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CASE REPORT

Gingival Angiosarcoma: A Case Report and Clinicopathologic Review of 32 Cases of Primary Gingival Angiosarcoma

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Abstract
Angiosarcoma is a malignant neoplasm of mesenchymal origin arising from vascular endothelium and most commonly involves extremities. Gingival angiosarcoma is a rare sporadic occurring tumor. We report a case of primary angiosarcoma of gingiva along with a review of 31 cases of primary gingival angiosarcoma reported in literature till 2018. A 30-year-old lady presented with recurrent gingival swelling over central mandible. She had no palpable cervical lymphadenopathy. She underwent central marginal mandibulectomy. Final histological analysis with immunohistochemistry was suggestive of the angiosarcoma of the gingiva. She is 50 months postoperative and doing well.

Introduction

Angiosarcoma is a malignant mesenchymal tumor originating from vascular endothelium, most commonly arising in extremities with long-standing lymphoedema. Oral and salivary gland angiosarcomas are rare, constituting only 1% of all angiosarcoma cases and mostly reported as case reports which occur commonly in tongue and lips [1]. Gingival angiosarcomas are still rarer. We present a case of angiosarcoma of gingiva along with a review of 31 reported cases in the literature.

Case Report

Thirty-year-old woman with no comorbidities presented with recurrent lower jaw gingival swelling. She underwent excision of the swelling four times elsewhere in the past 1 year. Family history was not significant. On examination, there was 1.5 cm × 1 cm fleshy swelling located centrally over gingiva of the lower jaw near incisor teeth (Fig. 1). There was no cervical lymphadenopathy. Histopathology of excision was done elsewhere, and slides reviewed at our hospital revealed features of angiosarcoma. Contrast-enhanced CT scan of neck and chest revealed a small (11 × 5 mm) heterogeneously enhancing lesion along gingival mucosa of a lower alveolus in the midline with no erosion of underlying bone; lungs were normal.

She underwent central marginal mandibulectomy with a 2-cm margin all around. Mobilization and approximation of floor of mouth mucosa with the lip mucosa to cover the exposed bone were done to close the defect. Rehabilitation was done by a removable partial denture. The final histopathological examination revealed polypoidal lesion lined by squamous epithelium; sub-

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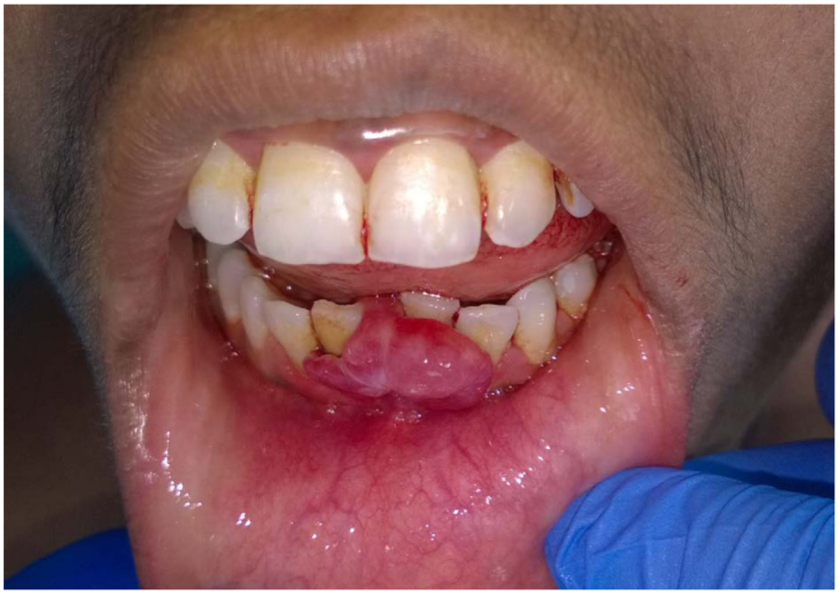

Fig. 1 Clinical photograph showing epilus like swelling arising from gingiva of mandible

epithelium tissue showed many thin congested vascular channels. The branching vascular channels were lined by round endothelial cells with atypia (Fig. 2). Stroma showed an inflammatory infiltrate of neutrophils, lymphocytes, and few atypical cells with scanty cytoplasm and hyperchromatic nuclei with 4–6 mitotic figures/10 HPF. Margins and bone were free of tumor. At high resolution (400×), pleomorphic tumor cells were seen (Fig. 3). Immunohistochemistry revealed strong positivity for CD 34(Fig. 4). Overall features were suggestive of well-differentiated angiosarcoma. The postoperative course was uneventful. Presently she is postoperative 50 months and doing well without any recurrence.

Review of Literature (Table 1)

All case reports of primary gingival angiosarcoma were reviewed, excluding head and neck, other oral cavities, and secondary angiosarcomas. PubMed and Google Scholar were searched using the keywords primary gingival angiosarcoma; 31 cases were found to the best of our knowledge. The present series highlights the clinical details, treatment, follow up, and prognosis of 32 patients (including the present case) reported in literature till 2018. Uchiyama et al. reviewed 12 cases of primary gingival angiosarcoma reported until 2009 [2]. Nagata et al. reviewed 15 cases of primary oral angiosarcoma reported until 2014 [3]. Details are given in Table 1.

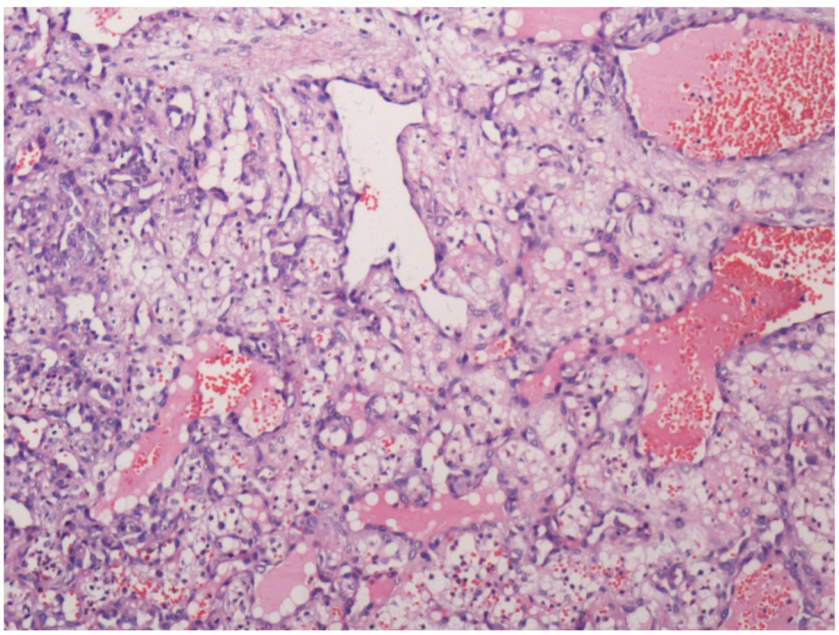

Fig. 2 Photomicrograph showing branching vessels lined by atypical cells (100×)

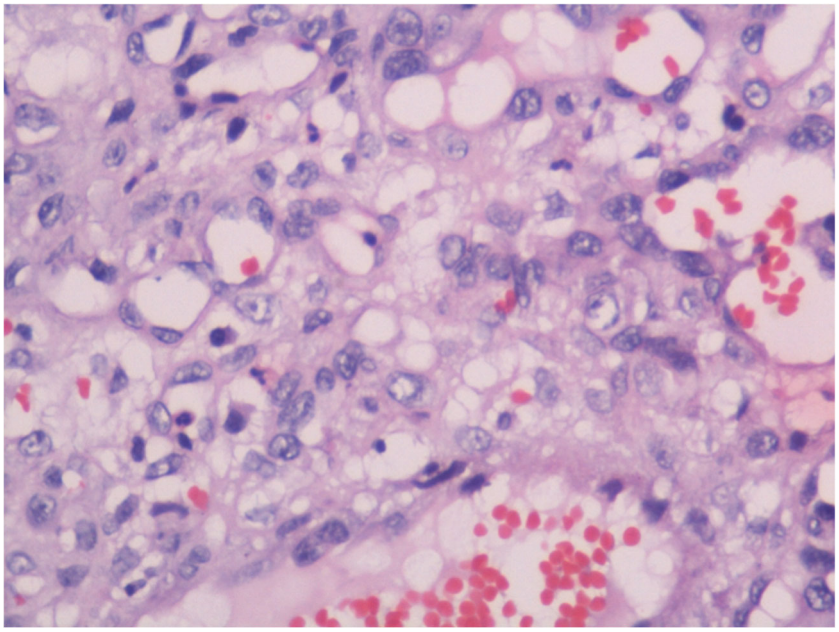

Fig. 3 Photomicrograph showing pleomorphic tumor cells (400×)

In the present series, the male to female ratio was 17:15. Age at presentation is extended from 3 months to 86 years, with a median of 62.5 years. The location of the tumor was mandibular gingiva in 21 cases (66%), maxillary gingiva in 9 (28%), and both mandibular and maxillary gingiva in 2 (6%).

Twenty-eight patients had non-metastatic disease (87.5%), and four metastatic disease at presentation (12.5%). Seventeen patients (53%) were treated by surgical modality alone (surgery arm), four patients by combined surgical modality and adjuvant therapy (combined arm) (16%), four primarily by radiation, chemotherapy, or electrofulguration modality (12%), 2 received no treatment (6%).

Seventeen patients who underwent primary surgical modality treatment, 4 died due to the disease at a median period of 5.5 months; two died due to causes unrelated to disease, 8 were disease free at a median follow up of 24 months (including the present case). Follow up was not available for three patients.

Five patients were treated by combined modality treatment with primary surgical treatment and adjuvant radiation therapy with or without chemotherapy. One was disease-free at 3-year follow up. Other patient treated by surgery and adjuvant chemotherapy underwent lobectomy for lung metastasis at 2 years posttreatment and was disease-free 10 months post-

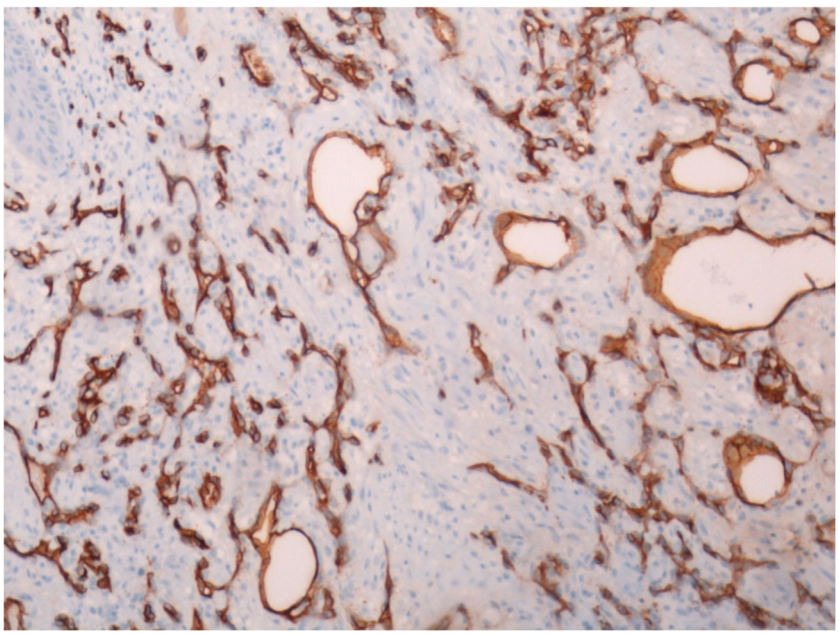

Fig. 4 Immunohistochemistry showing strong positivity for CD 34 highlighting vessels

Table 1 Depicting patients demographics and details of treatment and follow up

	Author, year	Age (years)/sex	Location	Treatment of primary tumor	Follow up
1	Henny 1949 [4]	3 months/M	Anterior part of maxilla	Electrocoagulation	Disease free till 2 years and 3 months
2	Blake and Blake 1956 [5]	26 M	First molar area of left mandible	Surgical excision	Disease free till 2 years and 4 months
3	Quinn et al. 1970 [6]	65 M	Maxillary and mandibular gingiva	Surgical excision, radiotherapy	Died after 1 month and 3 weeks (cause unknown)
4	Albright et al. 1970 [7]	34 M	Anterior part right mandible	Surgical excision	Disease free till 6 months
5	Wesley et al. 1975 [8]	18 F	Gingiva of left mandible	Enbloc resection of left mandible	Disease free till 2 years of surgery
6	Piscioli et al. 1986 [9]	86 F	Gingiva of the left mandibular molar area	Surgical excision	Died after 1 month due to cardiac failure
7	Carr and green 1986 [10]	66 M	Right maxillary gingiva with left upper arm, scalp, liver deposits	Nil	Died of renal failure, melena, abdominal pain and dyspnoea within few days of diagnosis (disseminated disease)
8	Kashima et al. 1994 [11]	39 M	Anterior part of right mandible	mandibulectomy	Died after 3 years (metastasis)
9	Margiotta et al. 1994 [12]	62 M	Right hemi mandible (chronic renal insufficiency)	Surgical excision	Follow up not available
10	Munoz et al. 1998 [13]	68 M	Mandibular molar area gingiva	Partial mandibulectomy	1-month post-surgery ➔ tonsillar, floor of mouth recurrence ➔Pharynx, larynx spread, denied any treatment ➔ Died within 2 months of surgery
11	Abdullah et al. 2000 [14]	60 F	Mandibular gingiva with scalp, shoulder and back deposits	Treatment Refused	Follow up not available
12	Loudon et al. 2000 [15]	68 F	Mandibular gingiva	Surgical excision	Died of local failure and complications (8 months)
13	Favia et al. 2002 [16]	65 F	Mandibular gingiva	Radiation plus chemotherapy	Died of disease (3 months)
14	Favia et al. 2002 [16]	82 F	Mandibular gingiva	Radiation plus chemotherapy	Died of disease (6 months)
15	Penner et al. 2002 [17]	16 F	Right mandibular gingiva	Enbloc resection ➔ right nodal dissection for neck nodal relapse after 3 months➔ Bimodal adjuvant chemotherapy and radiotherapy	Disease free 12 months post-surgery
16	Florescu et al. 2005 [18]	70 M	Mandibular gingiva	Surgical excision	Not reported
17	Driemel et al. 2008 [19]	63 M	Maxillary gingiva	None	Pleural and ileum metastasis (1 month)➔ ileal segmental resection ➔ died of intestinal bleeding due to disease 2 months post diagnosis.
18	Uchiyama 2009 [2]	59 M	Left maxilla	Chemotherapy including celmoleukin and teceleukin➔ partial maxillectomy➔ boron neutron capture therapy and lymphokine activated killer cell treatment	Disease free after 3 years post treatment
19	Mucke et al. 2010 [20]	72 M	Maxillary and mandibular gingiva	Surgical excision and then concurrent chemoradiation	Died of disease (6 months) Recurrence
20	Gordón-Núñez et al. 2010 [21]	17 F	Left mandibular gingiva	Surgery	Disease free after 14 months
21	Terada 2011 [22]	77 M	Mandibular gingiva	Enucleation, planned for radical surgery	Not reported
22	Suzuki et al. 2011 [23]	69 F	Right maxillary gingiva	Patient refused surgical treatment, so intra-arterial cisplatin and concurrent radiation	Died after 8 months with multiple lung metastasis
23	Sumida et al. 2012 [24]	55 F	Mandibular gingival (anterior part)	Wide excision	Disease free after 4 years
24	Aditya and lele 2012 [25]	75 F	Maxillary gingiva	Surgically unresectable. Patient declined further investigation and palliative radiation.	Not reported
25	Nagata et al. 2014 [3]	55 M	Mandibular gingiva	Segmental mandibular resection + left radical neck dissection	Thoracic vertebrae metastasis, died of disease (3 months)
26	Nagata et al. 2014 [3]	64 M	Maxillary gingiva	Maxillectomy + Bilateral radical neck dissection ➔ Chemotherapy (Cisplatin and Adriamycin)	Lung metastasis after 24 months ➔ lobectomy. No disease 10 months post lobectomy.
27	Sachadeva et al. 2015 [26]	52 F	Mandibular gingiva	Hemimandibulectomy	Died in few day (cardiac and respiratory issues)
28	Hunasgi et al. 2016 [27]	30 F	Mandibular anterior gingiva	Local excision ➔ Recurrence after 2 months ➔ Wide excision with 2 cm margin	Disease free till 2 years post radical surgery
29	Chamberland et al. 2016 [28]	83 M	Mandibular gingiva with bilateral tonsillar and bilateral neck nodal metastasis	Bilateral tonsillectomy and nodal puncture in right level IIa➔After 1 month, bone metastasis, right tonsillar relapse, and gross hematuria➔ paclitaxel 5 cycles + hemostatic RT➔ Mediastinal disease and compression	Died of disease after 4 months of diagnosis of disease.
30	Aljadeff et al. 2016 [29]	79 M	Maxillary anterior gingiva	Wide local excision ➔60 Gy of adjuvant radiation	Died 4 months after surgery due to respiratory distress presumably unrelated to disease.
31	Hartanto and Lau 2018 [30]	52 F	Right maxillary region with metastasis to lung, liver, bone, multiple lymph nodes at bilateral posterior triangle	Nil	Died in short time after confirmation of diagnosis.
32	Present case	30 F	Mandibular gingiva	Central marginal mandibulectomy	No disease (50 months)

lobectomy. Two patients died of disease unrelated to cancer, and one died of disease recurrence at 6 months.

Three of 4 patients treated by radiation and chemotherapy only without surgery died of disease at a median follow up of 6 months period posttreatment, one patient who underwent electrocoagulation ablative therapy was disease free at 27 months of follow up.

Two patients did not undergo any treatment for the primary. One patient developed pleural and ileum metastasis a month after diagnosis and later died of the disease. Others had unresectable maxillary gingival angiosarcoma with extension to paranasal sinuses and infratemporal area.

Discussion

Oral angiosarcoma constitutes only 2% of all angiosarcoma [1]. Among primary oral angiosarcomas, the most common site is tongue, salivary glands, and lip [1]. Gingiva is an infrequent site among all oral subsites for angiosarcoma. Angiosarcoma may present as a bluish macule on the face and scalp, or against a background of chronic lymphedema or in association with exposure to radiation or chronic pyothorax. Symptoms include swelling on gingiva with a history of the recent increase in size, frequently accompanied by bleeding.

Angiosarcoma is an aggressive tumor with an unfavorable prognosis that, despite aggressive multimodality, therapy tends to recur locally and metastasize early most commonly to the lung. Most of them occur within the initial 2–3 years from the diagnosis. The 2-year survival is 15–20% [2,3] It is chemotherapy and radiotherapy resistant. The role of adjuvant therapy is not known. Surgery remains the only form of curative treatment.

As shown in this study, surgery with or without adjuvant treatment, chemotherapy/radiotherapy is the only therapeutic option and remains the cornerstone of the treatment. Long-term survivors were only present in surgery containing arm. The current reviews also show that angiosarcoma is chemo-resistant and radio-resistant. Outcomes were not affected by adjuvant therapy. Neck dissection is necessary if there is any suspicion of lymph node metastases, although the use of prophylactic neck dissection is not warranted. Few selected patients with isolated pulmonary metastasis after a durable disease-free interval post-radical surgery for a primary tumor can be treated with metastasectomy with curative intent.

Owing to the rarity of the disease, only literature available is in the form of case reports. Biology of the disease needs to be studied in detail, and larger prospective multicentric studies need to performed to evaluate the optimal therapy, the role of adjuvant therapy.

Conclusion

Early diagnosis is crucial for survival as the wrong diagnosis can delay definitive treatment. Radical surgery is an only curative option. Even in recurrent cases, timely and adequate surgery can prolong survival. The chemotherapy/radiotherapy role is not established. The role of adjuvant treatment after surgery is not proven.

References

1. Fanburg-Smith JC, Furlong MA, Childers EL (2003) Oral and salivary gland angiosarcoma: a clinicopathologic study of 29 cases. Mod Pathol 16(3):263–271
2. Uchiyama Y, Murakami S, Kishino M, Furukawa S (2009) A case report of primary gingival angiosarcoma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 108(6):e17–e21
3. Nagata M, Yoshitake Y, Nakayama H, Yoshida R, Kawahara K, Nakagawa Y, Shinohara M (2014) Angiosarcoma of the oral cavity: a clinicopathological study and a review of the literature. Int J Oral Maxillofac Surg 43(8):917–923
4. Henny FA (1949) Angiosarcoma of the maxilla in a 3-month-old infant; report of case. J Oral Surg (Chic) 7(3):250–252
5. Blake H, Blake FS (1956) Angiosarcoma; report of a case. Oral Surg Oral Med Oral Pathol 9(8):821–825
6. Quinn JH, McConnell HA Jr, Leonard GL (1970) Multifocal angiosarcoma of the gingiva: report of case. J Oral Surg 28(3): 215–217
7. Albright CR, Shelton DW, Vatral JJ, Hobin FC (1970 Dec) Angiosarcoma of the gingiva: report of case. J Oral Surg. 28(12): 913–917
8. Wesley RK, Mintz SM, Wertheimer FW (1975) Primary malignant hemangioendothelioma of the gingiva: report of a case and review of the literature. Oral Surg Oral Med Oral Pathol 39(1):103–112
9. Piscioli F, Leonardi E, Scappini P, Cristofolini M (1986) Primary angiosarcoma of the gingiva. Case report with immunohistochemical study. Am J Dermatopathol 8(5):430–435
10. Carr RJ, Green DM (1986) Oral presentation of disseminated angiosarcoma. Br J Oral Maxillofac Surg 24(4):277–285
11. Kashima K, Igakura Y, Komura M, Hamada M, Arima R, Sakoda S (1994) Three gingival tumors derived from vascular endothelial cells: a case of hemangioendothelioma and two cases of angiosarcoma. Nihon Koku Shuyo Gakkaishi 6:251–261
12. Margiotta V, Florena AM, Giuliana G (1994) Primary angiosarcoma of the alveolar mucosa in a haemodialysis patient: case report and discussion. J Oral Pathol Med 23(9):429–431
13. Muñoz M, Monje F, del Hoyo JA, Martín-Granizo R (1998 Apr 1) Oral angiosarcoma misdiagnosed as a pyogenic granuloma. J Oral Maxillofac Surg 56(4):488–491
14. Abdullah BH, Yahya HI, Talabani NA, Alash NI, Mirza KB (2000) Gingival and cutaneous angiosarcoma. J Oral Pathol Med 29(8): 410–412
15. Loudon JA, Billy ML, DeYoung BR, Allen CM (2000) Angiosarcoma of the mandible: a case report and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol 89(4):471–476
16. Favia G, Muzio LL, Serpico R, Maiorano E (2002) Angiosarcoma of the head and neck with intra-oral presentation. A clinicopathological study of four cases. Oral Oncol 38(8):757–762

17. Penner C, Grist W, Müller S (2002) Epithelioid angiosarcoma presenting in the gingiva of an adolescent. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol 94(2):205–216
18. Florescu M, Simionescu C, Margaritescu C, Georgescu CV (2005) Gingival angiosarcoma: histopathologic and immunohistochemical study. Romanian J Morphol Embryol 46(1):57–61
19. Driemel O, Müller-Richter UD, Hakim SG, Bauer R, Berndt A, Kleinheinz J, Reichert TE, Kosmehl H (2008) Oral acantholytic squamous cell carcinoma shares clinical and histological features with angiosarcoma. Head Face Med 4(1):17
20. Mücke T, Deppe H, Wolff KD, Kesting MR (2010) Gingival angiosarcoma mimicking necrotizing gingivitis. Int J Oral Maxillofac Surg 39(8):827–830
21. Gordon-Nunez MA, Lopes MF, Maia AP, Galvão HC (2010) Intraoral epithelioid hemangioendothelioma: a case report and review of the literature. Med Oral Patolog Oral Cir Bucal 15(2):e340–e346
22. Terada T (2011) Angiosarcoma of the oral cavity. Head Neck Pathol 5(1):67–70
23. Suzuki G, Ogo E, Tanoue R, Tanaka N, Watanabe Y, Abe T, Iwamoto O, Kusukawa J, Hayabuchi N (2011) Primary gingival angiosarcoma successfully treated by radiotherapy with concurrent intra-arterial chemotherapy. Int J Clin Oncol 16(4):439–443
24. Sumida T, Murase R, Fujita Y, Ishikawa A, Hamakawa H (2012) Epulis-like gingival angiosarcoma of the mandible: a case report. Int J Clin Exp Pathol 5(8):830–833
25. Aditya A, Lele S (2012) A nodular growth on maxillary gingiva. Indian J Dent Res 23(1):116–119
26. Sachdeva SK, Dutta S, Rout P (2015) Angiosarcoma of mandible: An uncommon clinical entity. Int J Appl Basic Med Res 5(2):142
27. Hunasgi S, Koneru A, Vanishree M, Manvikar V (2016) Angiosarcoma of anterior mandibular gingiva showing recurrence–a case report with immunohistochemistry. J Clin Diagn Res 10(7):ZD01–ZD04
28. Chamberland F, Maurina T, Degano-Valmary S, Spicarolen T, Chaigneau L (2016) Angiosarcoma: a case report of gingival disease with both palatine tonsils localization. Rare Tumors 8(3):113–117
29. Aljadeff L, Fisher CA, Wolf SL, Byrd KM, Curtis W, Ward BB, Munz SM, Fullen DR, McHugh JB, Danciu TE (2016) Red exophytic mass of the maxillary anterior gingiva. Oral Surg Oral Med Oral Pathol Oral Radiol 122(4):379–384
30. Hartanto FK, Lau SH (2018) A case report of Angiosarcoma of maxillary gingiva: histopathology aspects. Sci Dent J 2(2):77–83