



ORIGINAL RESEARCH PAPER

Pathology

HEMANGIOMA OF THE ORAL CAVITY- A REVIEW

KEY WORDS:

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ABSTRACT

Benign lesion of the blood vessels or vascular elements is hemangioma. The majority of oral & oropharyngeal hemangiomas seem to be of a developmental nature often present at birth or shortly thereafter. In oral cavity hemangioma can occur at various sites, but they have strong preference for the occurrence in the tongue and floor of the mouth. Occurrence of hemangioma within the jaw bone is rare. The colour of hemangioma may vary from bluish to purple or fiery red. The present article reviews current theory, diagnosis & treatment of oral hemangioma.

INTRODUCTION-

The word “hemangioma” comes from the Greek haema-“blood”; angio, “vessel”,-oma, “tumor”.

The Greek suffix “oma” means cellular proliferation of a tumor & thus the term hemangioma is erroneous when used for malformations.

Hemangioma is benign & usually self involuting tumor of the endothelial cells that line blood vessels, & is characterized by increased number of normal & abnormal vessels filled with blood. Hemangiomas are the most common benign vasoformative tumor of infancy and childhood occurring in 4% of children by the age of 1 and greater frequency in girls. Hemangiomas are benign vascular tumors consisting of a collection of immature cells, including progenitor stem cells & disorganized blood vessels. They usually are manifested within the 1st month of life, exhibit a rapid proliferative phase during 1st year of life followed by slower but steady involution phase to near complete resolution.¹

The majority of hemangioma involve the head & neck. However, they are rare in the oral cavity but may occur on tongue, lips, buccal mucosa, gingiva, palatal mucosa, salivary gland, alveolar ridge & jaw bones. Clinically hemangioma appears as soft mass, smooth or lobulated, & sessile or pedunculated & may vary in size from a few mms to several cms. They are usually deep red & may blanch on the pressure & if large in size, might interfere with mastication.²

CLASSIFICATION

Hemangioma is a vascular tumor and it is NOT a vascular malformation.³

Hemangioma	Vascular malformation
appears in the early neonatal period	presents at birth
incidence of 2-3% in newborns and 10% by the end of first year of life [6]	incidence of 1.2% [7]
sex ratio: female/male is 3-5:1	sex ratio: equal
has a growth cycle with two phases [1]: - rapid growth induced by proliferation - slow regression induced by involution of hemangioma by the age of 5-10 (in great majority of cases) of three phases [4]. - rapid proliferating phase (0-1 year) - involuting phase (1-5 years) - involuted phase (5-10 years)	continues to grow at a rate proportional with the growth rate of the body, with no involution
“self-limited” tumor spontaneous regression can occur with or without sequelae: telangiectases, scars, atrophy or epidermal atrophy, hypopigmentation and/or redundant skin [3]	“self-perpetuating” embryologic tissue with malformed vessels never involutes
is a vascular tumor: endothelial cells proliferation	vascular abnormalities due to defects of embryogenesis (vasculogenesis/angiogenesis) with two subtypes: - extratruncal-the defect appears during earlier stage of embryogenesis (before formation of vascular trunk) - truncal - embryogenic defect is produced later [2]
the absence of recurrence phenomenon	recurrence can occur in extratruncal forms due to persistence of mesenchymal cells (angioblasts) that can proliferate triggered by trauma, pregnancy, surgical interventions
Duplex sonography and/or MRI in case of deep hemangioma mimicking vascular malformation	Duplex sonography and MRI attest the malformations

Table II. Differences between hemangiomas and vascular malformations [1].

- In 1966 this classification was modified by International Society for the Study of Vascular Anomalies (ISSVA)
- Presently ISSVA differentiates vascular tumors from vascular malformation⁴.

Table 1: Modified International Society for the Study of Vascular Anomalies (ISSVA) classification

Vascular tumors	Vascular malformation
Infantile hemangiomas	Slow (low) flow
Focal	Capillary malformations (CM)
Segmental	Port-wine stain
Indeterminate	Telangiectasia
Congenital hemangiomas	Angiokeratoma
Rapidly involuting congenital	Venous Malformations (VM)
Hemangioma (RICH)	Common sporadic VM
Non involuting congenital	Bean syndrome
Hemangioma (NICH)	Familial cutaneous and mucosal VM (VMCM)
Tufted angioma	Glomusvenous Malformation (GVM) or Glomangioma
Pyogenic granuloma	Maffucci syndrome
Dermatologic acquired vascular tumors	Lymphatic malformation (LM)
Kaposiform hemangioendothelioma	Lymphedema
Spindle cell hemangioendothelioma	Lymphangioma circumscriptum
NOS	Lymphangioma cavernosum
	Lymphangioma cysticum
	Fast (high) flow
	Arterial malformation (AM)
	Arteriovenous fistula (AVF)
	Arteriovenous malformation (AVM)
	Complex combined vascular malformations

DIAGNOSIS-

A thorough clinical history & physical examination leads to the accurate of hemangiomas. The diagnosis of OCH can be clinical; however, two physical examination maneuvers provide important information and reinforce the clinical diagnosis: The Diascopy and the HLMAC.

DIASCOPYY-

The diascopy is to compress a glass plate or blade over the lesion with finger pressure . The pressure exerted by the glass on the hemangioma compresses the blood vessels that it forms, causing the extravasation of the blood to the periphery vessels. The result of this maneuver causes a temporarily color change of the lesion, changing an important clinical feature of the lesion which is its usual reddish or purplish color, and after the maneuver, it resembles the color of the adjacent normal mucosa. After removing the pressure, the blood returns to the inside of this hemangioma and regains its original appearance.

HLMAC (Head Lowering Maneuver With Abdominal Compression)-

The HLMAC is based on the principle of blood redistribution to the other body parts, including the head. Thus, when the head is lowered, there is an accumulation of blood in the head. This is due to the absence of valves in the venous system of the head and neck, which is naturally aided by gravity in an upright posture, but during the execution of this mane maneuver, the head is near to the horizontal plane. This combination of factors promotes more blood supply to the OCH located in the head, which its clinical manifestation may present an increase in the volume and/or intensity of the red or purple color, or both of the OCH.

Routine imaging is not necessary but can be useful in deeper lesions & diagnostic challenges. MRI can be used to provide further information regarding the extent of involvement in local

tissue for deep disease.¹³ Ultrasound is useful to confirm diagnosis & is often sufficient as a singular imaging modality. Hemangioma will demonstrate a well defined mass with high vessel density, without abnormality of the surrounding fat, with uniform pulsatile, fast flow vascularity on Doppler with arterial & venous waveforms.⁵

MANAGEMENT-

Management of hemangioma depends on a variety of factors including the age of the patient and the size and extent of the lesions, as well as their clinical characteristics, and most true hemangioma requires no intervention. Some congenital lesions may undergo spontaneous regression at an early age. If superficial lesions are not an esthetic problem and are not subject to masticatory trauma, they may be left untreated.

However, 10–20% requires treatment because of the size, exact location, stages of growth or regeneration, functional compromise, and behavior. The potential for severe hemorrhage caused by the vascular nature of the lesion must be considered. The range of treatment includes surgery, flash lamp pulsed laser, intralesional injection of fibrosing agent, interferon alpha-2b, and electrocoagulation while cryosurgery, compression and radiation were used in the past.⁶ A combination of more than one treatment modality is often performed in larger or resistant lesions.

In last few year, beta-blockers, in particular propranolol, have dramatically altered the treatment paradigm. Propranolol is the mainstay of treatment for large or symptomatic IH, including subglottic and parotid disease. Typical dosing is 1–3 mg/kg/day divided into two to three doses. This is generally well-tolerated but may be associated with sleep disturbance, diarrhea, bronchial hyper-reactivity, and hypoglycemia. It is contraindicated in patients with bradycardia, heart block, hypotension, and asthma.

Early treatment during the proliferative & post proliferative phase is thought to be associated with improved outcomes. Over 90% of IHs respond to propranolol with reduction in size and color. Deeper components respond better than superficial ones.⁷

Corticosteroid therapy is an alternative option for patients who have contraindications or inadequate response to propranolol. Typical dosing is prednisone at 2–3 mg/kg daily and monitoring for side effects including adrenal axis suppression, cushingoid facies, irritability, stomach irritation, reduced growth rate, the head circumference, and weight gain is recommended. For localized IH, intralesional steroid injection can be considered and can be used in conjunction with the favorable responses obtained with propranolol.^{3,8}

Interferon alpha is indicated for the treatment of hemangiomas when they do not respond to corticotherapy. The mechanism of action of IFN is not understood fully. Interferon does inhibit endothelial cell migration and proliferation & thus, acts directly by inhibiting the angiogenic stimulus itself; by inhibiting the effect of specific growth factors on the proliferation of endothelial cells, smooth muscle cells, or fibroblasts; by decreasing the production of collagen; or by enhancing the production or release of endothelial cell prostacyclin. It acts as an inhibitor of endothelial proliferation, although its side effects are superimposed on its therapeutic effects, such as the neurological disorder (spastic diplegia), fever, malaise, diarrhea, neutropenia, anemia, and elevated transaminase.⁹

The use of sclerosing agents in the treatment of vascular abnormalities has been practiced for a long time. It is considered conservative, effective, safe, and inexpensive, being them or suitable for treatment of minor lesions. Sclerosing agent causes marked tissue irritation &/or thrombosis with subsequent local inflammation & tissue necrosis. The inflammation & tissue necrosis result in fibrosis with tissue contracture.¹⁰

The sclerosing agents most widely used are ethanolamine oleate, sodium morrhuate, polidocanol, sodium tetradecyl sulfate, absolute ethanol, sodium psyllate, quinidine urethane, hypertonic saline, and ethibloc. These substances may exhibit local and systemic complication potentially serious, such as anaphylactic shock and allergic reactions after administration of sodium morrhuate and

tetradecyl sulfate.¹¹

Sodium tetradecyl sulfate (sotradecol) is the sclerosing agent which has been used for years in the treatment of varicose vein, hemorrhoids and hemangioma. Intravenous injection causes intima inflammation and thrombus formation. This usually occludes the injected vein and subsequent formation of fibrous tissue results in partial or complete vein obliteration that may or may not be permanent. Minkow used a technique of intralesional injection of 0.1–0.5 ml of 3% STS in intraoral hemangioma at the interval of 2–4 weeks. Satisfactory results were reported in all patients with minimum side effects and disappearance of the lesions without scarring. The number of injections varied according to the size of lesion. The interval between the injections was usually 2–4 weeks. It allows the induration and inflammatory reaction to subside.¹¹

Absolute ethanol causes strong endothelial damage. Response rate is high, less expensive & easy to obtain but the injection is very painful & has a high complication rate. Penetrative effect on deep vascular layer is also high. The absolute ethanol offers high risk of complications and can cause tissue damage in case of leakage of the solution.

Polidocanol leads to over hydration of endothelial cells and is almost painless but it may induce irreversible cardiac arrest. The polidocanol produces a reduced sclerosing effect on endothelium in comparison with ethanolamine oleate, with less effective results.

Ethanolamine oleate primarily causes irritation in the endothelial intimal layer of the vein, producing an inflammatory response culminating in fibrosis of the vessel wall and possibly vein occlusion. Ethanolamine can diffuse through the venous wall, producing an extravascular inflammatory reaction and thus may induce venous sclerosis. There are reports of generalized urticaria that occurred after sclerotherapy for varicose veins with ethanolamine oleate in doses larger than 12ml per session, but this reaction can be controlled with antihistamines. Adverse reactions associated with the administration of ethanolamine oleate are related to the amount of the applied dose; it is being considered the amount of (0.4 ml/kg) the maximum safe dosage per patient. Surgical excision is reserved for ulcerative, bleeding, and significantly protruding hemangiomas. This can be performed alone or in combination with other treatments, especially when response to other treatments is limited or ineffective. Surgical treatment is indicated in cases that compromise the esthetic or interfere with the function of the region involved. Also, it is closely related to the possibility of complications such as bleeding, scarring, organ, and tissue dysfunction. Surgical treatment has a high rate of recurrence and exacerbation of lesion in the postoperative period.

Laser therapy is widely used as a therapeutic modality of hemangioma. Laser therapy provides the excision of the lesion with low degree of bleeding. The reduction of bleeding is caused by obliteration of blood vessels caused by the treatment; however, this surgical procedure can cause tissue necrosis, tissue atrophy, hyperpigmentation (transient or permanent), and scars, in addition to its high cost and high recurrence rate.

Cryotherapy has been indicated as a treatment for minor injuries but is rarely used as a therapeutic protocol for hemangiomas. It is a procedure that can be quite painful and can result in tissue atrophy, scarring, and hyperpigmentation. Cryotherapy also has a high cost because it requires specific equipment.

Embolization and radiotherapy are normally indicated for cases of intraosseous hemangiomas and/or large lesions, in which there is presence of blood vessels with large diameter. These procedures are associated with very important side effects.

DISCUSSION

Hemangiomas mean vascular-origin tumors that grow with cellular proliferation and they are the most common tumors of childhood. They are 7% of all benign tumors. Hemangiomas are seen one in ten children around age one. Generally, these lesions are not seen in birth but seen during the first months of life. 70-

90% of them are seen in the first 1-4 weeks. 80% of these lesions are single, while 20% of them are multiple lesions. Hemangiomas demonstrate a proliferation stage, then stabilization stage and finally involution stage. 50% of cavernous hemangiomas undergo involution around age 5, 70% around age 7, and the remainder around age 10-12. The earlier the involution stage starts, the sooner it is completed. They usually occur sporadically, but they have also been reported in autosomal dominant familial transmission. Hemangiomas can be diagnosed easily by inspection. However, contrast-enhanced MRI or angiography may be required to understand the depth of mass and to be informed about vascularization of large hemangiomas. Surgery, corticosteroids, sclerosing agents, radiation therapy, diathermy, electrocauterization, cryosurgery, laser, embolization, radiofrequency, and interferon are used in treatment of hemangiomas. Surgical procedures should be performed by physicians specialized in this field for the benefit of minimizing the risk of complications.

Surgical intervention should not be aggressive and surrounding vital formations should be protected. Total excision is often difficult, recurrences are seen. Nowadays multi-stage surgery is widely recommended. For the large hemangiomas making pressure on the airway, tracheotomy opening should be performed and steroids should be used.

As one of the treatment options, corticotherapy should be applied only in selected cases due to systemic side effects. Radiation therapy is another treatment option. Radiotherapy regresses hemangiomas, but it causes severe atrophy on tissues of the treated area especially on skin. It can also cause cancer in later years. For this reason, it is not preferred. Sclerosing agents can be applied into hemangiomas. Cryotherapy can be applied. However, the percentage of success is low. For superficial lesions it can give good results. RF was found to be a very safe and effective form of treatment since incisions are not required especially in shallow oral cavity hemangiomas, bleeding is minimal, it does not require suturing and pain is minimized.

CONCLUSION

Hemangioma is of benign origin & behavior, but hemangioma in the oral cavity is of clinical importance. It often mimics other lesion clinically & requires appropriate clinical diagnosis & proper management.

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