DOI: 10.7860/JCDR/2016/18497.8080

Case Report

Dentistry Section

Angiosarcoma of Anterior Mandibular Gingiva Showing Recurrence – A Case Report with Immunohistochemistry

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ABSTRACT

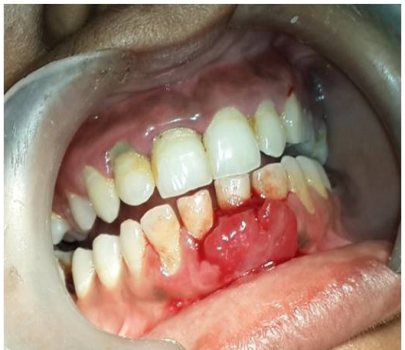
Angiosarcomas of oral cavity and salivary gland represent 1% of all cases reported in the literature and are therefore considered as extremely rare. To the best of our knowledge very few cases of angiosarcomas involving mandibular gingiva have been reported previously. Here, we report a case of angiosarcoma occurring in the gingiva with review of literature on clinical features. A 30-year-old female patient presented with a complaint of a small growing mass in relation to lower front teeth. Intraoral examination revealed a soft sessile growth arising from the labial gingiva in relation to 31 and 41 on the labial aspect extending distally to 32. The lesion was locally excised. Histolopathological analysis showed that the tumour was composed of spindle shaped to polygonal cells with hyperchromatic nuclei, conspicuous nucleoli and intracytoplasmic vacuoles, mitotic figure were also scattered. Immunohistochemical staining revealed that the tumour cells was positive for factor VIII-related antigen, CD31 and CD34. An excisional biopsy showed a diagnosis of angiosarcoma. After two months patient reported back with the same chief complaint. This present case is a 17th case report of angiosarcoma arising in anterior mandiblular gingiva.

Keywords: CD31, CD34, Factor VIII-related antigen, Gingiva, Malignant vascular tumour, Mandible

CASE REPORT

A 30-year-old female patient presented with a complaint of a small growing mass in lower front teeth in Local Private Dental Clinic, Raichur, Karnataka, India. The growth started two months ago, as a small sessile painless growth that progressively increased to attain the size of 3×3cm at the time of presentation. On provocation, the growth showed profuse bleeding. The past medical history was non-contributory and assessment of the head and neck region revealed no cervical or submandibular lymph node enlargement.

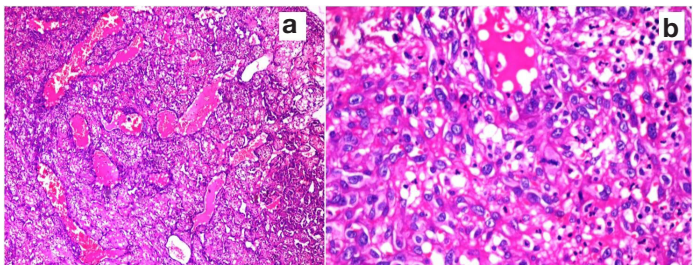
Intraoral examination revealed full complement of teeth. However, there was a soft sessile growth arising from the labial gingiva in relation to 31 and 41 on the labial aspect extending distal to 32 [Table/Fig-1]. Palpatory findings revealed swelling measuring 3×3cm which was soft to firm in consistency. Also, mobility was seen in relation to 31 and 41. Intraoral periapical radiograph in relation to 31 and 41 revealed loss of alveolar crestal bone interproximally [Table/Fig-2]. With the above said findings, a provisional diagnosis of pyogenic granuloma on the labial gingiva in relation to 31 and 41 was established. Peripheral giant cell granuloma and peripheral fibroma were considered in the differential diagnosis.



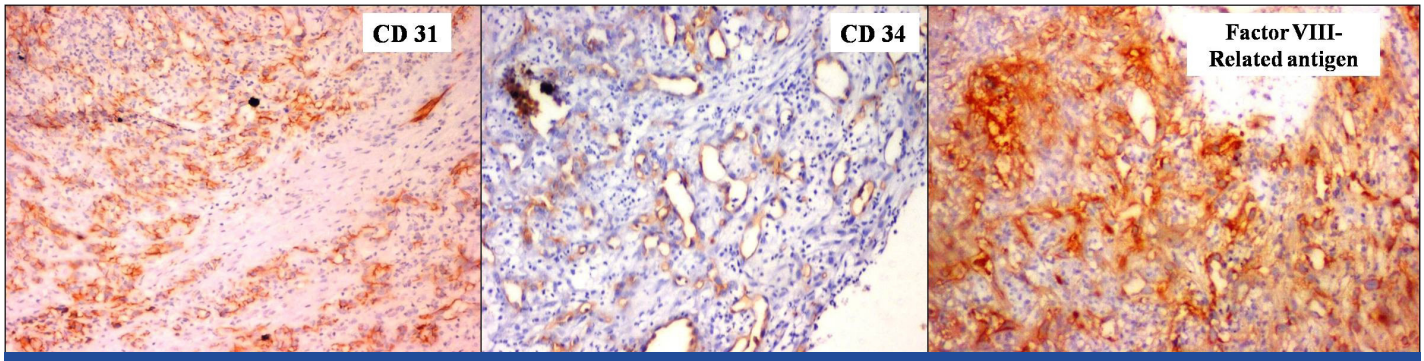
[Table/Fig-1]: Clinical photograph showing a soft sessile painless growth arising from the labial gingiva in relation to 31 and 41. **[Table/Fig-2]:** Intraoral periapical radiograph in relation to 31, 32, 41 and 42 revealed loss of alveolar crestal bone interproximally.

A local surgical excision was carried out under local anaesthesia and excisional biopsy was sent to Department of Oral Pathology, Navodaya Dental College, Raichur, Karnataka, India, for histopathological analysis. Serial sections revealed different microscopic aspects which confirmed that the lesion was pleomorphic. We observed large areas with distinctive vascular lumens, sometimes anastomosed. The tumour consisted of spindle to polygonal cells with hyperchromatic nuclei and conspicuous nucleoli with intracytoplasmic vacuoles and mitotic figure were also scattered [Table/Fig-3a,b]. Immunohistochemical staining revealed that the tumour cells were positive for CD1, CD34 and Factor VIII-related antigen [Table/Fig-4a-c]. A final histopathological diagnosis of angiosarcoma was given.

After two months, patient reported back with the same chief complaint. The growth was a soft exophytic nodular mass, with well-defined limits and a maximum diameter of 8 mm [Table/Fig-5]. The tumour was soft, white to pink in colour, with easy bleeding. A standard uptake value of 5.5 was observed during a PET scan examination (full body scan) and the report showed no metastasis to other areas. CT scan showed small soft tissue density lesion involving lower anterior teeth [Table/Fig-6]. Based on clinical, radiographic and histopathological findings, a recurrence of angiosarcoma was given. The operation was performed with



[Table/Fig-3a,b]: a) A photomicrograph showing large areas of distinctive vascular lumens, sometimes anastomosed (H & E, 10x). b) The tumour consisted of spindle to polygonal shaped cells with hyperchromatic nuclei and conspicuous nucleoli with intracytoplasmic vacuoles and mitotic figures are also seen (H & E, 20x).



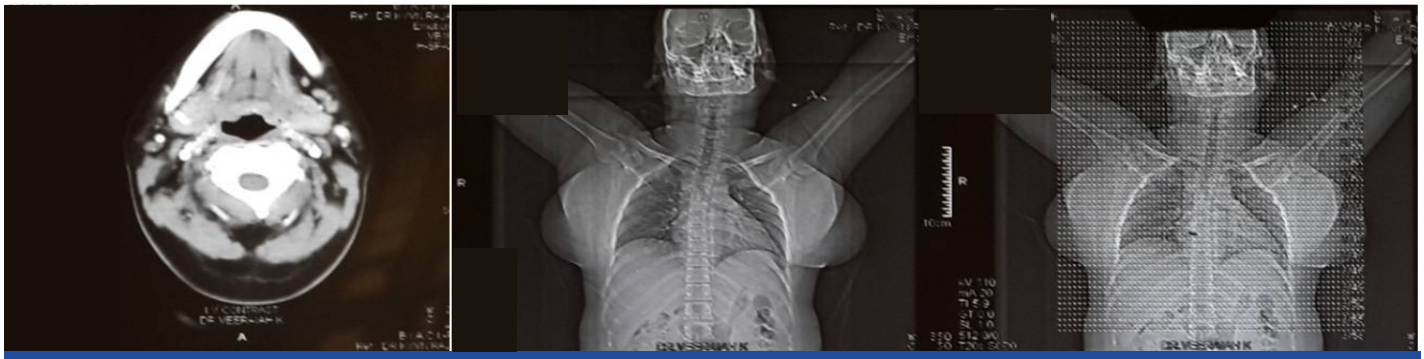
[Table/Fig-4a-c]: Immunohistochemical staining revealed that the tumour cells were positive for CD31, CD34 and Factor VIII-related antigen (10x).

[Table/Fig-5]: Clinical photograph of recurrence seen as a soft exophytic sessile mass, with well-defined limits and a maximum diameter of 8 mm with easy bleeding.

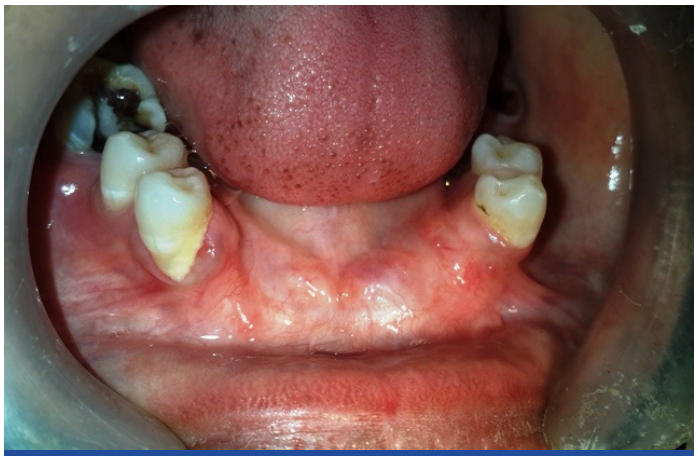
DISCUSSION

Angiosarcoma is a malignant mesenchymal tumour with a differentiation into vascular endothelium. Angiosarcomas constitute less than 1% of all malignant mesenchymal lesions. Although angiosarcoma can occur at any location, the most common sites are soft tegument areas and in the superficial soft tissues [1].

The angiosarcomas involving oral cavity and salivary glands correspond to 1% of all angiosarcomas reported in the literature and hence considered as particularly rare. This tumour can occur at any age, especially in elderly age group and affects males predominantly. Most of the time patients report at advanced stages with signs and symptoms of pain, tiredness, weight loss, bone pain, abnormal bleeding, intraoral lesion, anemia, enlarged lymph nodes, chest pain, pathologic fractures and difficulty in breathing [2].



[Table/Fig-6]: CT scan showing small soft tissue density lesion involving lower anterior teeth and PET examination (Full body scan) showed no metastasis to other areas.



[Table/Fig-7]: Follow-up photograph after two years showing uneventful postoperative course with no recurrence.

about a 20-mm surgical margin that was negative for tumour invasion along with extraction of 31, 32, 33 and 41, 42, 43. The postoperative course was uneventful. So far, after a two-year follow-up, no recurrence and metastatic lesions were found [Table/Fig-7].

Intraorally, angiosarcomas most of time present as well or ill-defined, polypoid nodular bluish or violet mass, reddish and soft to firm in consistency. Mucosal ulceration is not rare and is also related with bleeding on palpation and edema. Histopathologically, these tumours imitate the normal endothelial features and their appearance varies greatly, from the well-differentiated forms, similar with haemangiomas, to low differentiated forms- heavy to differentiate from the carcinomas or achromatic melanomas [3].

Angiosarcoma affecting oral cavity especially gingiva is particularly rare; there are only a few case reports and clinical review series in the literature [4]. Therefore, this case reports an epulis-like angiosarcoma of the anterior gingiva of mandible.

Angiosarcomas seen in oral cavity may occur in a range of tissues, for instance oral soft tissue, minor salivary glands and bones. Fanburg-Smith et al., in his review reported 22 cases of primary angiosarcoma seen in oral cavity and salivary glands. Among the cases nine were in the tongue, four in the parotid gland, four in the lip, three in the submandibular gland and one case in the palate [5].

A review of the English-language literature on oral angiosarcoma involving gingiva revealed only 16 cases with detailed histopathological confirmation were found. The clinical features,

Sl. No	Author	Year	Age/ Sex	Location	Primary Symptoms and Signs	Clinical findings	Treatment	Follow-up
1.	Henny [6]	1949	3mo/M	Anterior part of right maxilla	A small lump in anterior part of the right maxilla for one month	Firm, well-circumscribed mass with extension posteriorly to the palate and laterally to the cheek	Initial Incision Later: Electorocaguation	No recurrence after 2 years and 3 month
2.	Blake and Blake [7]	1956	26y/M	First molar area of left mandible	A lesion on the ridge of first molar area in the left mandible no pain for one month	A soft tissue mass of the first molar area in the left mandible lobular in appearance, round in shape, red in colour	Initial: Incision Later: "Removal	No recurrence after 2 years and 4 mo
3.	Quinn et al., [8]	1970	65 y/M	Maxillary and mandiblar gingiva	Multiple lesions in the oral cavity for 1 month	Multiple pedunculated superficially ulcerated large hemorrhagic friable lesion in the gingiva, painless	Excision, Radiotherapy	Died after 1 mo and 3 Weeks (unknown)
4.	Albright et al., [9]	1970	34 y/M	Anterior part of right mandible	A gingival mass in the right mandible for three month	An elevated hyperemic lobulated tumour on the lingual gingiva between the mandiblar right canine and premolar teeth	Initial: excision Later: wide removal	No recurrence after 6 months
5.	Piscioli et al., [10]	1986	86 y/F	Gingiva of the left mandibular molar area	A gingival mass for one week	A soft hemorrhagic nodule on the gingival of left mandibular molar area	Excision	Died after 1 month (heart failure)
6.	Carr and Green [11]	1986	66 y/M	Right maxillary gingiva	Bleeding from the gingival for 10 days	A large rubbery friable hemorrhagic mass on a broad base arising from the edentulous alveolus between the upper right canine and second molar teeth	Unknown	Died (metastases)
7.	Kashima et al., [12]	1994	39 y/M	Anterior part of right mandible	Pain for 10 months	Ulcer between the lower right central inclsor and the right lateral incisor	Mandibulectomy	Died after 3 years and 1 mo (metastasis)
8.	Kashima et al., [12]	1994	7 y/F	Left mandible	A painless mass for one month	Mass between the lower left lateral incisor and first molar teeth, dark violet in colour	Initial: Excision Later: Mandibulectmy	Died after 1 year and 1 month (metastasis)
9.	Margiotta et al., [13]	1994	62 y/M	Right mandible	A mass in the right mandible	An ovoid, sessile, ill-defined mass, painless	Excision	Unknown
10.	Muffoz et al., [14]	1998	68 y/M	Right mandible	A mass in the right retromolar trigone for one week	A non-ulcerated sessile slightly painful mass in the right retromolar trigone, brown in colour	Partial mandibulectomy	Died (recurrence)
11.	Abdullah et al., [15]	2000	60 y/F	Mandibluar gingiva	A slight elevated reddish-blue nodule in the oral cavity	A reddish-blue nodular mass on the lower Anterior gingiva	Refusal	Unknown
12.	Florescu M [3]	2005	70 y/M	Alveolar crest of mandible	The tumour was soft, white-gray colour, with disseminated areas of hemorrhage	A nodular mass, with undefined limits and maximum diameter of 4 cm.	Unknown	Unknown
13.	Uchiyama et al., [4]	2009	59 y/M	Left maxilla	Bleeding and swelling of the left maxillary gingiva for few months	A regular mass around the left upper molar area, violet in color	Initial: maxillotomy and chemotherapy. Later: boron neutron therapy and lymphokine activated killer cells treatment	No recurrence after 3 y
14.	Terada T [1]	2011	77y/F	Mandibular gingiva posterior to the front tooth	-	Polypoid reddish mass measuring 1.5 x 1.5 x 1cm in the mandibular gingival posterior to the front tooth	Radical operation	Unknown
15.	Sumida T [17]	2012	55y/F	Anterior region of the mandibular gingival	The epulis was a soft exophytic nodular mass, with well defined limits and a maximum diameter of 10 mm	The tumour was soft, whitepink in colour, with easy bleeding.	The operation was performed with about a 20-mm surgical margin that was negative for tumour invasion.	4-year follow-up, no metastatic lesions have been found
16.	Aditya A [18]	2012	75y/F	Gingival growth in the right maxillary region	Pain was present for the last 15 days; however, she could not indicate the onset and duration of the growth.	A lobulated, sessile mass involving the gingival and alveolar mucosa in the maxillary right molar region. The mass was 3 cm, soft to firm in consistency and slightly tender, with moderate bleeding.	The patient declined any therapy	Unknown
17.	Present case	2016	30 y/F	Mandibular anterior gingiva	The growth started 2 months ago, as a small sessile painless growth progressively increased to attain the size of 3×3 cm	soft sessile growth arising from the labial gingiva in relation to 31 and 41 on the labial aspect extending distal to 32	The operation was performed with about a 20-mm surgical margin that was negative for tumor invasion	2 years follow-up, no recurrence and metastatic lesions were found.

[Table/Fig-8]: A review of clinical features, treatment and prognosis of angiosarcoma involving primarily gingiva that was previously reported, together with the present case.

treatment and prognosis of these previously reported cases, together with the current case, is summarized in [Table/Fig-8] [1,3-18].

Histopathologically, there can be varied appearance, from well differentiated forms with formation of vessels lined of atypical endothelia, to low differentiated forms, composed by proliferation of epithelial-like cells, with polymorphous, hyper chromatic nuclei, with frequent atypical mitosis [1].

Three main patterns of growth are seen in angiosarcomas i.e., a spindle shaped cell pattern, an angiomatous pattern with epithelioid cell features and an undifferentiated or solid pattern. All these patterns can be seen in the same tumour. In the present case of angiosarcoma, there was existence of a vascular tumour despite the relatively benign vascular proliferation. The neoplastic cells seen were round to polygonal in shape, tall, with intense eosinophilic cytoplasm and round to ovoid pleopmorphic hyperchromatic nuclei with numerous mitotic figures [6].

According to the definition, the tumour cell of angiosarcoma has to show some degree of vascular differentiation, either seen at the light microscopic level or by immunohistochemical marker postivity. Earlier, positivity to Factor VIII-related antigen and lectins helped to aid in the diagnosis. Recently, expression of another antigen, CD31, has been used as a specific diagnostic marker for this malignancy [7,8].

Florescu et al., reported that utilization of CD31 and CD34 is sufficient for the identification of the majority of angiosarcomas, including the low differentiated forms and is the best means to deal with the diagnosis of these vascular neoplasms [3]. Thus CD31, CD34 with factor related antigen was analysed in the present case.

In the present case, the intense membrane-based uniform positivity of lesional cells was seen on CD31 and CD34 showed focal moderate cytoplasmic staining, together with a Factor VIII related antigen which was strong diffuse cytoplasmic staining of tumour cells of angiosarcoma. Positivity for these markers confirm the endothelial phenotype that is found in malignant vascular tumours.

Angiosarcomas seen in elderly patients, are very destructive, have a propensity to recur locally, spread extensive, and have an elevated rate of lymph node and systemic metastases, with tumour related-death. There is an universal agreement that the occasion of the tumor detection can be one of the prognostic factors of angiosarcoma of the oral cavity. However, studies showed that prognosis is not influenced by the histologic grade and mitotic activity [7]. The present case was diagnosed at an early age of 30 years and also showed recurrence after complete surgical excision. A two years follow-up showed no second recurrence.

CONCLUSION

Angiosarcoma is a rapidly progressing malignancy that rarely affects the oral and pharyngeal mucosa. However this is the 17th case report in the literature arising in anterior mandibular gingiva. The generally advanced stage of the tumor at initial diagnosis leads to a poorer survival of patients with mucosal angiosarcomas as compared with patients seen in cutaneous angiosarcomas. Tumor size and metastases are related to the prognosis of the disease. Early detection, therefore, is important. Published cases and recognition of new ones may be helpful in establishing timely treatment and better prognosis of this rare pathology.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Dec 22, 2015**
Date of Peer Review: **Feb 19, 2016**
Date of Acceptance: **Feb 28, 2016**
Date of Publishing: **Jul 01, 2016**