

# Vascular Malformations Of The Oral Cavity In Children And Young Adolescents – Insights Into Their Pathogenesis.

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## Abstract

Vascular anomalies are congenital errors in vasculogenesis. They comprise of vascular tumors (hemangiomas) and vascular malformations (venous malformations, arteriovenous malformations, lymphatic malformations). Lymphatic malformations or lymphangiomas are uncommon congenital malformations of the lymphatic vessels filled with a clear protein rich fluid containing few lymph rich cells. Large lymphangioma extending into tissue spaces of the neck is referred to as cystic hygroma. Advancements in the knowledge of pathogenesis of such vascular malformations is continuously changing their treatment protocols. Early recognition is of utmost importance for initiation of proper treatment, and avoiding serious complications. Lymphangiomas are further subclassified microscopically into capillary, cavernous, cystic and lymphangioendothelioma depending upon its histopathological features. Haemangiolymphangioma is a variant of lymphangioma showing vascular component. Herewith, we present a case of vascular malformation diagnosed as haemangiolymphangioma, histopathologically in a 5 year old girl. On the contrary, it is argued that instead of being a congenital malformation, lymphangioma is a true neoplasm resulting from transformed lymphatic endothelial cells and/ or stromal cells.

## INTRODUCTION

Vascular anomalies are congenital aberrancies in vascular development causing identifiable birthmarks of the skin and mucosa and a variable degree of underlying soft tissue abnormalities.<sup>1</sup> Under the global heading of vascular anomalies, these lesions predominantly occur within the head and neck and affect approximately 1 in 22 children.<sup>2</sup>

Previously termed ‘angiomas’ or vascular ‘birthmarks’, vascular anomalies are divided into two main categories: vascular tumours and vascular malformations. Infantile hemangiomas comprise the majority of vascular anomalies and are considered the predominant vascular tumour type composed of rapidly proliferating endothelial cells.<sup>2</sup> Blood vessel architecture is incomplete and surrounded by hyperplastic cells in hemangiomas and other vascular tumours. In contrast, vascular malformation do not contain hyperplastic cells but consist of progressively enlarging aberrant and ectatic vessels composed of a particular vascular architecture such as veins, lymphatic vessels, venules, capillaries, arteries or mixed vessel type. The latter comprises of lymphangiomas or lymphatic malformations which are congenital collections of ectatic lymph vessels that form endothelial lined cystic spaces.<sup>3</sup>

Lymphangiomas are benign, relatively rare tumors characterized by proliferation of lymphatic vessels. It represents about 6% of the total number of benign tumours of the soft tissue in patients aged less than 20 years.<sup>4</sup> The gender distribution of lymphangioma is equally divided between males and females with about 50% of the lesions being noted at birth and 90% developing by 2 years of age.<sup>5</sup>

Oral lesions may occur at various sites but they form most frequently on the anterior two-thirds of tongue. It may increase in size, producing macroglossia which may lead to difficulties in mastication, deglutition, and speech; and displacement of the teeth, with a resulting malocclusion. It may interfere with normal breathing, particularly during sleep, produce sleep apnea, and in certain instances, produce a life-threatening upper airway compromise.<sup>6</sup> It can also present in the palate, buccal mucosa, gingiva and lip.<sup>5</sup>

The tumor is superficial in location and demonstrates a white pebbly surface that resembles a cluster of translucent vesicles. The deeper lesion appears as a nodule or masses without significant change in surface texture or color.

We hereby present a case of lymphangioma with presence of a vascular component diagnosed as

hemangiolymphangioma.

## **CASE REPORT**

A 5 year old female patient reported to the department of Oral & Maxillofacial Pathology, I.T.S CDSR with a complaint of soft tissue growth with respect to left side of tongue. Patient had given a history of trauma and tongue bite three months back. Intra orally, the swelling was present on the left side of the dorsum of the tongue which was enlarging slowly in size without pain or tenderness. The swelling was initially small; peanut sized which increased to the present size of 2 x 1cm with a pebbly surface that resembled clusters of translucent vesicles. The lesion was pale pink in color, oval in shape with well defined margins. (Figure 1)

On physical examination, the child was in good general condition, without signs of any obstruction of superior respiratory tract. Routine haemogram of the patient was normal.

### **Figure 1**

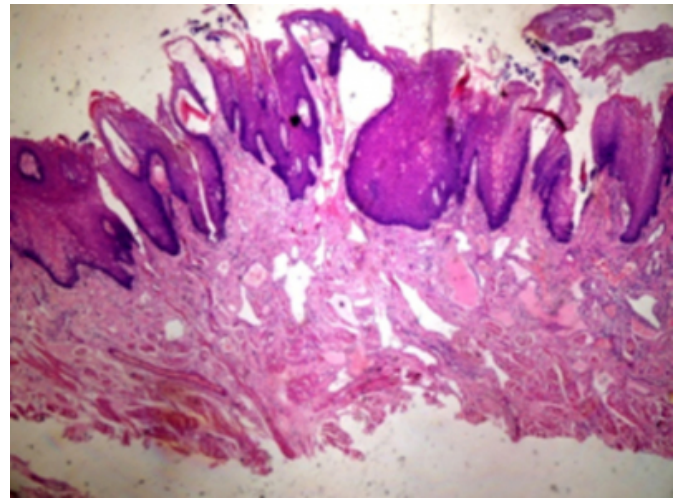
Figure 1: Intra oral photograph showing nodular swelling resembling cluster of vesicles on the left side of dorsum of tongue.



An incisional biopsy was performed and the tissue was histopathologically diagnosed as lymphangioma, since large lymphatic vessels lined by flattened endothelial cells pushing into the overlying epithelium were seen. (Figure 2)

### **Figure 2**

Figure 2: Photomicrograph of incisional biopsy showing large lymphatic vessels. (H&E, 10X)



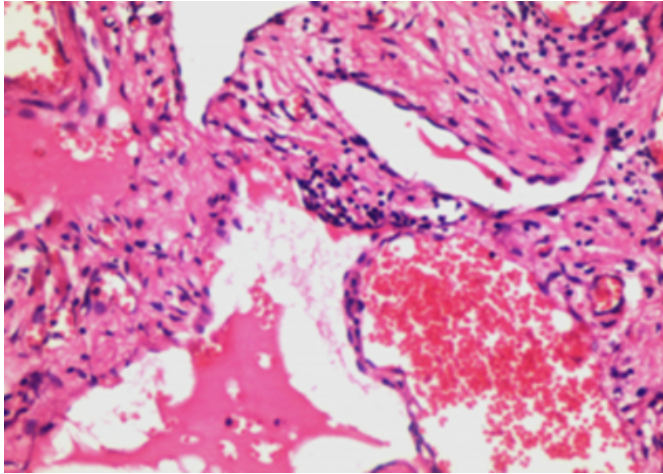
Patient was recalled after 4 days and a total excision of the lesion was performed under LA. The excised tissue was submitted to the department of Oral Pathology for histopathological examination.

On gross macroscopic appearance, the excised tissue was oval shaped measuring 1.5 x 1 cm in size, creamish brown in colour with a pebbly surface.

Microscopic examination of the excised lesion showed numerous large dilated lymphatic channels of irregular shape, lined by flattened endothelial cells, of which some of the vessels were filled with lymph. The channels were seen abutting and elevating the overlying epithelium. Numerous large to medium sized channels with thin endothelial lining, engorged with RBC's were also present in the deeper area of the connective tissue. (Figure 3) A confirmatory diagnosis of hemangiolymphangioma was given.

**Figure 3**

Figure 3: Photomicrograph showing large to medium sized lymphatic channels lined by thin endothelial cells containing lymph. Adjacent to it are channels engorged with abundant RBCs within the lumen. (H&E, 40X).



**DISCUSSION**

The origin of lesion is considered to be congenital abnormality of lymphatic system rather than true neoplasm. Portion of the jugular lymphatic sac are thought to sequestrate from the primary sacs during fetal development with failure to establish communications with other lymphatic system.<sup>7,8</sup>

The pathophysiology of vascular malformations, hemangioma and lymphangioma are interrelated. The classic sequence of events in embryology and development of vasculogenesis falls into three stages: the undifferentiated capillary network stage, the retiform developmental stage and the final developmental stage.<sup>9</sup> Two major theories have been proposed to explain the origin of lymphangiomas.<sup>10</sup> The first theory is that the lymphatic system develops from five primitive sacs arising from venous system. Concerning the head and neck, endothelial outpouchings from the jugular sacs spread centrifugally to form the lymphatic systems. Another theory proposes that the lymphatic system develops from mesenchymal clefts in the venous plexus reticulum and spread centripetally towards the jugular sacs. Finally, lymphangioma develop from congenital obstruction or sequestration of the primitive lymphatic enlargement.<sup>11</sup>

Several studies have been published regarding possible lymphangiogenic growth factor involvement in the etiology of lymphatic malformations. These factors include VEGF-C, vascular endothelial growth factor receptor 3 (VEGFR-3), and transcription factor Prox-1. VEGF-C and VEGFR-3

have been shown to be upregulated in lymphatic malformed tissue, and both are involved in lymphatic tissue proliferation.<sup>12</sup>

The misunderstanding on the nosologic distinction between oral haemangiomas and vascular malformations leads to diagnostic mistakes. Hemangiomas are differentiated from vascular malformations by their clinical appearance, histopathological features, and biologic features. The natural history of hemangiomas involves rapid proliferations for the first several months of life with subsequent spontaneous regression. Vascular malformations are often recognized at birth and grow proportionately with the child, with many becoming more prominent at puberty. Histologically, hemangiomas in the proliferating phase show endothelial hyperplasia and large number of mast cells. In contrast vascular malformations showed normal number of mast cells, and consist of mature, often combined, capillary, arterial, venous, and lymphatic elements.<sup>1</sup>

Lymphatic malformations/lymphangiomas are classified microscopically into four categories: Lymphangioma simplex (Lymphangioma circumscriptum), composed of small, thin walled lymphatics. Cavernous lymphangioma, comprised of dilated lymphatic vessels with surrounding adventitia. Cystic lymphangioma (cystic hygroma), consisting of huge, macroscopic lymphatic spaces with surrounding fibrovascular tissues and smooth muscle. In benign lymphangioendothelioma (acquired progressive lymphangioma), lymphatic channel dissect through dense collagen bundles.<sup>13</sup>

Occasionally channels may be filled with blood, a mixed hemangiolymphangioma, an uncommon developmental anomaly with a propensity to invade underlying tissues and to recur locally distinguishing it from the simple lymphangioma or hemangioma.<sup>14</sup> Although, histologically it is a benign disorder, local invasion into the muscle, bone, and underlying tissue can lead to severe deformity. In the present case numerous large sized lymphatic channels along with medium to large sized channels entrapped with RBCs, lined by endothelium were seen and hence it was subcategorized as hemangiolymphangioma.

We reviewed the archival cases of Lymphatic malformations in our department, the demographical information, location and histopathological features of which are shown in Table 1. The only significant difference in the three archival cases and the present case was in the histopathological features of



lymphangioma and hemangiolymphangioma.

**Figure 4**

Table 1. The demographic information, location and histopathological features are as follows:-

Case	Age/sex	Chief complaint	Histopathology	Diagnosis
1.	12/F	Recurrent pain and swelling in lower right cheek region since one and a half year.	Multiple intertwining lymph vessels in a loose fibrovascular stroma. Lymph vessels were seen extending in the epithelium and deep into the muscle tissue.	Lymphangioma
2.	10/M	Fluctuant swelling on the right side of floor of mouth extending upto the sub mandibular triangle region on the same side since one year.	Well defined connective tissue capsule with large dilated lymphatic vessels lined by single layer of endothelial cells.	Cavernous lymphangioma
3.	8/M	Nodular growth present on the tongue since six months.	Multiple dilated lymph vessels of different sizes in loose connective tissue papillae. Lymphatic spaces were lined by flattened endothelial cells.	Lymphangioma

Therapeutically, many approaches have been proposed. Spontaneous regression of the lesion is rarely encountered. Aspiration of the cystic content is a temporary measure to relieve airway obstruction.. Nd-Yag laser surgery has become widely preferred because of its advantages of less bleeding and edema. Surgical excision is the usual treatment of lymphangioma.<sup>15</sup> Because the rate of recurrence may be as high as 21%, long-term follow-up is essential.

## CONCLUSION

Vascular anomalies represent a wide variety of vessel abnormalities. Sometimes, the vascular lesions consist of both blood vessels and lymphatic vessels. Thus it can be

concluded that haemangiolymphangioma are lymphangioma only with a vascular component. Their correct classification and diagnosis is imperative to accurately ascertain prognosis and direct treatment.

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