Priority in selection of treatment methods used for lymphatic malformations affecting maxillofacial region

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Sulaimani Dental Journal

Abstract:

Objectives: The purpose of this paper was to discuss and evaluate the treatment plan selection and the outcomes of 82 cases of lymphatic malformation in oral & maxillofacial region.

Materials & methods: The analysis included of 82 cases of lymphatic malformation in oral & maxillofacial region during the period between January 2004 to November 2013 at maxillofacial department in Al-Hilla General Teaching Hospital. The treatment plans selection depend on details patient history, clinical examination & imaging investigations. Different techniques were used depended on age, extension, site & types of lymphatic malformation. The treatment methods were conservative treatment, surgery, use of sclerosing agents or combinations of them.

Results: Total number of the patients were 82 complains from different types lymphatic malformation, 30 were males constituting 36.5% while 52 were females constituting 63.5% . The youngest patient was 5 days, while the oldest one was 45 years. Forty case treated by sclerotherapy and surgery (48.7%) . Surgery alone as primary treatment done for 27 patients (32.9%) other 10 cases treated by sclerotherapy alone (12.1%) & 5 cases (6%) only needs observation .

Conclusions: Careful treatment plan selection depends on age, extension, type of lesion & experience of surgeon associated with good prognosis. Conservative resection was the most effective method in treatment of lymphatic malformation.

Keywords: *Vascular malformation, lymphangioma, sclerosing agent.*

Received*: April 2014,* ***Accepted****: September, 2014*

Introduction:

The lymphatic system develops during the 6th week of embryonic life [1]. Lymphatic malformation (LM) characterized by the size of the malformed channels which are microcystic, macrocystic, or combined. It's usually noted at birth or within the first 2 years of life. On occasion, LM first becomes evident in later childhood, adolescence, or even adulthood [2].

The Hamburg classification is currently the most accepted classification system. It is subject to continual improvement by the International Society for the Study of Vascular Anomalies (ISSVA)[3,4]. LM is most commonly located on the head and neck; other common sites are the axilla, chest, and perineum. LM typically causes deformity and psychosocial issues, especially when it involves the head and neck.

The two most common complications associated with LM are bleeding and infection. Intralesional bleeding occurs in up to 35% of lesions causing ecchymotic discoloration, pain, or swelling [5]. Oral lesions may lead to macroglossia, poor oral hygiene, and caries. Swelling due to bleeding, localized infection, or systemic illness may obstruct vital structures. Two-thirds of infants with cervicofacial LM require tracheostomy [6]. Bony overgrowth is another complication; the mandible is most commonly involved resulting in an open bite and prognathism [7]. These lesions are diagnosed by history and physical examination. Small, superficial or asymptomatic lesions do not require further evaluation and intervention as they are benign lesions.

Large or deep LMs are assessed by MRI to: (1) confirm the diagnosis; (2) define the extent of the malformation; (3) plan the treatment. LM appears as either a macrocystic, microcystic or combined lesion with septations of variable thickness [8,9]. Histological confirmation of LM is rarely necessary [10]. An infected LM often cannot be controlled with oral antibiotics and needs intravenous antimicrobial therapy with hospital admission. Intervention for LM is reserved for symptomatic lesions that cause pain, significant deformity, or threaten vital structures [5].

Sclerotherapy is first-line management for large or problematic macrocystic/combined LM and its preferred due to lower complications rate than attempted resection [11]. Several sclerosing agents are used to shrink LM likes doxycycline, sodium-tetradecyl sulfate (STS), ethanol, bleomycin, and OK-432 [9,12].

Excision of LM can cause significant morbidity: major blood loss, iatrogenic injury, and deformity [5,6]. Usually excision is usually subtotal because LM involves multiple tissue planes and important structures so recurrence is common (35–64%) [13]. In small, well-localized LM (microcystic or macrocystic) complete excision is recommended with preservation of the anatomy of the affected area. Subtotal excision

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of problematic areas, such as bleeding vesicles or a hyper-trophied lip should be carried out rather than an attempting "complete" resection that might result in a worse deformity than the malformation itself. Macroglossia may require reduction to return the tongue to the oral cavity or to correct an open-bite deformity [14]. In order to assess different modalities of treatment of lymphatic malformations affecting the maxillofacial area this study was done.

Materials and Methods:

Eighty-two patient treated by the same surgeon during the period between January 2004 to November 2013 at maxillofacial department in Al-Hilla General Teaching Hospital.

Patient records, treatment modality used, response to treatment, the period of treatment & its complications were reviewed. The diagnosis depends on physical examination, ultrasound, computed tomography & magnetic resonance imaging (MRI) study. According to MRI examination, the patients grouped into macrocystic (45 cases), microcystic (22 cases) & unicystic (15 cases). The treatment plan divided the patients in 4 groups (Table 1) depend on the types, site of the lesion &age of the patients as follows:-

1- Patients underwent surgery as primary treatment. Indicated in all unicystic & localized macrocystic or microcystic cases
2- Patients underwent pre-surgical treatment by percutaneous sclerosing agent injection (Ethanol or bleomycin). Indicated in diffuse Microcystic & macrocystic lymphangioma that's located in different tissues planes.
3- Patients underwent percutaneous sclerosing agent injection (Ethanol or bleomycin) alone. Indicated in cases of macrocystic & microcystic lymphangiomas. Its safety as compared to surgery that's may be at risk to damage important structures.

Figure 1: Clinical view of neck lymphangioma extend to floor of mouth & raise the tongue due to infection

4- Patients need observation & follow-up without treatment. Indicated in small lesion that's not affected the esthetic or function & without complication.

Ethanol (95%) 1mL/kg was used in pre-surgery & as primary sclerosing agent in the period from January 2004 till the end of 2009 while bleomycin was used between at the end of 2009 till November 2013.

The bleomycin diluted 1mg/1ml normal saline/kg after the fluid aspirated from the lesion the material injected into the lesion under deep sedation or general anesthesia. The procedure repeated each three weeks and in some cases the injection of sclerosing agent performed with ultrasonography guidance under deep sedation or GA.

Indications for treatment have based on tissue destruction or disfigurement (Fig.1) & obstruction of vital functions (Fig.6). The surgery in most of these cases represents the main modality of treatment as the first choice or follows different sclerosing agents treatment (Fig.5).

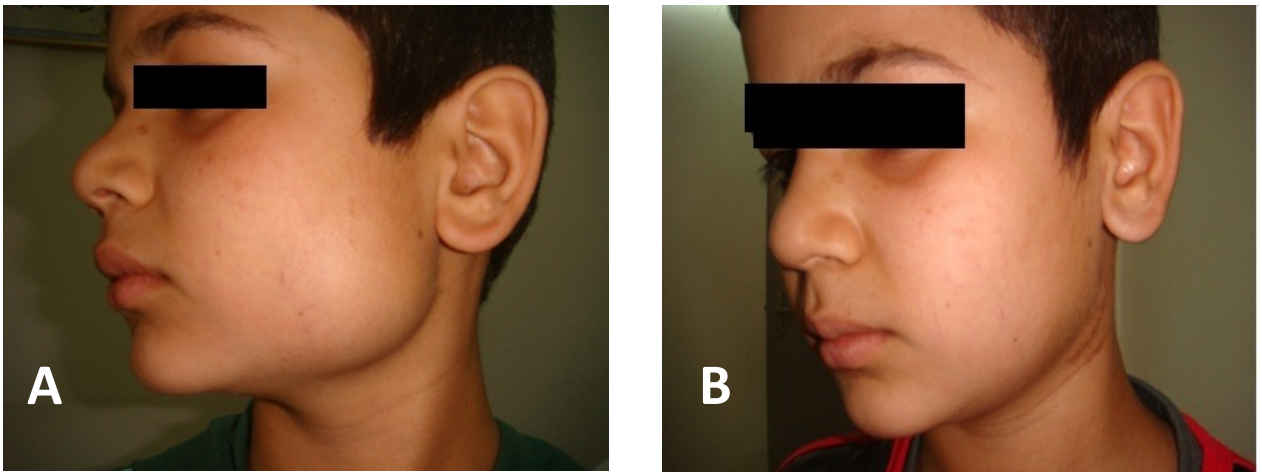

Figure 2: A : Clinical view of unicystic lymphangioma B: Post surgical excision (surgery primary treatment)

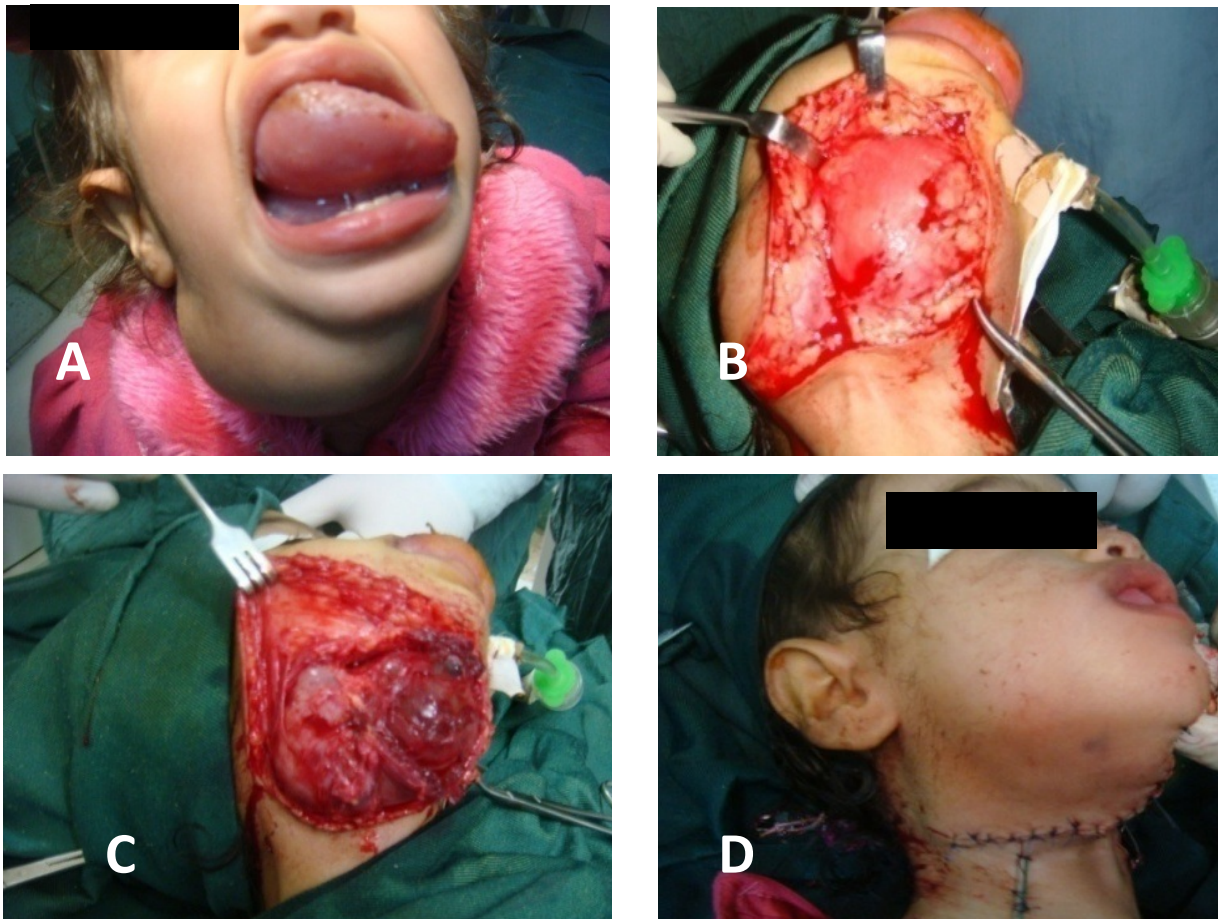

Figure 3: A- Clinical view of macrocystic lymphangioma, B- Surgical excision through submandibular approach, C- Multiple cystic appearance of the specimen, D- Immediate post surgical with reduction of macroglossia

Results:

Patients recorded in this study were 82 complains from different types lymphatic malformation 30 patients were males constituting 36.5% and 52 were females constituting 63.5% .

The youngest patient was 5 days while the oldest one was 45 years. Forty cases treated by sclerotherapy, followed by surgery (22 Ethanol & 18 bleomycin) represented (48.7%). Primary surgical excision used for 27 cases (15 unicystic, 7 macrocystic & 5 microcystic) represented (32.9%), while 10 cases treated by sclerotherapy alone (7 Ethanol & 3 bleomycin) represented (12.1%) & 5 case only needs observation (6%) as summarized by (Table 1).

Primary surgical excision was effective in 25 of 27 patients, most of them were unicystic and macrocystic. Ethanol pre-surgery was effective in 10 case, were

Table 1: Number of patient's distribution according treatment plan selection

Type Lymphangioma	No . of patients	Surgery	Ethanol pre-surgery	Bleomycin pre-surgery	Ethanol only as a sclerosing agent	Bleomycin only as a sclerosing agent	Observati-on only
Unicystic	15	15					
Macrocystic	45	7	10	11	5	2	
Microcystic	22	5	12	7	2	1	
Total	82	27	22	18	7	3	5

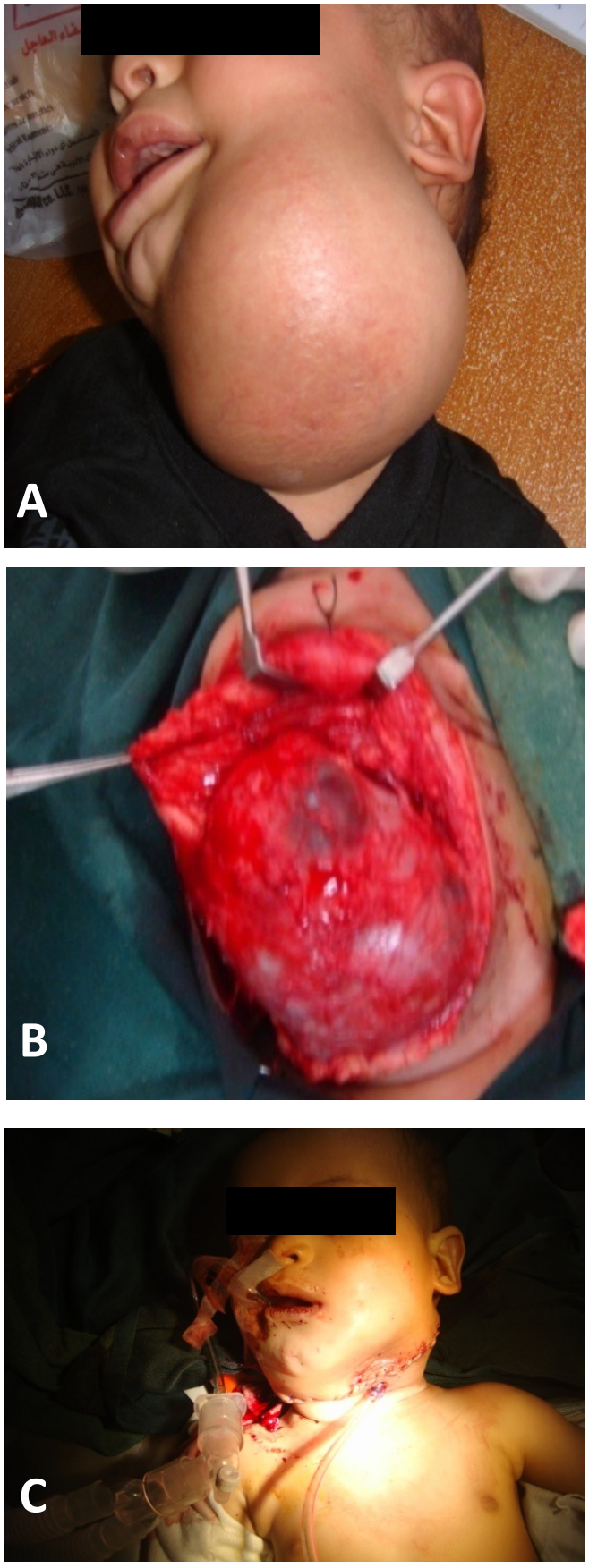

Figure 4: A- Clinical view of macrocystic lymphangioma, B- Surgical view of multicystic specimen, C- Post surgical view

Figure 5: Clinical view of huge macrocystic lymphangioma treated by bleomycin pre-surgical excision

Figure 6: A- Clinical view of macrocystic lymphangioma, B- Sclerosing agent used pre-surgical excision of the lesion

Table 2: The effectiveness of primary treatment according to the treatment plan modalities

The cure or permanent shrinkage percentage	Primary surgery 27 case	Ethanol pre-surgery 22 case	Bleomycin pre-surgery 18 case	Ethanol 7 case	Bleomycin 3 case
100% cure	25	10	9	0	0
> 70%	2	7	5	5	2
50-70%	0	5	4	2	1
<50%	0	0	0	0	0

Table 3: Complications according to type of treatment plan

Type of complication	Primary surgery 27 case	Ethanol pre-surgery 22 case	Bleomycin pre-surgery 18 case	Ethanol 7 case	Bleomycin 3 case	Total 82 case
Lymphorrhea	3	8	5	0	0	16
Airway obstruction	0	0	0	0	0	0
Infection	2	4	2	3	0	11
Tissue scar or ulceration	2	4	0	2	1	9
Facial nerve or any branch palsy	0	2	0	1	0	3
Total	7	18	7	6	1	39

completely cure other 7 case showed permanent shrinkage > 70% of their size & 5 cases had permanent shrinkage 50 - 70%.

The use of bleomycin pre-surgery was effective in 9 cases which were completely cure, other 5 cases had permanent shrinkage > 70% of their size & 4 cases showed permanent shrinkage 50 - 70% from their size.

Ethanol as a primary sclerosing agent was effective in 5 cases causing permanent shrinkage > 70% & 2 cases had permanent shrinkage 50 - 70% of the size of lesions.

Bleomycin as primary sclerosing agent was effective in 2 cases which had permanent shrinkage > 70% & 1 case show permanent shrinkage 50 - 70% of the size of lesion (Table 2).

Complication after primary surgical excision included lymphorrhea (3 cases), infection (2 cases) and unacceptable tissue scar (2 cases). The complication after ethanol pre-surgical excision included lymphorrhea (8 cases), infection (4 cases), palsy of mandibular & cervical branches of facial nerve (2 cases), and tissue scar (4 cases). The complication after bleomycin pre-surgical excision included lymphorrhea (5 cases), infection (2 cases). The complication after ethanol as a primary treatment alone included infection (3 cases), palsy of mandibular branch of facial nerve (1 case) and tissue scar (2 cases). The complication after bleomycin as a primary treatment alone included skin scar in one case (Table 3). The ethanol has a greater incidence of adverse side-effects than bleomycin. The major side-effect is skin necrosis & Severe pain that does not occur following the injection of bleomycin and there are fewer adverse reactions.

Discussion:

Based on the size of the lymphatic lumen, LMs (previously termed lymphangiomas) can be divided into microcystic lesions (previously termed lymphangioma circumscriptum), macrocystic lesions (previously termed cystic hygromas) (fig.4) and a combined form. Hence the term cystic hygroma has now been replaced by the term macrocystic. The most important diagnostic tool in lymphatic malformations is clinical examination and information from magnetic resonance scanning (MRI), which demonstrates the extent of the lesion and helps to differentiate between it and other vascular lesions.

Doppler ultrasound can confirm the flow of the lesion [15] and in this study the diagnosis depended on history , physical examination and MRI in majority of cases, but its cost and some time limited availability make the CT scan & ultrasonic used in diagnosis the lesions & classify them into macrocystic , microcystic & unicystic lesions.

Indications for treatment depend on the size, location and symptoms of the lesion. Cosmetic disability, presence of recurrent infection, oozing, crusting, ulceration and pain are the most frequent

indications for treatment. This indications supported by surgical excision is recommended for resectable lesions, there is a high recurrence rate [11].

Raveh *et al* reported a recurrence rate of 22% in 74 children treated with primary surgical excision, but in our study Cure rates were superior in the group having primary surgical excision in type with low complication rates [16]. The effectiveness of treatment were superior in the group having surgery with sclerotherapy (ethanol & bleomycin) similar result were observed by Kim *et al*. [17] & approximately similar result in ethanol & bleomycin pre-surgery but the complication with ethanol more than bleomycin were used presurgery.

Sclerotherapy is the first-line management for large or problematic macrocystic/combined LM [11]. In this study the sclerotherapy (ethanol & bleomycin) used as a first line of treatment only in macrocystic 7 cases & 3 microcystic cases with similar acceptable outcome but the complication with ethanol is more than bleomycin. Five cases did not need treatment, just observation alone without any intervention; this fact supported by Dasgupta *et al.* that patients with asymptomatic macrocystic LMs of the head and neck, who underwent interventional procedures had a higher complication and recurrence rate compared to patients who were managed by observation alone [18]. Priority should be placed on preservation of normal function and restoration of a normal appearance. Microcystic lymphangioma are diffuse, located in different tissues planes, and it is difficult to distinguish involved tissue from normal tissue. Macrocystic lesions on the other hand are more localized and are more easily excised this result supported by other study & surgical management in some cases associated with correction of macroglossia [14] .

Conclusions:

Careful treatment plan selection depends on age, extension, type of lesion and experience of surgeon associated with good prognosis. Conservative resection was the most effective method in treatment of lymphatic malformation and the macrocystic lesions are most easily excised. Diffuse microcystic lesions are more difficult and may require multiple operations. Care should be taken to identify and preserve important structures, because tissue planes are often damaged.

References:

1. *Mulliken JB, Young A. Vascular birthmarks: hemangiomas and malformations. Philadelphia: WB Saunders; 1988.*
2. *Marler JJ, Fishman SJ, Upton J, Burrows PE, Paltiel HJ, Jennings RW, et al. Prenatal diagnosis of vascular anomalies. J Pediatr Surg. 2002; 37:318–26.*
3. *Lee BB, Laredo J, Lee TS, Huh S, Neville R. Terminology and classification of congenital vascular malformations. Phlebology. 2007; 22: 249-52.*
4. *Mattassi R, Loose DA, Vaghi M. Hemangiomas and Vascular Malformations, An Atlas of Diagnosis and Treatment. Springer Verlag. 2009.*
5. *Padwa BL, Hayward PG, Ferraro NF. Cervicofacial lymphatic malformation: clinical course, surgical intervention, and pathogenesis of skeletal hypertrophy. Plast Reconstr Surg. 1995;95:951–60.*
6. *Edwards PD, Rahbar R, Ferraro NF, et al. Lymphatic malformation of the lingual base and oral floor. Plast Reconstr Surg. 2005;115:1906–15.*
7. *Greene AK, Burrows PE, Smith L. Periorbital lymphatic malformation: clinical course and management in 42 patients. Plast Reconstr Surg. 2005;115:22–30.*
8. *Finn MC, Glowacki J, Mulliken JB. Congenital vascular lesions: clinical application of a new classification. J Pediatr Surg. 1983;18:894–900.*
9. *Choi DJ, Alomari AI, Chaudry G. Neurointerventional management of low-flow vascular malformations of the head and neck. Neuroimag Clin N Am. 2009;19:199–218.*
10. *Florez-Vargas A, Vargas SO, Debelenko LV. Comparative analysis of D2–40 and LYVE-1 immunostaining in lymphatic malformations. Lymphology. 2008;41:103–10.*
11. *Smith MC, Zimmerman B, Burke DK. Efficacy and safety of OK-432 immunotherapy of lymphatic malformations. Laryngoscope. 2009;119:107–15.*
12. *Burrows PE, Mitri RK, Alomari A. Percutaneous sclerotherapy of lymphatic malformations with doxycycline. Lymphat Res Biol. 2008;6:209–16.*
13. *Alqahtani A, Nguyen LT, Flageole H. 25 years' experience with lymphangiomas in children. J Pediatr Surg. 1999;34:1164–8.*
14. *Grimmer JF, Mulliken JB, Burrows PE, Rahbar R. Radiofrequency ablation of microcystic lymphatic malformation in the oral cavity. Arch Otolaryngol Head Neck Surg. 2006;132:1251-6.*
15. *Marler JJ, Mulliken JB. Current management of hemangiomas and vascular malformations. Clin Plast Surg. 2005;32:99–116.*
16. *Raveh E, de Jong AL, Taylor GP, Forte V. Prognostic factors in the treatment of lymphatic malformations. Arch Otolaryngol Head Neck Surg. 1997;123:1061–5.*
17. *Kim KH, Sung MW, Roh JL, Han MH. Sclerotherapy for congenital lesions in the head and neck. Otolaryngol Head Neck Surg. 2004;131:307–16.*
18. *Dasgupta R, Adams D, Elluru R, Wentzel MS, Azizkhan RG. Non interventional treatment of selected head and neck lymphatic malformations. J Pediatr Surg. 2008;43:869–73.*