for the precise assessment of lesion depth, vascularity, and extension; Diode Laser transmucosal photocoagulation to promote volume and vascular supply reduction with subsequent Diode Laser-assisted surgical excision; histological examination withimmunohistochemical analysis too.

Results: 7 paediatric cases with histologically confirmed LC of the tongue were treated, all demonstrating comparable clinical and radiological characteristics; after surgery, complete healing was observed in all cases without complications.

Conclusion: Data from literature mainly describe invasive procedures for LC treatment, lacking standardization and often unsuitable for paediatric populations. The proposed protocol demonstrated substantial clinical value as a minimally invasive, safe, and reproducible approach for the diagnosis and management of LC of the tongue in paediatric patients.

1. Introduction

Lymphatic Malformations (LMs) are abnormal accumulations of dilated lymphatic vessels that give rise to cystic spaces lined by endothelial cells [1]. Early identification and precise management are essential to mitigate potential risks and prevent long-term functional and aesthetic complications. The impact of these

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anomalies varies depending on factors such as lesion number, size, anatomical location, and extent, emphasizing the importance of a tailored, multidisciplinary approach to treatment.

Although the precise aetiology remains elusive, as for the other vascular malformations (VMs), LMs are inherently congenital, with 65–75 % identified at birth and 80–90 % from the second year of life onwards. The most frequently affected area is the head, which is involved in approximately 90 % of cases. [2]. Multiple classification systems have been proposed to categorize vascular anomalies (VAs). A comprehensive framework, based on cellular features, flow characteristics, and clinical behaviour, was updated in 2018 during a meeting of the International Society for the Study of Vascular Anomalies (ISSVA) and is now globally recognized as the official system for classifying congenital vascular disorders [3]. Before the adoption of ISSVA system, VAs were frequently misdiagnosed, mismanaged, and poorly understood [4]. LMs classification is based on the presence of macrocystic (>1 cm) or microcystic spaces (<1 cm), or a combination of both [1,3].

Lymphangioma circumscriptum (LC) is a distinct clinicopathological variant within the wide spectrum of lymphangiomas, a group of benign VAs characterized by proliferating malformation of the lymphatic vessels, originally described by Redenbacher in 1828 and now widely classified as congenital VMs rather than true neoplastic lesions, in accordance with ISSVA [5,6]. These lesions predominantly affect the skin and mucous membranes and, although rare, they clinically present with or without symptoms, with isolated reported cases of malignant transformation. [7]. Despite the widespread adoption of the ISSVA classification system which provides a widely accepted framework for categorizing LMs into macrocystic, microcystic, and mixed variants, it lacks a clearly defined criterion for the macroscopic dimensions. The absence of a size-based classification may limit the clinical applicability of the system, particularly in the targeted surgical planning and prognostic evaluation. When lymphangiomas present as small, well-circumscribed lesions, the term “circumscriptum” is appropriately used to denote their localized nature and defined boundaries. Massive lesions with infiltrative behaviour toward surrounding tissues may frequently represent the clinical manifestation of underlying systemic or syndromic conditions. Their presence should prompt thorough diagnostic evaluation to rule out broader pathological processes [3,4].

LC generally exhibits a slow growth over a period of years, though it may rapidly expand within days, particularly during infections or hormonal changes such as puberty, resulting in a significant mass. Upon physical examination, LCs typically present as fluid-filled and non-compressible, a characteristic feature that aids in differentiating them from venous malformations. In some cases, the mucosal and skin surfaces may be affected by clusters of translucent, thin-walled vesicles often described as resembling a “frog-spawn” appearance. The formation of vesicles may lead to complications such as bleeding, lymphatic fluid leakage, and pain [1,2].

Diagnosis is typically established in childhood, and whether not evident at birth, it often manifests during infections that induce swelling due to increased lymphatic flow. A comprehensive imaging approach is essential for characterizing lesions, assessing parameters such as size, vascular flow velocity, flow direction, anatomical relationships with adjacent structures and lesion composition [2,8–11].

Spontaneous resolution of LMs is rarely reported in a small percentage of cases. In non-regressive lesions, surgical approach is required, as their natural course typically involves progressive enlargement. While localized lesions may be favourable to complete surgical resection, extensive lesions present significant challenges due to several factors: they frequently involve lip, cheek, and tongue; complete excision may lead to severe tissue defects with both aesthetic and functional defects and uncontrolled bleeding; lesions are poorly delineated and the walls of lymphatic vessels within LMs are fragile and prone to rupture [12].

A wide range of therapeutic strategies are reported, ranging from minimally invasive techniques to advanced surgical interventions incorporating adjunctive therapies too. In complex cases, a multimodal approach is often necessary, including combinations such as sclerotherapy followed by Laser therapy or initial surgical approach followed by adjuvant Laser or sclerotherapy to address residual lesions [13–15].

This study proposes an advanced clinic-pathological and therapeutic High-Tech protocol combining High-Definition Intraoral Ultrasonography (IHDUS) and Diode Laser technology for the integrated management of lingual LC in paediatric patients treated at the Complex Unit of Odontostomatology, University of Bari “Aldo Moro.” Also, a comprehensive analysis of the existing literature has been performed.

2. Materials and methods

This study was conducted according to the principles of the Declaration of Helsinki (protocol approved by Independent Ethical Committee of the University of Bari “Aldo Moro” - study number 4576, protocol number 143, date of approval 15-10-2014) and involved all paediatric patients (age≤18) with a clinical diagnosis of lingual LC treated at “Aldo Moro” University of Bari from 2015 to 2025.

Parents of enrolled paediatric patients provided informed consent for both the proposed therapeutic procedure and the utilization of their clinical data for scientific research purposes. During initial evaluation, a comprehensive medical history was gathered, alongside a detailed clinical assessment with the objective of identifying potential trauma, syndromic associations, comorbidities, and concurrent pharmacological treatments that could influence management strategies. Furthermore, data concerning anatomical distribution, bleeding propensity, and pain intensity were documented. To assess functional and aesthetic impact, patients filled structured questionnaires designed to evaluate impairments affecting daily activities. Functional defects were defined as disturbances in essential orofacial functions. These findings contributed to determining the necessity and urgency of the procedure.

The protocol consists of the following sequential procedures:

1. **IHDUS** – To assess the vascular blood component, extension, depth of the lesion and flow intensity.
2. **Diode Laser Transmucosal Photocoagulation** – To reduce lesion size and minimize vascular supply.
3. **Diode Laser Surgical Excision** – To remove the lesion.

As a first approach, all lesions underwent IHDUS to assess depth and extent of the malformation. Imaging was performed using an advanced ultrasound system (Logic 9, General Electric Healthcare, Chicago, IL, USA) equipped with a high-frequency linear “Hockey Stick” probe (18 MHz) which was covered with a latex protection and filled with ultrasound gel for intraoral lesions [15,16]. Doppler imaging was integrated into the evaluation to characterize hemodynamic vascular patterns. Based on ultrasonographic findings, lesions were further stratified by depth. Only patients with lesions extending beyond 5 mm underwent MRI for further anatomical characterization and treatment planning.

A preliminary photocoagulation protocol was implemented using a Diode Laser (Lasotronix, Poland), emitting light at a mean wavelength of 980 nm through a flexible quartz fiber with a diameter of 320 μm. Photocoagulation was performed using a power output of 4–6 W/cm^2 in pulsed mode (t-on = 250 ms,

t-off = 250 ms), with the tip positioned 2–3 mm above lesion surface. To ensure optimal tissue response, fiber tip was continuously moved across the lesion to avoid prolonged exposure at any single point, while monitoring for signs of tissue constriction and blanching; to mitigate the risk of thermal injury and optimize procedural safety, ice packs were applied.

In the same operative session, following photocoagulation, the final stage involved surgical excision using the same Laser device. Procedure was performed in continuous wave mode with an energy output of 4–8 W at a wavelength of 980 nm.

Optical fiber was applied in direct contact with the tissue, optimizing cutting efficiency while simultaneously achieving haemostasis through laser-induced coagulation, thereby minimizing intraoperative blood loss. To prevent excessive thermal diffusion and potential collateral damage to deeper structures, fiber was meticulously oriented parallel to the mucosal surface throughout the excision. Excised sample was submitted for histopathological examination at the Institute of Pathological Anatomy of "Aldo Moro" University of Bari. Tissue samples were formalin-fixed and paraffin-embedded (FFPE), tissue samples were cut as 3 μm thick sections, mounted on glass slides, and firstly stained with Haematoxylin and Eosin (H&E). Immunohistochemical coloration for CD31 (Leica, clone 1A10, RTU), CD34 (Dako, clone QBEnd10, 1:500), podoplanin/D2-40 (Abcam, clone GP36, 1:4000) and VIII-related antigen (FVIII-RAG) were also performed to further investigate the vascular nature of the lesion. FVIII-RAG counts were made determining the number of vessels per mm^2, thereby allowing for the calculation of counted microvessel density (CMVD), a validated parameter for evaluating the extent of microvascular proliferation within histological specimens.

2.1. Literature analysis

A comprehensive analysis of the literature was conducted across three major biomedical databases—PubMed, Scopus, and Web of Science—to identify relevant studies published between January 1999 and April 2025. The search strategy incorporated a structured combination of Medical Subject Headings (MeSH) and free-text terms, specifically: "Lymphangioma Circumscriptum" AND "Oral" OR "Lymphangioma Circumscriptum" AND "Tongue". Duplicates were removed, and titles and abstracts were screened for relevance. Full-text articles were retrieved for studies meeting inclusion criteria.

Eligibility was determined based on the following criteria: (1) paediatric patients; (2) studies reporting a histopathological confirmed diagnosis of LC; (3) articles published as case reports, case series, or reviews; (4) studies providing sufficient clinical and therapeutic information. Studies were excluded if they lacked histological confirmation, did not specifically address oral presentations, were based on animal models, or contained insufficient clinical data.

3. Results

3.1. Case series

7 paediatric patients with histopathological confirmation of LC localized to the tongue were enrolled in the present study. Data are summarized in Table 1.

3.2. Case 7

A 14-year-old male patient was referred for the evaluation of a dorsal tongue lesion. The lesion had been present since early childhood and was associated with occasional bleeding following trauma or functional activities. No pain or other symptoms were reported.

Intraoral examination revealed a well-circumscribed, roundish swelling located on the dorsal surface of the tongue, characterized by a papillary surface texture, affected by clusters of translucent vesicles. The lesion exhibited a reddish coloration with purplish areas, measured approximately 3.5 cm at its greatest dimension, and was firm, non-tender, and non-haemorrhagic upon palpation. The remainder of the oral mucosa appeared unremarkable and within normal clinical limits (Fig. 1A).

IHDUS revealed a hypoechoic area measuring 2.22 × 0.38 cm, with low to absent vascular signal on Color Doppler imaging (Fig. 1B). Transmucosal photocoagulation using a Diode Laser was employed to obtain volumetric reduction of the lesion and attenuation of its vascular supply (Fig. 1C and D). Surgical excision was performed in continuous wave mode with an energy output of 6–8W at a wavelength of 980 nm and application of intramuscular suture (vicryl 2/0) to promote the closure (Fig. 1 E). The latter was achieved by primary intention using 0-silk sutures (Fig. 1 F). Clinical follow-ups at 1 month showed complete healing of the treated area (Fig. 1 J). Histopathological examination confirmed diagnosis of LC along with the immunohistochemical analyses which revealed a strong podoplanin/D2-40 expression in endothelial cells and CD31 positivity (Fig. 2 A, B, C). The histopathological specimen demonstrated a strong correlation with the corresponding ultrasonographic image (Fig. 2 D).

3.3. Literature analysis

From search protocol, only 10 studies met the inclusion criteria. A total of 11 individual clinical cases were identified which are described and summarized in Table 2.

4. Discussion

LMs are benign congenital anomalies of the lymphatic system, histologically characterized by thin walled, dilated vascular channels lined by inconspicuous endothelial cells and filled with proteinaceous lymphatic fluid; despite their well-documented morphological features, LMs precise aetiology remains unclear; although their congenital origin, only 65–75 % of cases are diagnosed at birth, with the head and neck region being the most affected site (90 %) [1–26].

The most widely accepted classification system, revised during the 2018 ISSVA meeting, is based on cellular characteristics, flow dynamics, and clinical behaviour. Recent advances in molecular biology have identified several lymphatic endothelial cell markers, such as lymphatic vessel endothelial hyaluronan receptor-1 (LYVE-1) and podoplanin, as well as lymphangiogenic growth factors responsible for lymphatic vessel proliferation and maintenance. These include vascular endothelial growth factor C (VEGF-C), vascular endothelial growth factor receptor 3 (VEGFR-3), and the transcription factor Prox-1 [18]. Both VEGF-C and VEGFR-3 have been shown to be upregulated in LM tissue, with both factors playing roles in lymphatic tissue proliferation [15,16,26–29]. Additionally, Prox-1 is involved in the upregulation of VEGFR-3 in lymphatic endothelium and may contribute to the separation of lymphatic vessels from the venous system during embryonic development [17,28,29]. Embryologic development of the lymphatic system remains a subject of active research. Due to the incomplete understanding of such process, elucidating the causal factors underlying LMs is still challenging [27].

LMs accurate diagnosis requires a multimodal imaging approach, incorporating conventional radiography, High-Definition US, and MRI. Panoramic radiograph plays a limited role in the diagnosis and

Table 1
Data of patients treated at Complex Unit of Odontostomatology of "Aldo Moro" University of Bari.

Nr	Year	Age	Gender	Location	Medical History	Clinical aspect	US	MRI	Treatment	Immunohistochemical features	Recurrences
1	2016	10	F	Dorsal tongue	None	Well-defined roundish swelling with focal areas of translucent vesicles	Hypoechoic heterogeneous small-size area measuring 0,76 × 0,45 cm and low vascular signal on color Doppler	None	Preliminary diode laser photocoagulation + diode laser excision	CD31 (++), CD34 (+), podoplanin/D2-40 (+++), FVIII-RAG (+)	No recurrences at 8 years
2	2017	14	M	Dorsal tongue	Previous orthodontic treatment	Hyperplastic lesion with multiple pink to blue papules and "frog-egg" appearance"	Hypoechoic area witch cystic appearance measuring 2,63 × 0,54 cm and low vascular signal on color Doppler	Focal well-circumscribed hyperintense lesion	Preliminary diode laser photocoagulation + diode laser excision	CD31 (++), podoplanin/D2-40 (+++), FVIII-RAG (+)	No recurrences at 7 years
3	2018	12	M	Dorsal tongue	Orthodontic treatment	Verrucous-like lesion with irregular multiple pink to blue vesicles	Hypoechoic heterogeneous cystic lesion with low vascularity on color Doppler measuring 2,11 × 0,34 cm	None	Preliminary diode laser photocoagulation + diode laser excision	CD31 (+), podoplanin/ D2-40 (+++), FVIII-RAG (+)	No recurrences at 6 years
4	2021	6	F	Dorsal tongue	None	Roundish enlarging swelling measuring 5 cm with irregular papillary surface	Cystic hypoechoic lesion measuring 3,36 × 0,59 cm with moderate vascularity at color Doppler	Focal well-circumscribed hyperintense lesion	Preliminary diode laser photocoagulation + diode laser excision	CD31 (++), CD34 (+), podoplanin/D2-40 (++), FVIII-RAG (+)	No recurrences at 4 years follow-up
5	2021	11	M	Dorsal tongue	None	Verrucous-like swelling with numerous soft irregular vesicles	Hypoechoic cystic lesion measuring 1,8 × 0,21 cm with low vascularity on color Doppler	None	Preliminary diode laser photocoagulation + diode laser excision	CD31 (+), podoplanin/ D2-40 (+++), FVIII-RAG (+)	No recurrences at 4 years
6	2022	12	F	Dorsal tongue	Orthodontic treatment	Defined roundish lesion with irregular and papillary surface	Cystic hypoechoic lesion measuring 3,2 × 0,57 cm with moderate vascularity at color Doppler	Localized well-defined lesion with cystic appearance	Preliminary diode laser photocoagulation + diode laser excision	CD31 (+), podoplanin/ D2-40 (+++), FVIII-RAG (+)	No recurrences at 2 years
7	2025	14	M	Dorsal tongue	None	Well-circumscribed, roundish swelling measuring 3,5 cm with papillary surface and clusters of translucent vesicles	Hypoechoic heterogeneous area measuring 2.22 × 0.38 cm, with low vascular signal on color Doppler	None	Preliminary diode laser photocoagulation + diode laser excision	CD31 (+), podoplanin/ D2-40 (+++), FVIII-RAG (+)	No recurrences at 1 month follow-up

+++: positivity ranged from 75 % to 100 %.
++: positivity ranged from 35 % to 74 %.
+: positivity <34 %.

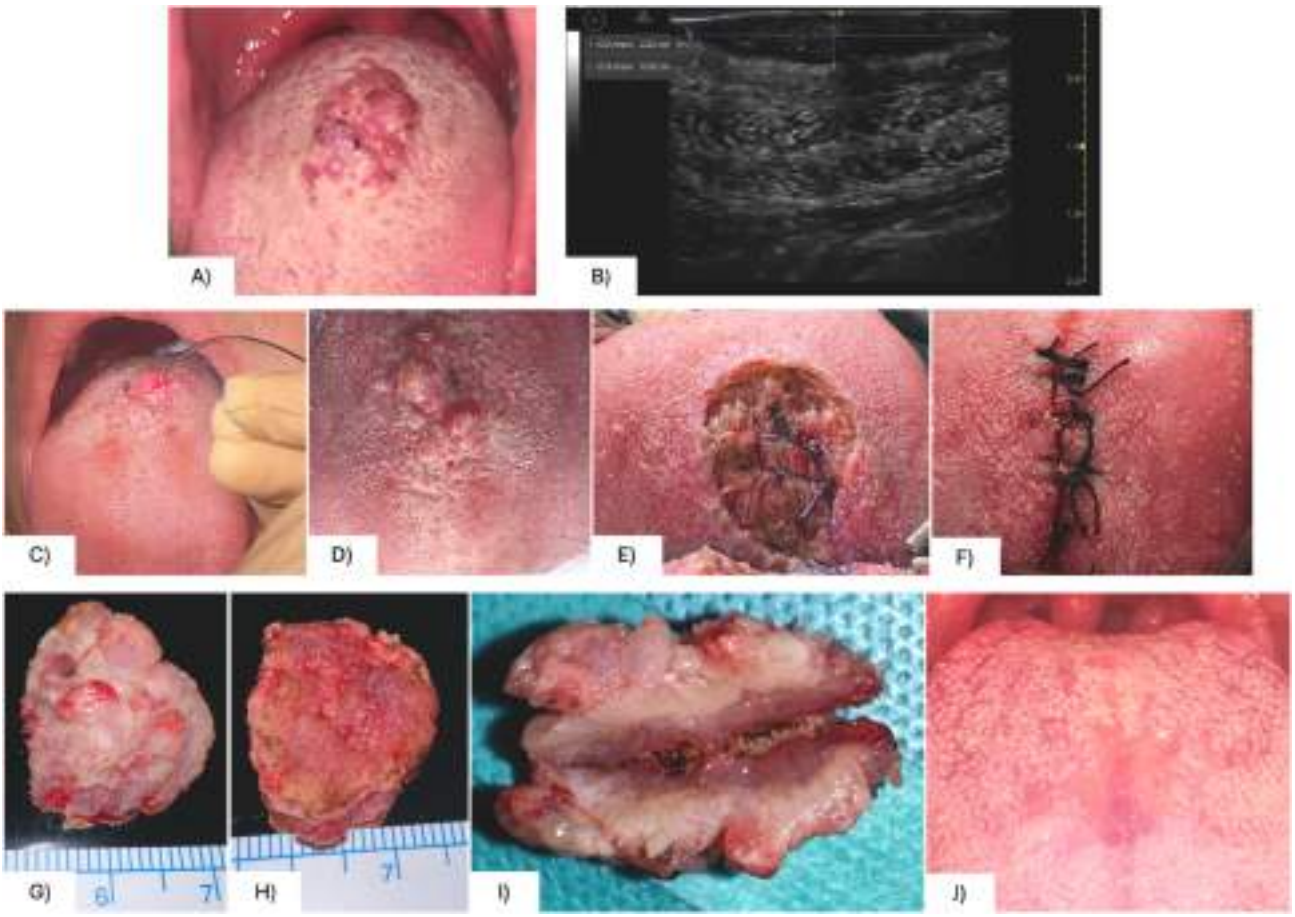

Fig. 1. A) 3.5 cm well-circumscribed, roundish swelling located on the dorsal surface of the tongue, with papillary surface texture and clusters of translucent vesicles; **B)** Hypoechoic area measuring 2.22 × 0.38 cm; **C and D)** Clinical appearance post-transmucosal photocoagulation with a Diode Laser, demonstrating well-demarcated coagulated tissue with initial signs of healing, including blanching and no bleeding; **E)** immediate postoperative appearance following surgical excision with a Diode Laser. Residual tissue shows clean margins, absence of active bleeding, and initial tissue blanching consistent with photothermal coagulation; **F)** 0-silk suture was placed to promote healing; **G and H)** surgical specimen excised using Diode Laser, with clear delineation of the excised tissue and coagulated edges consistent with laser-assisted resection; **I)** excised specimen resected with a scalpel; **J)** 1 month follow-up showing healing of the treated region.

classification of LMs as it only provides valuable insights into osseous involvement. Findings such as bone erosion, sclerosis and periosteal reaction suggest skeletal involvement, although whether confined in oral soft tissues, it is generally insufficient for accurate diagnosis and characterization [8]. MRI delineates well-demarcated cystic masses with fluid attenuation, lobulated architecture, and septations. The varying degrees of contrast enhancement correspond to different vascular and blood components within the lesion. Additionally, MRI plays a critical role in therapeutic decision-making by identifying relationships with adjacent vital structures. Furthermore, serial MRI assessments provide an objective and quantitative method for monitoring treatment outcomes by evaluating changes in lesion size and segmental characteristics over time [5]. Ultrasound (US) is the imaging modality of choice for suspected VMs due to its accessibility, cost-effectiveness, non-invasiveness, and absence of ionizing radiation [9]. The assessment begins with grayscale imaging to delineate lesion boundaries. LC typically appear as hypoechoic or heterogeneous lesion in approximately 80 % of cases. The primary objective of US is to differentiate between microcystic and macrocystic LMs; in addition, Color and Power Doppler distinguish high- flow and low-flow malformations [10]. Magnetic resonance imaging (MRI) is the gold-standard imaging technique for evaluating extensive LMs [11]. Therapeutic strategies range from minimally invasive techniques to advanced surgical interventions, often requiring a combination of approaches [14,15,30–33]. As a first approach, ultrasound-guided aspiration may be employed to reduce lesion volume and alleviate pressure-related symptoms. However, this is only a temporary measure, as recurrence rates are high, with risks of secondary infection. Aspirated fluid—typically milky, serous, serosanguinous, or straw-coloured—can be sent for cytological analysis to evidence malignant cells. Recently, Laser technology is increasingly utilized for the treatment of small, microcystic, and superficial lesions, particularly in the larynx and oral cavity. Laser therapy offers advantages such as minimal bleeding, reduced postoperative pain, precise tissue ablation, and repeatability. The carbon dioxide (CO_2) laser is the most commonly used in the oral cavity due to its strong absorption by water and oral mucosa. Additionally, other laser devices, including neodymium-doped yttrium aluminium garnet (Nd:YAG, 1064 nm, near-infrared) and Diode Lasers, have been reported as effective in treating oral cavity VMs. Diode Laser exhibits minimal absorption by water while demonstrating a strong affinity for haemoglobin. Due to its low water absorption, the High-Level Diode Laser can penetrate tissues to a depth of approximately 4–5 mm and its energy is selectively absorbed by haemoglobin, leading to localized heat generation. This thermal effect induces coagulation, extending to a depth of approximately 7–10 mm, in a process known as photocoagulation [13,14].

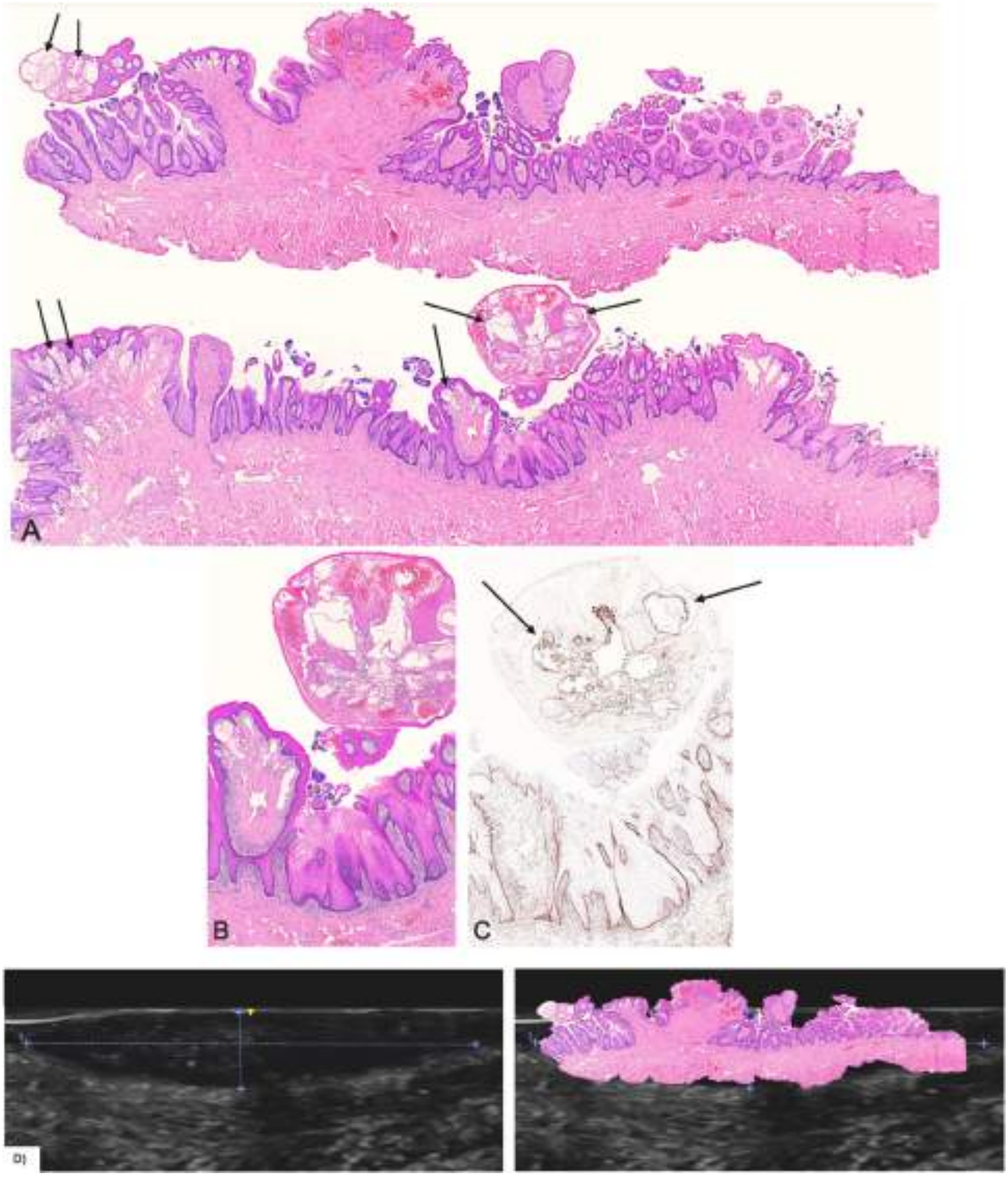

Fig. 2. At low-power magnification, the "**A**" detail reveals a microcystic lesion extending from mucosa to muscolar layers; it is predominantly made up of variably sized (0,2–0,6 mm), irregular shaped lymphatic spaces clustered within the superficial layers of the chorion (as highlighted by the arrows), resulting in a multifocal polypoid verrucoid-like protrusions of the overlying mucosa. Lymphatic spaces are lined by a monolayered endothelium, are mostly devoid of a muscular wall and may appear either empty or fluid-filled; occasionally, they contain red blood cells (ematic venous vessels intermingled) (**B**). The surrounding epithelium is thinned, because of the physical distention exerted by the lesion, while the adjacent oral mucosa exhibits reactive changes (papillomatous hyperplasia, acanthosis and mild chronic inflammation) (H&E) (**B**). The immunohistochemical analyses of the same field revealed a strong podoplanin/D2-40 expression in vascular vessels which is helpful to confirm the lymphatic nature. (**C**). Correspondence between microscopical tissue architecture and ultrasonographic image (**D**). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 2
Paediatric Lingual LC from literature analysis.

Nr	Year	Author	Age	Gender	Location	Clinical aspect	US	MRI	Treatment	Recurrences
1	1999	*Joel Schwab* et al. [16]	14 months	M	Tip of the tongue	White verrucous lesion	None	No evidence of extension to surrounding tissues	Surgical biopsy	NS
2	2006	*Arika Bansal* et al. [17]	7 yo	F	Dorsal tongue	Asymptomatic swelling, occasional episodes of severe bleeding	None	None	Surgical biopsy	NS
3	2012	*Yazeed Alghonaim* et al. [18]	6 yo	M	Right tongue margin	4 cm, pedunculated, painless, irregular, white/grey, multi-cystic lesion firm consistency and non-tender on palpation	None	Defined mass with no bony or muscular extension	Excisional biopsy + radiofrequency ablation	None at 18 months follow-up
4	2013	*Chakravarti A.* et al. [19]	5 yo	F	Dorsal tongue	Numerous small vesicles containing straw coloured fluid with some haemorrhagic fluid	None	None	Surgical biopsy + three doses bleomycin 0.75U/mg/kg given at monthly intervals	No recurrences at 18 months follow-up
5	2013	*Chakravarti A.* et al. [19]	4 yo	M	Anterior part of tongue	Small vesicles containing clear fluid with some containing haemorrhagic fluid	None	None	Surgical biopsy + three doses bleomycin 0.75U/mg/kg given at monthly intervals	No recurrences at 12 months follow-up
6	2014	*Nikolaos Katsoulas* et al. [20]	12 yo	F	Right dorsal tongue	Sessile tumor with papillary surface, red with white areas, measured approximately 0.5 cm in greatest diameter, asymptomatic, no bleeding	None	None	Surgical excision	No recurrences at 18 months follow-up
7	2017	*Jungil Hwang* [21]	10 yo	F	Dorsal tongue	Approximately $70 \times 35 \times 20$ mm reddish, verrucous, protruded lesion	None	$50 \times 35 \times 25$ mm ill-defined lesion	Incisional biopsy + triamcinolone and bleomycin directly injected at monthly intervals + intralesional bevacizumab	No recurrences at 3 years follow-up
8	2021	*Samaneh Mozafarpoor* et al. [22]	18 yo	F	Dorsal tongue	Hyperplastic lesion (1×2 cm2)	None	None	3 sessions of pulsed-dye laser (PDL) therapy+ 3 sessions of long-pulsed Nd:YAG laser therapy	NS
9	2022	*Naqoosh Haidry* et al. [23]	12 yo	F	Dorsal tongue	Multiple pink to blue papules resembling a pebbly, vesicle-like surface - the so- called “frog-egg” or “tapioca pudding appearance"	Multiple hypoechoic centres showing minimum vascularity	None	Intralesional injection of 0.2 ml of 3 % sodium tetradecyl sulphate	No recurrences
10	2023	*Dimitrios Andreadis* et al. [24]	6 yo	M	Dorsal tongue	Hyperplastic overgrowth characterized by small soft irregular vesicles with a red-brownish-yellow color	None	Area of T2 signal with maximum diameter of 2.3 cm and cystic texture in the middle and frontal left tongue region	Immediate preoperative direct embolization sodium tetradecyl sulphate + surgical excision of the abnormal surface of the tongue	NS
11	2024	*Jain A.* et al. [25]	12 yo	F	Dorsal tongue	Enlarging painless raised, irregular, greyish-white, multi-cystic lesion. Vesicles contained straw-coloured fluid or haemorrhagic fluid	None	Iso to hyperintense on T1 and hyperintense on T2 defined lesion	Surgical excision + radiofrequency ablation	No recurrences at 1 year follow-up

NS: Not Stated.

Intralesional sclerotherapy, which involves the injection of sclerosing agents to induce localized inflammation and thrombosis within the vascular malformation, is a widely utilized treatment modality. Various sclerosing agents have been proposed, each exhibiting distinct properties, indications, and risk profiles, particularly in the management of oral VMs. Although this method demonstrated variable success, it is associated with potential complications, including fever, pain, and transient lesion enlargement [14,15].

Surgical excision remains the gold standard for LMs treatment. Highest resolution rate is described for focal macrocystic lesions, although selected microcystic cases might also benefit from resection to improve aesthetic and functional outcomes. Surgical management of complex lesions is challenging, particularly whether they extend into deep anatomical spaces or have thin, finger-like projections. Due to the infiltrative nature of LMs, particularly their tendency to involve adjacent structures, achieving complete surgical resection remains challenging, even for experienced surgeons. Postoperative complications occur in approximately 15–30 % of cases, with recurrence rates ranging from 10 to 15 % [12].

In the present study, IDHUS as a first approach to LC management proved to be an effective imaging modality for assessing lesion extension, depth and vascularization, thereby reducing the number of patients requiring MRI execution. Primary objective of any therapeutic approach is to preserve functional integrity while achieving an optimal aesthetic outcome. Although complete surgical excision remains the gold standard for treating LC, it is often challenging due to their infiltrative behaviour and complex integration with surrounding tissues. In cases where surgical removal is impractical due to deep infiltration into critical anatomical structures, sclerotherapy is the preferred alternative. [31,34,35]. Table 2 provides a synthesis of reported cases of lingual LC from the existing literature, highlighting a predominance of surgical interventions—primarily excisional biopsy—and intralesional administration of pharmacologic agents, most commonly bleomycin. However, the evidence supporting the efficacy of these approaches remains confined to small-scale case series, thereby limiting their generalizability [31,36,37]. Notably, only a single study by Samaneh Mozafarpoor et al. (2021) reported the use of a laser-based treatment protocol comprising three sessions of pulsed-dye laser (PDL) therapy in combination with Nd:YAG laser therapy, reflecting the highly limited application of laser modalities in the management of LC [22]. Furthermore, none of the reviewed studies employed immunohistochemical analysis, underscoring a significant methodological gap that undermines the diagnostic and interpretative reliability of the available data. In 2022, Wiegand et al. reported that one-third of the referred patients with LMs in their study was previously treated at other hospitals, although most common therapeutic procedures in their study were conventional surgical resection (47.0 %), laser therapy (17.4 %) and sclerotherapy with OK-432 (8.3 %), watch-and-wait procedure was adopted in 27.7 % of the patients [36].

Diode Laser-assisted excision approach demonstrated significant advantages, including precise tissue removal, reduced the intraoperative bleeding, and shortened surgical time. Additionally, postoperative complications—such as scarring, pain, inflammation, and discomfort—were minimal, further highlighting the efficacy and safety of this technique [13,31–33,38].

The herein described protocol represents a promising and effective treatment modality for LC, offering a minimally invasive alternative with optimal functional and aesthetic outcomes.

Our findings, in conjunction with existing literature, indicate the absence of a clearly defined sex-related predominance in LCoccurrence. Described case series highlight the potential role of previous or concurrent orthodontic treatment as a significant local traumatic factor contributing to lesion development—an association that has not been previously emphasized in the literature. Furthermore, although some authors have proposed the utilization of MRI as a valuable adjunct in the diagnostic workflow, literature lacks consensus regarding standardized diagnostic protocols. In fact, aside from one report describing the application of US, most published cases do not detail a comprehensive diagnostic workflow, underscoring the need for greater methodological protocol and uniformity in clinical evaluation.

The correspondence between microscopical architecture and ultrasonographic image underscores the diagnostic accuracy and reliability of IHDUS in characterizing lesion macroscopic texture and tissue composition. This correlation between imaging and histology further validates the integration of US as a valuable adjunctive tool in the diagnostic workflow, also with an accurate immunohistochemical analysis to confirm the lymphatic origin. FVIII-RAG is widely regarded as one of the most specific immunohistochemical markers for vascular endothelial cells and is commonly employed in the assessment of CMVD—a well-established method for quantifying microvascular proliferation. This technique typically involves enumerating stained microvessels within regions exhibiting the highest degree of neovascularization, under standardized magnification settings [39]. In our series, FVIII-RAG positivity was observed at relatively low levels, counting <34 %, also with CD34, a marker for blood vascular endothelia. By contrast, immunoreactivity for CD31 was consistently high across all cases, indicating robust endothelial expression and supporting their reliability as endothelial markers. Additionally, podoplanin expression, a specific lymphatic endothelial marker, ranged from 75 % to 100 %, further reinforcing its value in delineating lymphatic vascular components within LC. To date, and to the best of our knowledge, the available literature does not report any diagnostic-therapeutic approach similar to the proposed protocol in this study. Published cases predominantly describe more invasive interventions, such as intralesional administration of sclerosing agents or surgical excision—methods that may pose considerable risks, particularly in paediatric patients. The treatment strategy presented herein is both minimally invasive and conservative offering a potentially safer and more tolerable alternative for LC managing.

This study is subject to limitations that warrant consideration: due to the rarity of lingual LC, sample size from our Institute is reduced, thus limiting the applicability of our findings to broader populations; also, to our knowledge, the integration of IHDUS with Diode Laser as a combined diagnostic and therapeutic protocol has not been previously documented in the scientific literature, thereby limiting comparative analysis and confining outcome evaluation exclusively to our case series; literature analysis revealed a limited number of cases, many of which lacked long-term follow-up, thus impeding a comprehensive and statistically significant interpretation of data. A further methodological limitation refers to the inherent bidimensionality of ultrasonographic imaging, which may compromise the accurate characterization of the lesion architecture. This limitation becomes especially pronounced in the context of large-volume lesions, where the depth and internal heterogeneity may exceed the resolving capacity of conventional 2D imaging, thereby affecting both diagnostic precision and therapeutic planning.

Despite these limitations, this is the first study which explored the combined application of Diode Laser photocoagulation and Diode Laser surgical excision for the comprehensive management of LC, previously assessed with IHDUS examination. We propose an innovative High-Tech diagnostic-therapeutic protocol designed to optimize treatment outcomes also with immunohistochemical

analysis. Our findings suggest that this approach is universally applicable across LC but also effective in managing both minor and extensive tongue lesions. Additionally, no complications were observed, highlighting its favourable safety profile; aesthetic and functional outcomes were deemed satisfactory. Given such promising findings, we suggest that the High-Tech protocol represents a safe and effective minimally invasive diagnostic and therapeutic strategy for LC management.

Data statement

The original contributions presented in this study are included in the article. Also, collected data were downloaded from the following databases: PubMed (https://pubmed.ncbi.nlm.nih.gov; URL accessed on 1 February 2025), Scopus (https://www.scopus.com; URL accessed on 1 March 2025), and Web of Science (https://clarivate.com/academia-government/scientific-and-academic-research/research-discovery-and-referencing/web-of-science/; URL accessed on 1 April 2025). Further inquiries can be directed to the corresponding authors.

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References

[1] Buckmiller LM, Richter GT, Suen JY. Diagnosis and management of hemangiomas and vascular malformations of the head and neck. Oral Dis Jul 2010;16(5):405–18.
[2] Sham ME, Sultana Nishat. Vascular anomalies in maxillofacial region – review. J Oral Maxillofac Surg Med Pathol 2012;24:137–46.
[3] ISSVA classification of vascular anomalies ©2025 international society for the study of vascular anomalies.
[4] Enjolars O, Wassef M, Chapot R. Introduction: ISSVA classification; venous malformations (VM). In: Enjolars O, Wassef M, Chapot R, editors. Color atlas of vascular tumors and vascular malformations. New York: Cambridge University Press; 2007. p. 1–11. 168-223.
[5] Neville BW, Damm DD, Allen CM, Bouquot JE. Soft tissue tumors. In: Neville BW, editor. Oral and maxillofacial pathology. 2nd ed. New Delhi, Philadelphia: Saunders Publishers; 2002. p. 475–7.
[6] Stănescu L, Georgescu EF, Simionescu C, Georgescu I. Lymphangiomaof the oral cavity. Rom J Morphol Embryol 2006;47:373–7.
[7] Miceli A, Stewart KM. Lymphangioma. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
[8] Hydoh H, Hori M, Akiba H. Peripheral vascular malformations: imaging, treatment approaches, and therapeutic issues. Radiographics 2005;3:S157–71.
[9] Paltiel HJ, Burrows PE, Kozakewich HP, Zurakowski D, Mulliken JB. Soft tissue vascular anomalies: utility of US for diagnosis. Radiology 2000;214:747–54.
[10] Trop I, Dubois J, Guibaud L. Soft-tissue venous malformations in pediatric and young adult patients: diagnosis with Doppler US. Radiology 1999;212:841–5.
[11] Poldervaart MT, Breugem CC, Speleman L, Pasmans S. Treatment of lymphatic malformations with ok- 432(picibanil): review of the literature. J Craniofac Surg 2009;20(4):1159–62.
[12] Lowe LH, Marchant TC, Rivard DC, Scherbel AJ. Vascular malformations: classification and terminology the radiologist needs to know. Semin Roentgenol 2012:106–17.
[13] World Health Organization. Pathology and genetics of tumours of soft tissues and bone, vol. 158; 2002.
[14] Zhou Q, Zheng JV, Mai HM, Luo QF, Fan XD, Su LX, et al. Treatment guidelines of lymphatic malformations of the head and neck. Oral Oncol 2011;47:1105–9.
[15] Colbert SD, Seager L, Haider F, Evans BT, Anand R, Brennan BA. Lymphatic malformations of the head and neck—current concepts in management. Br J Oral Maxillofac Surg 2013;51:98–102.
[16] Schwab J, Baroody F. Lymphangioma circumscriptum: an unusual oral presentation. Clin Pediatr 1999;38(10):619–20. https://doi.org/10.1177/000992289903801012.
[17] Bansal A. Lymphangioma circumscriptum of the tongue. Indian Pediatr 2006 Jul;43(7):650–1. PMID: 16891689.
[18] Alghonaim Y, Varshney R, Sands N, Daniel SJ. Coblation technique as an alternative treatment modality for oral lymphangioma. Int J Pediatr Otorhinolaryngol 2012 Oct;76(10):1526–7. https://doi.org/10.1016/j.ijporl.2012.06.014. Epub 2012 Jul 20. PMID: 22819484.
[19] Chakravarti A, Bhargava R. Lymphangioma circum- scriptum of the tongue in children: successful treatment using intralesional bleomycin. Int J Pediatr Otorhinolaryngol 2013;77:1367–9.
[20] Katsoulas N, Tosios KI, Argyris P, Koutlas IG. A. Sklavounou Lymphangioma circumscriptum, angiokeratoma, or superficial vascular ectasia with epithelial hyperplasia? Oral Surg Oral Med Oral Pathol Oral Radiol 2014;118(2):e53–7.
[21] Hwang J, Lee YK, Burm JS. Treatment of tongue lymphangioma with intralesional combination injection of steroid, bleomycin and bevacizumab. Arch Craniofac Surg 2017 Mar;18(1):54–8. https://doi.org/10.7181/acfs.2017.18.1.54. Epub 2017 Mar 25. PMID: 28913305; PMCID: PMC5556746.
[22] Mozafarpoor, Asilian A, Goodarzi A, Ebrahimi Z, Mokhtari F, Moqaddam ZR. Treatment of tongue lymphangioma circumscriptum with non-ablative long-pulsedNd:YAG laser: a case report and review of literature. Iran J Dermatol 2021;24:242–8.
[23] Haidry N, Shivhare P, Vaidyanathan A, Ahmad Mokhtar E, Ghimire AC. Lymphangioma of the oral and maxillofacial region: a report of three cases. Cureus 2022 Dec 15;14(12):e32577. https://doi.org/10.7759/cureus.32577. PMID: 36654537; PMCID: PMC9840748.
[24] Andreadis D, Ndreu A, Tsekos A, Panta P. Diagnostic and therapeutic challenges of a large tongue lymphangioma in a child: a case report. Cureus 2023 Oct 20;15(10):e47363. https://doi.org/10.7759/cureus.47363. PMID: 38022192; PMCID: PMC10657479.
[25] Jain A, Kumar Rai A, Kaur J, Abbas SZ, Bansal H. Treatment of oral lymphangiomas by coblation. Indian J Otolaryngol Head Neck Surg 2024 Aug;76(4):3543–7. https://doi.org/10.1007/s12070-024-04603-0. Epub 2024 Mar 14. PMID: 39130350; PMCID: PMC11306697.
[26] Orvidas LJ, Kasperbauer JL. Pediatric lymphangiomas of the head and neck. Ann Otol Rhinol Laryngol 2000;109:411–21.
[27] Wiegand S, Eivazi B, Barth PJ, Berens D von Rautenfeld, Folz BJ, Mandic R, et al. Pathogenesis of lymphangiomas. Virchows Arch 2008;453:1–8.
[28] Itakura E, Yamamoto H, Oda Y, Furue M, Tsuneyoshi M, et al. VEGF-C and VEGFR-3 in a series of lymphangiomas: is superficial lymphagioma a true lymphangioma? Virchows Arch 2009;454:317–25.
[29] Pavlov KA, Dubova EA, Shchyogolev AI, Mishnyov OD. Expression of growth factors in endotheliocytes in vascularmalformations. Bull Exp Bio Med 2009;147:366–70.
[30] Angiero F, Benedicenti S, Romanos GE, Crippa R. Treatment of hemangioma of the head and neck with diode laser and forced dehydration with induced photocoagulation. Photomed Laser Surg 2008;26:113–8.
[31] Romeo U, Del Vecchio A, Russo C, Palaia G, Gaimari G, Arnabat-Dominguez J, et al. Laser treatment of 13 benign oral vascular lesions by three different surgical techniques. Med Oral Patol Oral Cir BucalMar 2013;18(2):e279–84. 1.
[32] Limongelli L, Tempesta A, De Caro A, Maiorano E, Angelelli G, Capodiferro S, et al. Diode laser photocoagulation of intraoral and perioral venous malformations after tridimensional staging by high definition Ultrasonography. Photobiomodul Photomed Laser Surg 2019;37:722–8 [CrossRef].
[33] Angelelli G, Moschetta M, Limongelli L, Albergo A, Lacalendola E, Brindicci F, et al. Endocavitary sonography of early oral cavity malignant tumors. Head Neck 2017;39:1349–56 [CrossRef].
[34] Blei F. Congenital lymphatic malformations. Annl N Y Acad Sci 2008;1131:185–94.
[35] Swetman GL, Berk DR, Vasanawala SS, Feinstein JA, Lane AT, Bruckner AL. Sildenafil for severe lymphatic malformations. N Engl J Med 2012;366(4):384–6. https://doi.org/10.1056/NEJMc1112482.
[36] Wiegand S, Wichmann G, Dietz A. Efficacy of sirolimus in children with lymphatic malformations of the head and neck. Eur Arch Otorhinolaryngol 2022;279(8):3801–10. https://doi.org/10.1007/s00405-022-07378-8.
[37] Wiegand S, Wichmann G, Dietz A, Werner JA. Association between malformation type, location and functional deficits in lymphatic malformations of the head and neck in children. Eur Arch Otorhinolaryngol 2023 May;280(5):2535–40. https://doi.org/10.1007/s00405-023-07844-x. Epub 2023 Jan 25. PMID: 36695910; PMCID: PMC10066143.
[38] Tempesta A, Dell'Olio F, Siciliani RA, Favia G, Capodiferro S, Limongelli L. Targeted diode laser therapy for oral and perioral capillary-venous malformation in pediatric patients: a prospective study. Children 2023;10:611. https://doi.org/10.3390/children10040611.
[39] Kohlberger PD, Obermair A, Sliutz G, Heinzl H, Koelbl H, Breitenecker G, et al. Quantitative immunohistochemistry of factor VIII-related antigen in breast carcinoma: a comparison of computer-assisted image analysis with established counting methods. Am J Clin Pathol 1996 Jun;105(6):705–10. https://doi.org/10.1093/ajcp/105.6.705. PMID: 8659444.