

## Cellular hemangioma: A rare case report

Rupali R Vaidya<sup>1</sup>, Avinash L Kashid<sup>2\*</sup>

<sup>1</sup>Junior Resident, <sup>2</sup>Assistant Professor, Dept. of Dentistry, Swami Ramanand Teerth Rural Government Medical College, Ambajogai, Maharashtra, India

\*Corresponding Author: Avinash L Kashid

Email: [avinash.kashid@gmail.com](mailto:avinash.kashid@gmail.com)

### Abstract

Cellular hemangioma is rare immature form of capillary hemangioma.

**Keywords:** Hemangioma, Buccal mucosa.

### Introduction

Hemangioma is the benign tumour of infancy. It is characterized by a rapid growth phase with involution.<sup>1</sup> The malformations have a normal endothelial cell growth cycle that affects the veins, the capillaries, or the lymphatics, and they do not involute.<sup>2</sup> Hemangiomas are more common in females than males (2:1).<sup>1</sup>

The most common locations are head and neck accounting for 60% of cases and it is relatively rare in the oral cavity but may occur on tongue, lips, buccal mucosa, gingiva, palatal mucosa, salivary glands, alveolar ridge, and jaw bones.<sup>3</sup> They are classified mainly cavernous and capillary types.<sup>4</sup>

Cellular hemangioma is an immature form of capillary hemangioma whose increased cellularity and brisk mitotic activity may provide false impression of angiosarcoma.<sup>5</sup> Cellular hemangioma of infancy, is a benign tumor which characterized by the formation of vascular tubes of endothelial cells. These tumors are differentiated from one another by the predominant cell type found on histopathologic examination. Cellular hemangioma is a rare tumor of oral cavity.<sup>6</sup>

### Case Report

A female patient aged 17 years, reported to dental department with a chief complaint of a extraoral swelling on left cheek region since birth (Fig. 1,2) and intraoral growth on left buccal mucosa since 5-7 months (Fig. 3), she also complaints of difficulty on eating and brushing teeth. The growth was asymptomatic; the patient's medical history was non-contributory.

On examination 54mm x 8mm x 54mm sized solitary, diffuse extra-oral swelling with smooth surface was seen on left cheek region. The overlying skin was pigmented. On palpation, the swelling was non-tender, soft in consistency and blanched on pressure. A left-sided hemihypertrophy of face was observed. Her mouth was deviated toward the right side of her face. No other similar lesions were clinically visible in the head and neck region. Moreover, no lymph nodes were palpable. Intraoral examination showed a mass on left buccal mucosa, which was soft in consistency. Periodontal examination revealed mild and localised

gingivitis with plaque accumulation and presence of supragingival calculus. There was no evidence of dental caries. Based on clinical signs and symptoms, a provisional diagnosis of vascular lesion was given and differential diagnosis of hemangioma, lymphangioma, pyogenic granuloma, A-V malformation was given.

The patient was advised routine blood investigations which came out to be within normal limits. After which patient was advised Ultrasonography which was suggestive of lymphangioma, further patient was advised an incisional biopsy under local anesthesia for more improvised diagnosis and the histopathological diagnosis of cellular hemangioma was given.



**Fig. 1:** Extraoral view



**Fig. 2:** Extra oral view

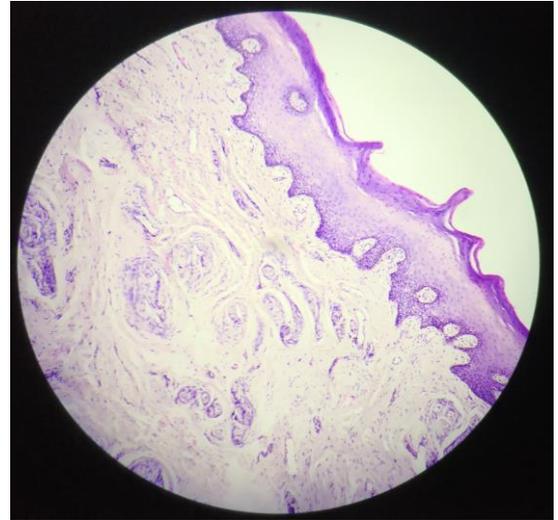


**Fig. 3:** Intraoral view

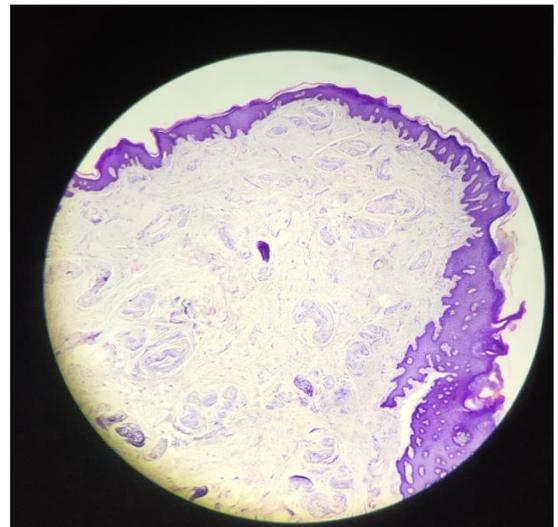
### Histopathology Report

The H and E stained sections showed, hyperkeratotic, hyperplastic lining of stratified squamous epithelium. Underneath shows fibrocollagenous stroma characterized by plump endothelial cells that lined numerous small sized vascular spaces with small inconspicuous lumens. The capillary size vessels imperfectly canalized giving the impression of solid nests of endothelial cells. The intervening collagenous stroma shows individually scattered oval to spindle cells intermixed with sparse inflammatory cells. (Fig. 4 & 5).

The histopathological diagnosis of cellular hemangioma was given.



**Fig. 4:** Histopathologic section (×10)



**Fig. 5:** Histopathologic section (×10)

### Discussion

Vascular lesions are the most common congenital abnormalities which are divided into two categories: Hemangioma and Vascular malformations.<sup>6</sup> The differentiation between hemangioma & vascular malformations is made on the basis of clinical appearance, histopathology and biological behaviour.<sup>8</sup> Hemangiomas are usually self involuting tumour, growing lesions that eventually disappears whereas malformations are enlarged or abnormal vessels present at birth and essentially permanent.<sup>13</sup> There are many ways to classify hemangioma. According to Enzinger and Weiss, hemangiomas are classified into Capillary, Cavernous, and misselleneous form like verrucous, veneous and artriovenous hemangiomas.<sup>10</sup>

Among hemangiomas, the most common are cavernous & capillary hemangiomas. Cellular hemangioma is subtype of capillary hemangioma which is characterized by recurrence potential & cellular immaturity.<sup>6</sup>

Hemangiomas are common soft tissue tumours in infancy that often congenital or develop in the neonatal

period and grow rapidly<sup>7</sup>. Seven percent of total benign tumours of infancy and childhood are hemangiomas.<sup>8</sup> Hemangiomas are found on all regions of body but most commonly they occur in head and neck region (60%), followed by Trunk (25%) and then extremities in (15%).<sup>12</sup>

Etiology of hemangiomas is unknown. Although origin of pathogenesis is incompletely understood various theories have been proposed to explain mechanism and pathogenesis of hemangioma. Aberrant and focal proliferation of endothelial cells results in haemangioma. The placental theory of haemangioma origin has been described by North et al., who studied various histology and molecular markers such as GLUT1, Lewis Y Antigen, Merosin, CCR6, CD15, IDO, FC, and gamma Receptor II. Positive staining for GLUT1 is considered highly specific and diagnostic for haemangioma, and it is useful for making differential diagnosis between haemangioma and other vascular lesions clinically related to it. More recently, somatic mutational events in gene involved in angiogenesis are related to haemangioma growth. Growth factors specifically involved in angiogenesis such as VEGF, b-TGF, and IGF are often increased during the proliferation phases of haemangioma growth. Moreover, it has been noted that during the involution phase of haemangioma, there is a decrease in angiogenic molecules (VEGF, PCNA, Type IV collagenase, Lewis V antigen, CD 31), while there is increase in concentration of marker for apoptosis (T4, TUNNEL, INF, Mast cells, and TGF). Thus, role of molecular signalling is now clear in haemangioma development.<sup>3</sup>

Hemangiomas are characterised by endothelial proliferations and its natural course can be divided into following phases.

1. Rapid Proliferation Phase(0-1 year)
2. Involuting Phase 1-5 years)
3. Involuted Phase(5-10 years)<sup>13</sup>

The cellular hemangioma of infancy is a form of capillary hemangioma. It occurs in infancy at the rate of about 1 in every 200 live births. Although primarily infants and children are affected, it is also observed in middle-aged and other individuals, such lesions are called senile hemangiomas.<sup>5</sup> As a rule, the senile form is less cellular than the infantile form and often demonstrates progressive luminal ectasia of the vascular element.<sup>5</sup> The evolution of these lesions is characteristic. Although described as congenital they actually appear within a few weeks after birth and rapidly enlarge over a period of several months, achieving the largest size in about 6-12 months.

The histologic appearance of hemangiomas fluctuates with the stage of the life cycle of the tumor and can be divided into the proliferative phase and the involutive phase. The proliferative hemangiomas show a proliferation of endothelial cells. The basal lamina is thickened and multilaminar underneath the endothelial cells forms syncytial masses with or without lumens. Light micrographic findings demonstrate a large number of vascular plexus consist of capillaries, venules and small veins. The proliferative endothelial cells are active with hypertrophy and a pale staining nucleus. The

nuclei show occasional mitotic figures, and the number of mast cells is much higher than normal tissue. The involuting phase hemangioma demonstrates diminished cellularity with a flattening of the lining endothelial cells. As the endothelium flattens, there is a relative dilation of the vessels supplying the tumor and progressive deposition of perivascular, intralobular, and interlobular fibrous tissue. The basement cell membrane is still multilaminar and the number of mast cells gradually returns to normal. Complete involuted hemangioma has a "sponge-like" structure, with scattered thin-walled blood vessels lined with flat endothelial cells. The basement membranes remain multi-laminar and the number of mast cells returns to normal amounts.<sup>12</sup>

### Treatment

The treatment of hemangiomas is dependent on the various stages of growth.

(1) Small isolated or multiple skin lesions on the face found after birth should be treated as soon as possible in order to prevent its progress into the proliferative phase; (2) Proliferative hemangiomas should be treated step by step, including systematic drug therapy (oral propranolol, oral prednisone, topical use of imiquimod, subcutaneous injection of interferon a-2a or 2b) →laser therapy (argon laser, pulsed dye laser and Nd:YAG laser, semiconductor laser etc.) →sclerotherapy (intratumoral injection of steroids, pinyangmycin, interferon a). For deep or large hemangiomas, a comprehensive approach must be taken into consideration, e.g. drug therapy combined with laser therapy. (3) Close observation is indicated for involutive hemangiomas. Surgical excision should be taken for residual lesions, scar, hypertrophy, or pigmentation. (4) For residual lesions of involuted hemangiomas, surgical trimming or laser treatment is feasible. The treatment of hemangiomas should be considered cautiously and with consultation of the child's parents.<sup>12</sup>

### Wait and see

"Wait and see" is mainly indicated in involuting hemangiomas or small, stable hemangiomas in non-vital sites, without significant impacts on appearance and function. The growth of the lesions should be observed, recorded and photographed in the follow-up period. Treatment should immediately be taken when the following occurs: (1) fast growth of hemangioma; (2) hemorrhage, infection or ulceration complicated with huge hemangioma; (3) functional problems, such as dysfunction of feeding, breathing, swallowing, hearing, vision, excretion or sports etc.; (4) it involves facial vital structures, e.g. eyelids, nose, lips etc.<sup>12</sup>

### Cryotherapy

CO<sub>2</sub> rime and liquid nitrogen used to be applied in treatment of superficial hemangiomas with some effects in 1960s.<sup>12</sup>

### Laser therapy

Laser therapies treat hemangiomas by acting on intravascular oxyhemoglobin, resulting in vascular injury. There are several types of lasers available for management of hemangiomas, including argon laser, pulsed dye laser and Nd:YAG laser, etc. Laser therapy is indictable for treatment

of early, superficial hemangiomas or the superficial portion of the compound hemangiomas because of the limited penetration depth less than 5 mm, it is not suitable for management of deep-seated hemangiomas.<sup>12</sup>

### Drug therapy

Pharmacotherapy is indicated for multiple hemangiomas, rapidly proliferative hemangiomas, and hemangiomas that are affecting vital organs or life threatening. Several drugs have been documented in the literatures including propranolol, corticosteroids, alpha-interferon, anti-cancer drugs (cyclophosphamide, vincristine, pinyangmycin), imiquimod, and etc. Induction of early involution and freedom from the side effects of steroid therapy seem encouraging for using propranolol as a first line treatment modality in the management of troublesome hemangiomas.<sup>12</sup>

### Oral corticosteroid

Oral corticosteroids have been used for more than 30 years. They used to be the first-line treatment for severe, multiple hemangiomas, potentially disfiguring hemangiomas or hemangiomas involving vital structures as well as for patients with congestive heart failure, consumptive coagulopathies, and thrombocytopenia prior to the serendipitous discovery and subsequent wide clinical application of propranolol. The initial oral dose of prednisone is 4 mg/kg per day for 7 days. If the tumors stop growing or become smaller, the same dose continues for 3 weeks. Conversely, the dose is increased to 5 mg/kg per day for 7 days, then is tapered down gradually and ceased after 4 to 8 weeks.<sup>12</sup>

### $\alpha$ -interferon (IFN- $\alpha$ )

Interferon- $\alpha$  is used to treat rapidly growing, life-threatening hemangiomas which have failed to respond to systemic corticosteroids. It is usually used at a dosage of 3 million U/m<sup>2</sup>, given subcutaneously per day for more than 3 months. The response rate is varied between 80% and 90%. Compared with oral corticosteroid, IFN- $\alpha$  can be used for both proliferative and involutive hemangioma. However, due to the potential severe adverse effects, IFN- $\alpha$  administration should only be considered in patients with massive or life-threatening hemangiomas.<sup>12</sup>

### Propranolol

Accidentally found that propranolol can effectively control the proliferation of severe hemangioma and promote its regression, which was also confirmed subsequently by other physicians. Propranolol is a nonselective beta-blocker used in treating cardiac arrhythmias, angina and hypertension. The possible mechanisms for treatment of infantile hemangiomas are unclear. The most important advantages of oral propranolol over glucocorticoids and anti-cancer drugs are efficacy and safety, with fewer side effects and low cost.

- Gill JS, Gill A Bharadwaj, Grover HS. Oral haemangioma. Case report in Medicine. 2012, Article ID 347939, 4 pages, 2012.

Propranolol has replaced corticosteroids as first-line therapy for both proliferative and involutive hemangioma.<sup>12</sup>

The suggested dosage is 2 mg/kg per day, divided into 2 to 3 doses; the mean treatment duration is 6-8 months; and the time to discontinue propranolol is 12 months of age unless complete resolution occurred earlier, and therapy was tapered off over the last month. Combined low-dose oral propranolol 1.5 mg/kg/day as first-line therapy and oral prednisolone 2 mg/kg/day might be useful in avoiding adverse effects of propranolol in young infants.<sup>12</sup>

### Surgical therapy

Surgical excision of hemangiomas is no longer the first choice treatment. But residual deformities after conservative, or laser, therapy can be corrected surgically. The aim of surgery is to remove or re-contour the residual deformity, scar, hypertrophied tissues, hyperpigmentation, or fibrofatty tissues to improve cosmetics and function.<sup>12</sup>

In summary, the treatment of hemangiomas should be individualized. Factors affecting the decision to treat include: size, location, depth, growing stage, and trend of the lesion. A successful regime should be widely adaptable to various types and sizes of hemangiomas. Unfortunately, none of the currently available treatment modalities are refractory to standard therapy. For some patients, single method treatment may achieve perfect effects; while for extensive or multiple hemangiomas, combined treatment is often mandatory. The major principles of management are outlined as follows: (1) preventing or treating life-or function-threatening complications; (2) preventing permanent disfigurement or face defects after hemangioma regression; (3) preventing or adequately treating ulceration to minimize scarring, infection, and pain; (4) minimizing psychosocial stress for patient and family; (5) avoiding over-treatment to lesions which could regress spontaneously with a good prognosis.<sup>12</sup>

### Conclusion

Haemangioma is of benign origin and behaviour, but haemangioma in the oral cavity is of clinical importance. It often mimics other lesion clinically and requires appropriate clinical diagnosis and proper management.<sup>3</sup>

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None.

### Conflict of interest

None.

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