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Review Article

Guidelines for the treatment of head and neck venous malformations

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Abstract: Venous malformation is one of the most common benign vascular lesions, with approximately 40% of cases appearing in the head and neck. They can affect a patient's appearance and functionality and even cause life-threatening bleeding or respiratory tract obstruction. The current methods of treatment include surgery, laser therapy, sclerotherapy, or a combined. The treatment of small and superficial venous malformations is relatively simple and effective; however, the treatment of deep and extensive lesions involving multiple anatomical sites remains a challenge for the physicians. For complex cases, the outcomes achieved with one single treatment approach are poor; therefore, individualized treatment modalities must be formulated based on the patient's condition and the techniques available. Comprehensive multidisciplinary treatments have been adapted to achieve the most effective results. In this paper, based on the national and international literature, we formulated the treatment guidelines for head and neck venous malformations to standardize clinical practice. The guideline will be renewed and updated in a timely manner to reflect cutting-edge knowledge and to provide the best treatment modalities for patients.

Keywords: Head and neck, venous malformation, treatment guidelines

Introduction

Venous malformation is one of the most common vascular malformations together with lymphatic malformation. It exhibits a low flow rate because they are post-capillary lesions and have no arteriovenous (AV) shunts. The lesions grow in proportion with the body, demonstrating lifelong development, and do not regress spontaneously. The incidence of venous malformation is approximately 1:5,000-10,000; approximately 40% of them occur in the head and neck regions. The vast majority of these malformations are sporadic and more commonly occur in the mouth, airway tract and muscle [1]. Venous malformation is not only disfiguring but is also usually associated with complications, such as pain, ulcers, bleeding, and the compression or invasion of adjacent structures. These complications have severe impact on speech, swallowing, and respiratory function and may even lead to death due to bleeding and suffocation [2].

The pathogenesis of venous malformation is unclear. It is speculated to be caused by developmental defects of the venous system. TIE2 receptor mutation has been found in some patients with venous malformation syndrome (such as blue rubber bleb nevus syndrome) and multiple myocutaneous and venous malformations [3]. Familial venous malformation is char-

acterized by autosomal dominant inheritance related to mutation of the 9P locus and is rarely seen clinically [4]. Further studies showed that somatic mutations in angiopoietin receptor gene TEK presented in various single or multiple venous malformations and led to loss of TIE2 receptor function [5], and upregulated expression of other vascular endothelial growth factors, such as βTGF and βFGF, which exacerbated the severity of the lesion [6].

A significant increase in the number of nerve cells is found in some venous malformation lesions; the underlying etiology requires further investigation [7]. Pain is common with venous malformations in the upper face and is largely secondary to these static malformed venous pools leading to spontaneous thrombosis and resultant phlebitic syndrome in the area of thrombosis. In addition, the expression of matrix metalloproteinase-9 was recently found to be increased in intramuscular venous malformations, suggesting that venous malformations have the capability for invasive growth and angiogenesis while expanding slowly due to the increase in hydrostatic pressure. Progesterone receptors are highly expressed in venous malformations, which might be one of the reasons for the rapid increase in the number of lesions when hormonal levels change [8].

There are various kinds of treatment methods for venous malformation, including surgery, sclerotherapy, laser therapy, cryotherapy, electrocoagulation treatment, and treatment with copper needles. All of these methods have advantages and disadvantages [9-11]. In principle, an individualized treatment modality should be designed according to the location, size and extent of lesion, speed of venous drainage, and technical availabilities. Large venous malformations in the head and neck can seriously affect patients' physical and mental health. Single treatment approach is not able to achieve satisfying outcomes. Therefore, multidisciplinary treatments are required to achieve the desired therapeutic effects. Consequently, comprehensive multidisciplinary treatments are recommended for the treatment of complex and extensive venous malformations. To standardize the treatments for head and neck venous malformations, we formulated the guideline for diagnosis and treatment of head and neck venous malformations based on published literatures and clinical experiences [12]. With the development of medical science and technology, new methods, technologies, and drugs will continue to emerge. The guideline will be revised regularly and updated according to the latest clinical evidence and scientific research.

Histopathological and clinical features

Histologically, venous malformations (VMs) may be ectatic or micro-venular. They can be malformed in many varying sizes. The degree of ectasia increases with advancing age, but the rate at which this takes place is variable. Calcification and formation of phleboliths occur through dystrophic calcification of organizing thrombi, as a result of stasis in these low-flow lesions. The thrombus may become infected and cause pain and tenderness.

The location of the venous malformation can be superficial or deep, and they can involve single or multiple anatomical sites. The commonly affected sites include the cheek, neck, eyelids, lips, tongue, soft palate, parapharyngeal space, and floor of the mouth. The color of the skin or mucous membrane may be normal or appear blue or dark purple when the entire dermis is involved. The boundary is not clearly defined, and the lesion is soft, compressible and occasionally phlebolith can be palpated. When a child is crying or the patient lowering his/her head below the heart level, the lesion is significantly congested with venous blood and enlarged.

Venous malformations can be noted at birth when located superficially. Deep intramuscular VMs are not seen at all. Nothing may even be suspected if there is no enlargement of the muscle(s) involved. Usually, there are no symptoms when the lesion is small. If the lesion continues to expand for various reasons, it can result in deformities of the face, lips, or tongue and functional disorders. In cases of trauma, secondary infection, abrupt hemorrhage of the lesions, or changes in hormonal levels can lead to pain, swelling, and even bleeding [13]. Venous malformations in parapharyngeal space, tongue, and soft palate may be accompanied with swallowing, speech, and airway problems.

Venous malformations can also occur within muscles (such as the temporal muscle, masseter muscle and tongue muscle), which are

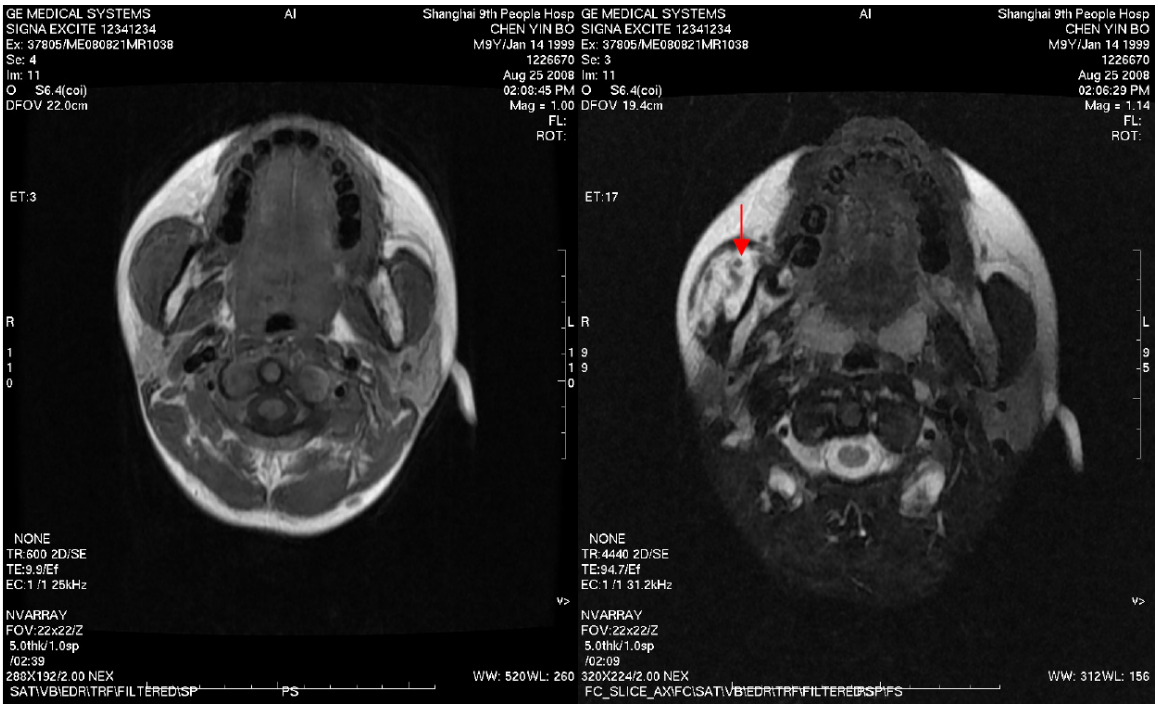

Figure 1. Venous malformation with a phlebolith located in the right masseter muscle area in a 9-year-old boy. The lesion was irregular and not well defined. A. Axial T1-WI demonstrated the intermediate intensity of the mass. MR T-1 imaging sequences are worthless for VM imaging, diagnosis, and evaluation after treatment for follow-up; B. Axial T2-fs (the fast short tau inversion recovery sequence) demonstrated a soft-tissue mass with a hyperintense signal and foci of low signal corresponding with phlebolith (arrow). Bright signal in the VM surrounded by lower signal muscle makes the lesion stand out and be very obvious. Immediately anterior to the masseter is the subcut fat that has equal signal intensity to the VM in the muscle. Therefore, VMs can be totally missed if they reside in the subcutaneous fat without T-2 weighted imaging without fat suppression. The right masseter is larger than the left one due to VM.

known as intramuscular venous malformations. Some lesions in the pterygopalatine fossa and infratemporal fossa are difficult to detect when in the early stages of development. When the head is lower than heart level, the lesions recruit blood, resulting in bulges and a visible mass.

Diagnosis

Venous malformations occurring in superficial areas are usually easy to diagnose by clinical examination. However, for those lesions that are deep in the face and neck, it is sometimes difficult to make a correct diagnosis through clinical examination alone. Imaging studies using B ultrasound (US), CT, MRI are the best diagnostic scans [14].

CT scans are a much inferior imaging modality for VMs. MRI using STIR and T2 weighted with fat suppression with no contrast is always completely diagnostic in defining the VM and its anatomical extent. Also, it is the only method to study the patient to determine the efficacy of treatment. STIR sequences are also diagnostic and have an important role in diagnosis and follow-up after treatment. Aspiration after direct needle puncture of the mass revealing venous blood is usually diagnostic.

Phleboliths are often found in venous malformations of the face and neck by clinical and X-ray examinations. The mandible may be involved. X-ray examinations may reveal jaw bone lesions as a soap bubble-like or honeycomb-shaped low-density image.

Magnetic resonance imaging (MRI) is the optimal method for confirming the size of the venous malformation and thereby assists in making the treatment plan. Venous malformations on MRI T1-weighted images appear as an entity mass of intermediate signal intensity, and T2-weighted images display high signal intensity and homogeneous mass. Phleboliths

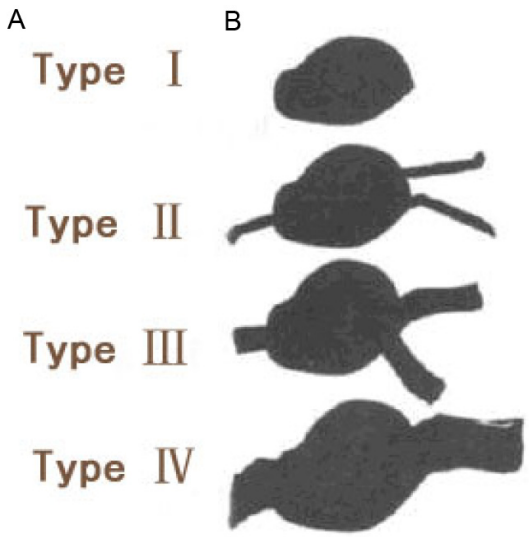

Figure 2. Imaging classification of venous malformations according to the draining vein.

are commonly seen in scans. The calculi are opacified on CT and display high-density scattered calcification, which appears as low-signal or void on T1-weighted and T2-weighted MRI images (**Figure 1**).

In T2-weighted images, venous malformations can appear as "venous lakes". MRI sectional images can avoid signal overlap and thereby demonstrate the relationship between the lesion and the deep structure. MRI is therefore superior to CT in demonstrating the relationship between the extent of the lesion and normal tissue. Consequently, MRI guides the performance of sclerotherapy [15, 16]. Large head and neck venous malformations reveal a tendency for deep penetration and expansion along the fascia. MRI and particularly T2-weighted images can demonstrate the relation between the lesion and surrounding structures. CT can effectively reveal phleboliths in venous malformations but without enhancement in the lesion itself; therefore, it is difficult to determine the relationship between the lesion and surrounding tissue.

In recent years, the application and development of 64-slice spiral CT angiography (CTA) combined with virtual endoscopy (VE) has provided a non-invasive vascular screening for patients, which has certain advantages in the diagnosis of venous malformations. It can help to visualize the extent of the lesion, blood drainage and relationships with nearby vessels, muscles, bone structures, etc. (from multiple angles and in three dimensions). This not only reduces patient suffering during examination but also allows clinicians to make more accurate and rapid diagnoses.

According to the imaging features of the draining veins, venous malformation is divided into four types [15] (**Figure 2**): Type I, isolated malformation without venous drainage; Type II, malformation with drainage into normal veins; Type III, malformation with drainage into dilated veins; and Type IV, dysplastic venous ectasia. This proposed classification scheme is helpful for selection of sclerosing agents. For type I and type II lesions, mild sclerosants such as pingyangmycin should be considered first; for type III and type IV lesions, strong and aggressive sclerosants such as ethanol is more suitable due to the fast vein drainage.

Treatment of venous malformations

The signs and symptoms will depend on the sites involved and the extent of the venous malformation. The treatment goal should be to cure the venous malformation; however, cure may only be obtained in case of small, focal lesions [17]. Multifocal or extensive venous malformations are rarely cured but the symptom and signs can be controlled. Patients with incurable venous malformations should be told that repeated treatments throughout life are necessary. With proper treatment the venous malformations can be shrinking but will persist and reexpand when there is trauma and/or hormonal influence (puberty, pregnancy, birth control pills, etc).

Pain is a common problem with venous malformations especially in the upper face and temple areas. Controlling the pain should be a goal but it may be difficult to accomplish. Bleeding and airway compromise is common with extensive head and neck mucosal lesions and the goal is to decrease the chances of bleeding and to improve the airway.

Various methods have been used to treat venous malformations, including conservative treatment such as head position elevation, sclerotherapy, laser therapy, and surgery. Due to the variety of treatment methods and different manifestations in individual patient, it is

suggested that multidisciplinary approach should be performed in patients with complicated lesions. Treatment should be delivered by a team of experts in vascular malformations.

Conservative treatment is primarily suitable for small, isolated, asymptomatic venous malformations. Head elevation is very important in alleviating the hydrostatic pressure that leads to expansion of the deformity and can reduce airway obstruction, swelling and pain. Other beneficial conservative treatments include local compression, anti-infection therapy, pain control, etc.

Sclerotherapy

Sclerotherapy has become the current mainstream treatment for venous malformation [18, 19]. It can be used alone or combined with surgery and/or laser therapy. For large lesions, multiple treatments are necessary. Recurrence is seen, this may possibly happen with some sclerosing agents that incompletely treat the VMs being injected. The sclerosants commonly used are 5% sodium morrhuate, pingyangmycin (PYM), anhydrous ethanol and lauromacrogol. They work by destroying the endothelial cells of blood vessels, accelerating protein coagulation in the blood of the lesions, promoting platelet adhesion to the vascular wall during thrombosis formation and causing vascular occlusion through thrombotic mechanisms. After treatment with sclerosing agents recurrence is common. The possible reasons include insufficient doses and the presence of residual lesions. In addition, after injection, the thrombus formed is absorbed or dissolved, which leads to lumen recanalization and eventually, recurrence [20].

Sodium morrhuate: 5% sodium morrhuate was historically the sclerosing agent used most commonly in the treatment of venous malformations.

Because sodium morrhuate is irritating, can induce severe reactions or even tissue necrosis, it is seldom used nowadays.

Pingyangmycin (PYM): PYM is an anticancer drug extracted from gram-positive *Streptococcus*, which has a chemical structure similar to that of bleomycin A_5. The major histological changes observed after intralesional injection of PYM include injured vascular endothelial cells, various degrees of vascular wall thickening and luminal occlusion [20], while thrombosis formed within the lumen and inflammatory response outside the lumen are not as obvious as after injection of sodium morrhuate. Therefore, the side effects (e.g., local swelling and pain after treatment) are mild. This treatment is suitable for treating type I, II and mucosal venous malformations.

Injection procedures: PYM injection at a concentration of 2 mg/ml is prepared by diluting 8 mg PYM powder with normal saline, adding 2% lidocaine and dexamethasone and then mixing uniformly. The dosage for each injection should not exceed 8 mg. For large lesions, PYM injection can be repeated at an interval of 2 to 3 weeks [21].

For superficial lesions, a 25 gauze needle is inserted into the normal tissue adjacent to the lesion and enters the lesion horizontally. The drug is injected into the lesion until the lesion turns pale and swells. The injection should not begin from the surface of the lesions to avoid bleeding or drug effusion, which might reduce the treatment effects. For deep venous malformation, direct puncture should be performed first to confirm that blood can be withdrawn and the needle is in the lesions rather in normal tissues using ultrasonography guidance or fluoroscope. For lesions localized in the eyelids and lips and superficial lesions, each injection dosage should not exceed 4 mg at a concentration $\leq$ 1 mg/mL to avoid local tissue necrosis. After injection, effusion of solution should be avoided by applying pressure to the injection sites with sterile cottons for 2 to 3 min. For large or multiple lesions, injection should be conducted in multiple sessions. Generally, the periphery lesion is injected first, followed by injection of solution into the central part of the lesion, to prevent further expansion of the lesion during treatment.

For venous malformations with a diameter less than 1.5 cm, one injection is usually sufficient; but for larger lesions or multiple lesions, 3 or more injections are needed to achieve acceptable outcomes. The treatment effect can be observed 7-30 days after injection.

Absolute ethanol: Absolute ethanol is a strong sclerosant with a long history of clinical application [22], and it is used to treat venous malfor-

mations due to its ability to destroy vascular endothelial cells, which induces hemoglobin denaturation, intravascular thrombosis and fibrosis, thus leading to occlusion of the draining veins and formation of embolisms within the lesions. Because of its lower cost, quick metabolism, good results and low recurrence rate when used in the sclerotherapy of venous malformations, absolute ethanol has been used widely to treat any types of venous malformations under fluoroscope, especially extensive or complicated lesions. Preoperative percutaneous venogram can be used to confirm the diagnosis, determine the size and compartments of the lesion, number of draining veins and return velocity, thereby providing important information for estimating the sclerosant dosage and prevention of complications. Absolute ethanol can be used alone or in combination with other sclerosants, such as PYM or lauromacrogol, to reduce the dose and improve the efficacy [23].

Absolute ethanol is strongly irritating to tissue; therefore, a minor mistake may lead to serious complications. The injection should be implemented under digital substraction angiography (DSA) direct visualization [24]. After proper sterilization, a butterfly needle is used percutaneously and the needle is advanced into the VM via US or fluoroscopic guidance. Blindly burying needles of varying lengths to the hub in the vicinity of the VM is never tried. Accurate placement of the needle into the VM is advocated. The needle's depth and direction should be adjusted until automatic outflow of blood through the connecting tube of the butterfly needle. Contrast medium is then injected until the draining veins are demonstrated. The dosage of absolute ethanol is approximately 1/2 to 2/3 of the amount of the contrast used. For large venous malformations involving multiple anatomical sites, injection can be done simultaneously in different areas. The cumulative total dose of serial injections of ethanol in a single procedure should not exceed 1 ml ethanol/ kg body weight of the patient [25]. After quick injection of ethanol into the compartments, the patient's blood pressure and heart rate should be monitored. If the venous return velocity is fast, compression should be applied to the draining veins during injection to prevent a great quantity of ethanol flowing into the pulmonary circulation in a short time and minimize complications, such as pulmonary artery spasm, pulmonary hypertension and pulmonary embolism. Preoperative and postoperative injection of dexamethasone can ease tissue edema. For patients undergoing injection at a dose more than 0.5 ml/kg, the blood pressure and the amount of urine after operation should be observed. A balanced salt solution and sodium bicarbonate should be given intravenously to alkalinize urine to prevent acute renal failure caused by hemoglobinuria. Antibiotics are given when necessary.

Particular attention should be paid during ethanol injection listed as follows [26]. (1) It is of outmost importance to inject ethanol into the compartments rather than into the surrounding tissues or major blood vessels under DSA guidance; (2) When performing ethanol injection in the upper 1/3 of the face, the possibility of accidental embolization of the cavernous sinus should always be considered. Facial venous connections may connect to the angular vein. This in turn drains superiorly to connections to the superior ophthalmic vein (SOV). This then drains into the cavernous sinus. Merely manually compressing the angular vein against the maxilla to prevent upward flow to the eye, or compressing the vein connections around the glabella of the upper nasal area will simply and effectively prevent flow into the cavernous sinus. While doing either compression maneuver they should repeat the VM direct puncture angiographs to prove that the maneuver is successful in preventing flow into the cavernous sinus; (3) Caution should be taken when the injection is near the parotid gland to avoid damaging the facial nerve and subsequent facial paralysis. It is in the medial third of the parotid gland that the 7th nerve traverses. Not all areas are dangerous. Further, large doses in this area are to be avoided. Small doses with repeated procedures, rather than large injections with few procedures greatly reduce the chances of facial palsy. An alternative is using ethanol to occlude the draining veins, followed by administration of PYM to eliminate the compartments; (4) For type III or IV venous malformations, the draining veins should be compressed to prolong the staying time of the sclerosis agent within the compartments and prevent pulmonary complications; (5) For patients with venous malformations in the tongue, floor of the mouth, parapharyngeal area and soft palate, the airway may be compromised postoperatively. If necessary, a prophylactic tracheotomy may be

performed, or prolonged endotracheal intubation considered.

Polidocanol: also known as lauromacrogol or aethoxysclerol (chemical name: lauryl alcohol polyoxyethylene), is a more moderate form of ethanol [27] most commonly used in European countries. It is an effective sclerosing agent that consists of 95% hydroxypolyethoxydodecane and 5% ethyl alcohol and is known to have a low risk of complications. Injection of lauromacrogol can damage vascular endothelium cells, promote thrombosis, occlude blood vessels and induce aseptic inflammation and subsequent fibrosis, resulting in obliteration of the vascular channels and elimination of the compartments. It can be used alone to treat smaller superficial type I or II lesions, or in combination with ethanol to treat large type III or IV venous malformations.

After proper disinfection, a 25 gauze needle is inserted into the lesion from the adjacent normal tissue until blood can be withdrawn. For larger lesions, multiple injections will ensure uniform distribution of the drug within the lesion. The injection should continue until the lesion surface turns pale and swells. After injection, compression is applied to the insertion sites with sterile cottons for 2-3 min to prevent effusion of the drug. The total dosage is determined by the location and size of the lesions and the patient's age, with no more than 3 ml at each injection (less than 1 ml for children). For patients with lesions that fail to complete response, injection is repeated at an interval of 1 to 2 weeks but not more than 5 consecutive sessions.

Lauromacrogol injection is a simple, time-saving, safe and effective way for venous malformations. Lauromacrogol has definite anesthetic effect; the injection is painless and well-tolerated by the patients. Furthermore, allergic reactions are rare, and hemolysis seldom occurs, which largely reduces the possibility of pigmentation. Therefore, it is suitable for treating head and neck venous malformations. The main disadvantage is necrosis and ulceration may occur if the solution leaks out into the skin or mucosa.

Lauromacrogol can also be mixed with a certain amount of air (the most commonly used liquid-to-air ratio is 1:4) as sclerosing foam [28], which reduces the dosage and concentration of the sclerosant. Additionally, the selectivity of action on endothelium of the foam reduces the risk of tissue damage while the sclerosant runs off the vessels. However, the rate of relapse after treatment with sclerosing foam is higher compared with liquid sclerosant [29], and the complication may occur with use of "foam" VM embolization causing strokes by flowing foam bubbles going through patent ductus arteriosus (PDA) and the like.

The concentration of lauromacrogol used to produce foam sclerosing agent is 0.25% to 4%, depending on the size of the malformation and hemodynamic characteristics of the lesions. A higher concentration (3% to 4%) is used for intramuscular venous malformations, and lower concentrations (0.25% to 0.5%) for the peripheral portions of huge venous malformations. 1% to 2% lauromacrogol is chosen for residual lesions after treatment [29].

Sclerotherapy can also be combined with other treatment modalities. For large venous malformations or lesions with a fast drainage, selective ligation of the connecting veins, suture around the lesions and mixing the agents with tissue glue [30] may help to increase local drug concentration and prolong the sclerosing effect. Preoperative sclerotherapy is often used to create thrombosis of the lesions and reduce blood loss during operation. Sclerotherapy is used for treating residual lesions after laser therapy or surgical excision.

Other drugs used as sclerosing agents in the treatment of venous malformations include sodium tetradecyl sulfate, ethanolamine, gliadin, diatrizoate acid, quinoline, poppy oil, hypertonic glucose, tetracycline or doxycycline, Ethibloc, urea and OK-432 [30]. These drugs are presently used less frequently or used as a combination [31].

Sclerotherapy of venous malformations is a relatively safe and reliable treatment modality, and its efficacy is related to the type and dose of sclerosing agent, as well as type and extent of the lesion.

Complications of sclerotherapy include allergic reactions, cutaneous or mucosal necrosis, and sensory nerve or motor nerve injuries such as facial paralysis. These complications occur more often after injection of absolute ethanol and sodium morrhuate but seldom PYM injec-

tion [32, 33]. Thus, PYM is suitable and usually selected for the treatment of superficial lesions. In addition, patients may develop more severe swelling after sodium morrhuate or absolute ethanol injection. Airway obstruction caused by postoperative swelling should be considered when treating lesions on the base of the tongue, floor of mouth, soft palate, pharynx and larynx, and the patients are usually hospitalized for treatment and observation for 2 to 3 days.

Absolute ethanol injection can be extremely painful; therefore, it is recommended that the injection be administered under general anesthesia or sedation to alleviate patients' suffering. By adding radiopacity agent into the sclerosing agent, the puncture site can be monitored through the fluorescent screen to determine whether the sclerosing agent was injected into the lesions and how it was distributed within the lesions, which is helpful to minimize complications. Because ethanol sclerotherapy can give rise to serious complications, although rarely encountered in head and neck cases, such as pulmonary artery spasm or pulmonary embolism, it should only be performed by physicians with significant clinical experience and excellent skills and in specialize medical centers or hospitals with adequate equipment and technical capability. In addition, ethanol injection of less than 0.14 ml/kg body weight every ten minutes obviates the occurrence of cardio-pulmonary collapse [25].

Fever often occurs after PYM injection; this can be alleviated with symptomatic treatment. The main side effects of PYM injection are interstitial pneumonitis and pulmonary fibrosis related to endothelial cell damage in pulmonary capillaries. These complications are closely related to the total amount of drug used. No reports on the use of PYM to treat venous malformations leading to pulmonary fibrosis have been published that we are aware of. Very rare patients may experience acute allergic shock during injection. Therefore, care must be taken to prevent this fatal complication, and first aid treatment must be available on the spot, including intravenous infusion, and anti-shock treatment, anti-allergy treatment [21].

Laser treatment

Neodymium (Nd): YAG laser is most commonly used, but potassium titanyl phosphate (KTP) laser can also be used [34]. The Nd: YAG laser is a 1064 nm wavelength laser that utilizes invisible light from the infrared portion of the spectrum, which can be transmitted through the thin optic fiber to targeted sites from the mouth to the larynx. The absorption of laser energy by hemoglobin generates a high localized temperature, which results in coagulation and immediate shrinkage of the lesions. It should be pointed that lasers can only penetrate 1-3 mm. VMs often are much larger and thicker than 3 mm and can never be affected by laser treatment. Thus, the superiority of ethanol and liquid sclerosants to flow throughout VMs is distinct and thus be treated. Thermal injuries to nerves and skin scarring due to laser treatments of superficial lesions are to be avoided.

Non-contact mode: Adult patients are anesthetized with 2% lidocaine block anesthesia combined with infiltration anesthesia; while infants are usually given 4-8 mg/kg of ketamine hydrochloride through intramuscular injection. The assistants use suction to keep the airway patency and pump out the smoke generated by laser beam. Surgeons, nurses and assistants should wear safety glasses, and the patients' eyes should be covered by protective eyewear before treatment. The laser power is usually adjusted to 10-30 W [35]. During treatment, the laser probe is set 0.5 to 1.0 cm away from the lesions with a spot size of 1.5 to 3.0 mm. Duration time is around 0.5 sec. The lesions are lasered perpendicularly. Venous malformations mostly involve the mucosa and skin; they are easily compressed, and appear as dark-blue. After laser irradiation, the lesions shrink immediately and appear as gray-white or gray-black, and then may disappear after repeated laser treatments. The power setting is determined by the patient tolerance and location. For mucosal lesions and those located in the pharynx and larynx, lower power energy is applied first. Then, according to the severity of shrinkage after coagulation, the laser power is slowly increased to achieve a complete photocoagulation. The treatment pattern should be in a polka-dot pattern to avoid mucosa or skin necrosis. Because of melanin in skin, necrosis and scarring can occur when treated.

Interstitial Nd: YAG laser: This method is suitable for small and medium venous malformations with extensive communicating branches in deep layers [36]. Before treatment, the opti-

cal probe should be positioned under ultrasound guidance. During surgery, incisions of the skin and subcutaneous tissue are made to expose the lesion. Generally, this type of lesion has a thin fibrous capsule and is compressible. Signal changes of the color Doppler ultrasound (CCDS) reflect the extent of lesion revascularization, intensity of the reaction and coagulation effect. After inserting a 16 gauze puncture needle and adjusting the laser power to approximately 10 W, the laser probe is inserted into the needle to the inclined plane of the tip; the probe and needle are then inserted into the lesion. If the lesion contains large amount of fibrous tissues like spongy structure with many small sinuses, the lesions will shrink instantly, and the laser power can be increased slowly. Subsequently, the laser probe is inserted radially in different directions, and laser treatment is performed simultaneously. The duration of the laser exposure is determined by the lesion size. During treatment, the laser cable should be pulled out frequently to determine how carbonized the laser probe is. Benzalkonium bromide, not alcohol, is used to wipe and wash the fiber surface because the fiber and probe are flammable. As the optical fiber is very brittle, it must be moved gently and should not be distorted during the procedure.

Severe contraction of the lesions results from the laser thermal effect, which also leads to 1st degree tissue injury. The oral mucosa appears gray-white, and local swelling occurs within 24 hours. Normal tissue surrounding the lesion will exhibit hyperemia and blisters with liquid exudation in the lasered area. After rupture of the blisters, ulceration forms, or the wound will be covered with a pseudomembrane. Tissue swelling reaches its peak 2 to 3 d after treatment; 1.5% hydrogen peroxide or chlorhexidine can be used and oral hygiene must be maintained by rinsing the mouth frequently.

After interstitial laser treatment, exudation and swelling are more severe; fever and mild pain may occur, accompanied by an increased amount of leukocytes, which can be treated by appropriate use of antibiotics. Corticosteroids can be given intravenously for lesions located in the oropharynx to decrease airway problems. After Nd: YAG treatment, the wound usually heals 5 to 15 d later than the surgical incision. The incrustation and necrotic tissue should be removed promptly, and secondary bleeding from the wound should be monitored closely.

Nd: YAG laser therapy is relatively simple and easy to be performed with little or no bleeding. An optical fiber is used for Nd: YAG laser therapy and allows the light beam to accurately focus and then coagulate the lesion with minimal damage to normal tissue, which is more applicable to venous malformations in the oral mucosa, oropharynx and base of the tongue, especially in infants and children. Patients with small lesions exhibit a minor response after treatment and only require minimal postoperative care. For patients with extensive venous malformations in the oropharynx or supraglottis, treatment can be performed over the course of several sessions.

Surgical treatment

In most cases, surgical treatment is considered primarily as an adjuvant to improve the function and appearance [17]. Localized or limited venous malformations can be removed surgically [37]. For large lesions, partial excision can be considered after sclerotherapy to improve cosmetics. Some large venous malformations may be resectable if the MRI reveals a definitive border with only low draining veins. Before operation, MRI should be performed to define the extent of the lesion and venous drainage. Blood transfusion should be prepared because blood loss can be significant. In cases with extensive tissue defects caused by surgical removal, a skin graft or flap should be transplanted for reconstruction. For patients with large tongue lesions, surgery can first be done to reduce the size of the tongue, followed by a shortened course of sclerotherapy. After treatment of large venous malformation with absolute ethanol sclerotherapy, patients may have fibro-fatty tissue remnants, which may necessitate surgical correction. During surgery, laser treatment can also be used to remove the residual lesions. Preoperative sclerotherapy leads to occlusion of malformed veins and reduces blood loss during surgery; however, fibrosis and scarring can give rise to more difficulties in identifying important nerve and blood vessels, which should be fully considered and estimated by the surgeons before operation.

In addition to the above-mentioned methods, some centers have also successfully used copper needle embolism [11] treatment for venous malformations.

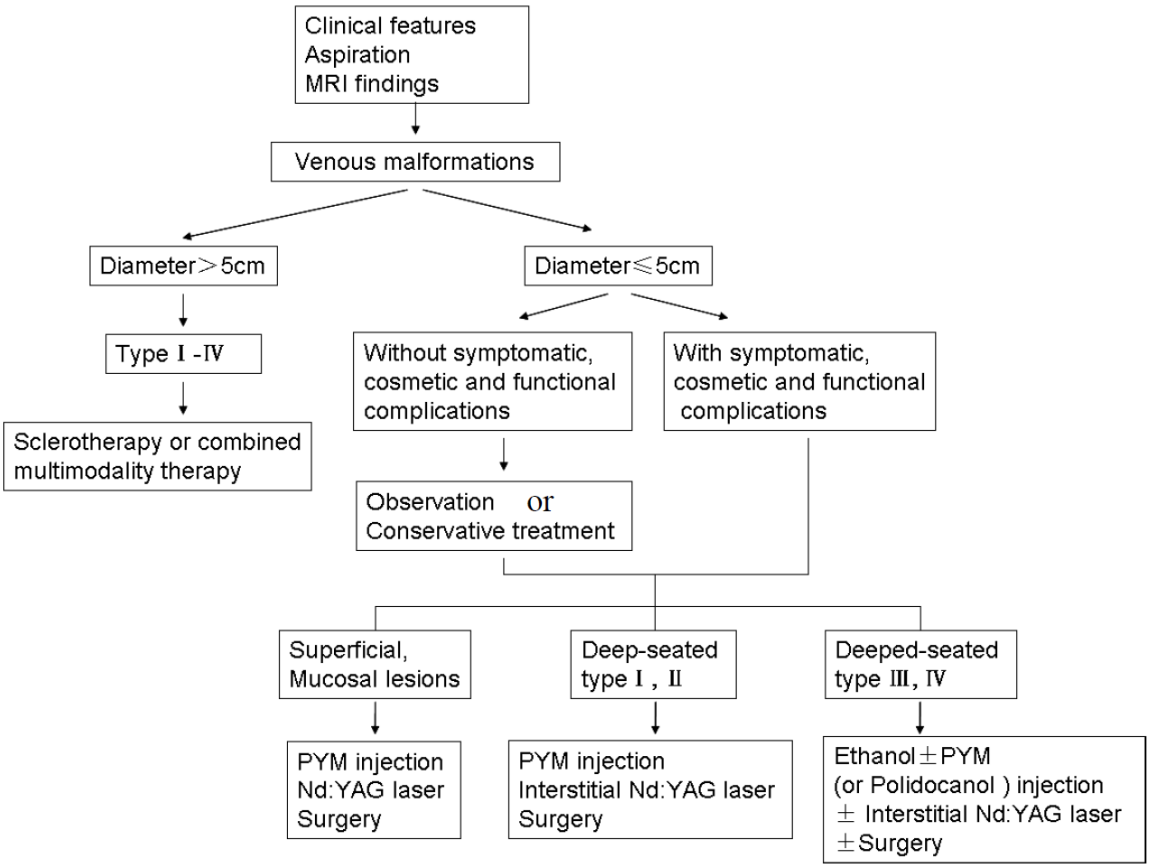

Figure 3. Algorithm for decision-making related to the treatment of head and neck venous malformations.

Large venous malformations, usually involving multiple tissue layers (including the skin, mucosa and muscle) and important structures, such as vital nerves, eyes and larynx, are still therapeutic challenge for the physicians. Currently, comprehensive treatment with a variety of methods is advocated. During the treatment process, attention should be paid to maintaining the upper airway patency [38].

Selection of treatment modality

This will depend somewhat on the experience of the team and equipment available.

Mucosal and superficial venous malformations

Treatment options include intralesional injection of PYM, or Bleomycin, Nd: YAG laser therapy and surgical excision. The first choice is PYM intralesional injection, which is easy to perform. With proper application, tissue necrosis is generally not an issue, with very few complications and good recovery in terms of appearance and function.

Deep type I and II venous malformations

Intralesional injection of PYM, Nd: YAG laser therapy, and surgery represent favorable treatment options. The first choice is intralesional injection of PYM.

Deep type III and IV venous malformations

Absolute ethanol sclerotherapy is recommended alone or with laser therapy, surgery or PYM injection. Surgery is mandatory for extensive lesions.

Deep and superficial mixed-venous malformation

One of the treatments described above is selected based on lesion depth and location. Sclerotherapy can be considered as the main treatment to be used in combination with laser therapy, surgery or other treatments.

Treatment of venous malformations in the mouth and oropharynx

For patients with venous malformations in the floor of the mouth, base of the tongue, oropharynx, and larynx, appropriate methods including sclerotherapy, Nd: YAG laser treatment, surgery and combined treatments should be selected based on the extent of the lesion. Treatment should be conducted under general anesthesia to ensure airway patency. For large tongue lesions, sclerotherapy can be first conducted to reduce intraoperative blood loss associated with surgical debulking of macroglossia. Laser and further sclerotherapy are subsequently applied. Another alternative involves sclerotherapy first; glossoplasty followed. For cases undergoing a tracheotomy, the tracheal tube is preserved after treatment. After 24 to 48 h of observation, extubation or a preventive tracheotomy is conducted to prevent upper airway obstruction that can be caused by postoperative swelling.

The treatment flowchart of head and neck venous malformations is shown in **Figure 3**.

Evaluation of treatment effectiveness

There is still no gold standard for evaluating the effectiveness of the treatment of venous malformations. Therefore, establishing comprehensive criteria for the evaluation of life quality appears to be extremely urgent for patients with venous malformations of the head and neck. Achauer et al [39] proposed a 4-grade scale based on improvement of volume, color, and texture of infantile hemangioma (superficial only): scale: 1, poor (0 to 25 percent); 2, fair (26 to 50 percent); 3, good (51 to 75 percent); and 4, excellent (76 to 100 percent). This scale can be modified and used to evaluate the treatment outcome of venous malformation. In addition, treatment efficacy is closely related to the primary site; therefore, the anatomical site should be fully described and considered. Multiple lesions with involvement of several anatomical areas should be illustrated independently. Lesion size and treatment efficacy are closely related. The size of the lesions should be measured precisely. For superficial lesions of the skin and mucosa, size can be represented directly by the two largest diameters. For deep lesions, size can be measured using a B-mode ultrasonography and/or MRI.

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Conflict of interest

None.

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