

Metastatic Maxillary Gingival Angiosarcoma with Aggressive Growth: A Case Report

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Angiosarcoma is a rare malignant tumor of endothelial origin. It is an aggressive neoplasm with early metastasis and poor prognosis and accounts for approximately 2% of all soft tissue sarcomas. Primary tumors arising in the oral cavity account for only 1% of all angiosarcomas. Here, we report a rare case of metastatic angiosarcoma of the gingiva originating from a primary mediastinal lesion. The patient was an 83-year-old man who presented with a maxillary interincisor tumor; it was a painless mass with rounded superficial necrosis measuring 23 mm × 17 mm on the labial side and 20 mm × 17 mm on the palatal side. The histopathological diagnosis was of an epithelioid angiosarcoma. Imaging revealed lesions in the mediastinum, lungs, liver, and skin. The primary lesion was considered a mediastinal lesion. As the tumor had spread throughout the body, palliative therapy was administered. However, the patient's general condition deteriorated rapidly, and he died 3 weeks after the first visit. Identifying oral metastatic malignancies may result in detection of malignant tumors at other sites; thus, oral and maxillofacial surgeons must maintain a heightened awareness of angiosarcoma.

Key words: angiosarcoma, soft tissue sarcoma, metastatic oral tumor, maxillary interincisor tumor, palliative therapy

INTRODUCTION

Angiosarcoma is a rare vascular neoplasm arising from endothelial cells and accounts for approximately 2% of soft tissue sarcomas [1]. The most common primary site is the skin, with occurrences commonly in the head and neck region [2, 3]. The mean age of patients with angiosarcoma is 65.7 years (range, 52–83 years), with most patients being male (5 : 1) [1]. The National Cancer Intelligence Network reports that the prevalence of angiosarcoma is approximately two in a million [4]. It is a very aggressive neoplasm with high rates of local recurrence, early metastasis, and poor prognosis [1, 5]. Angiosarcoma is often associated with distant metastases at the initial diagnosis and progresses rapidly before a definitive diagnosis is made [1, 5–7]. Up to 32% patients have had metastatic lesions at the time of diagnosis [6, 7]. The 5-year overall survival rate is 35–45% [2, 7]. Angiosarcomas that metastasize to the oral cavity have rarely been reported.

Metastatic oral tumors are very rare, accounting for <1% of oral malignancies [5]. Most of them are located the jawbone and rarely metastasize to the gingiva [8]. Herein, we report a rare case of a patient with angiosarcoma who presented to our hospital with the chief complaint of a gingival mass that showed rapid general deterioration.

CASE REPORT

An 83-year-old Japanese man visited our hospital with a chief complaint of a gingival mass that had grown rapidly over the past month. The patient had been visiting a nearby clinic for a subcutaneous abdominal mass over the past several months. He had a medical history of colon cancer, hypertension, and aortic valve replacement. Intraoral examination revealed a painless dumbbell-shaped mass with rounded superficial necrosis measuring 23 mm × 17 mm on the labial side and 20 mm × 17 mm on the palatal side that protruded from the maxillary midline interdental papilla (Fig. 1A). Occlusal radiographs and computed tomography (CT) showed an impacted maxillary central supernumerary tooth, but there was no bone resorption around the teeth associated with the mass (Fig. 2A, B). The lesion could not be evaluated using CT because of dental metal artifacts. No lymphadenopathy was observed in the cervical region. Magnetic resonance imaging revealed a high signal intensity in short T inversion recovery and a contrast-enhancing effect.

As malignancy was suspected, we resected the maxillary gingival mass on the labial side at its base for biopsy (Fig. 1B–D). Rapid mass regrowth was observed at the wound site within 2 weeks of biopsy (Fig. 1E, F). Histopathologically, the surface layer of the lesion was

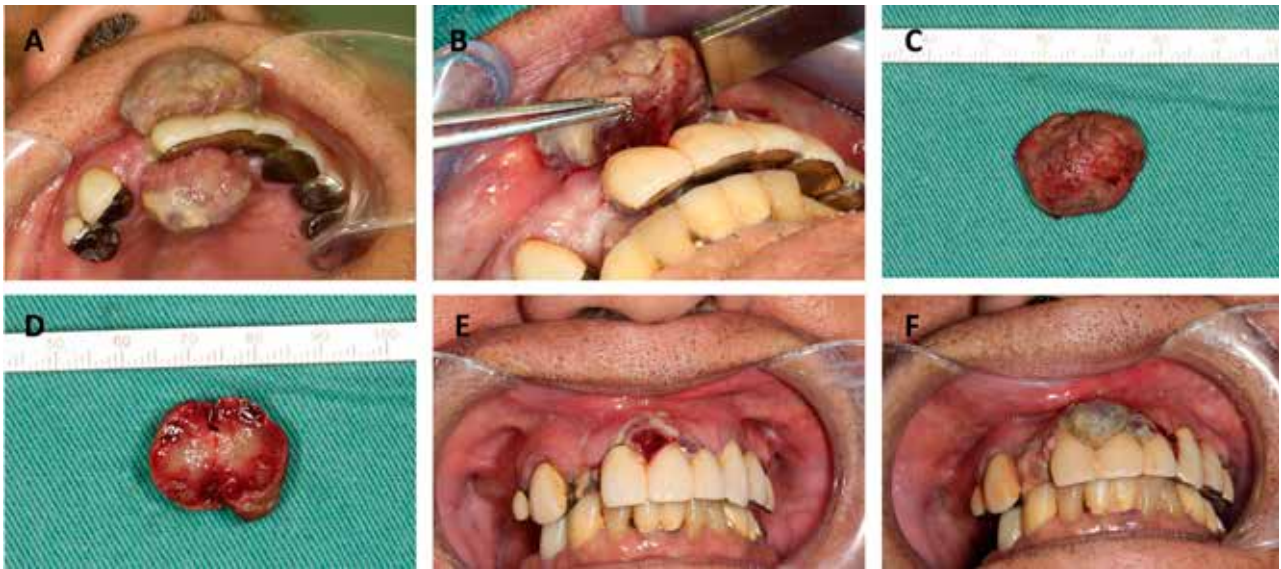


Fig. 1 Intraoral and biopsy findings.

A) At the first visit. B-D) Biopsy findings. E) One week after biopsy. F) Two weeks after biopsy.

Intraoral examination revealing a painless mass protruding from the interdental papilla, measuring 23 mm × 17 mm on the labial side and 20 mm × 17 mm on the palatal side (A). We have resected the pedunculated mass on the labial side of the base (B). Showing the specimen after resection. The tumor surface was eroded and indurated (C) Showing the section of the lesion, the interior was a solid white lesion (D). The resection site appeared raised and superficial necrosis was observed within one week (E). Furthermore, the lesion became larger and spread laterally, within two weeks. After biopsy, it showed rapid growth (F).

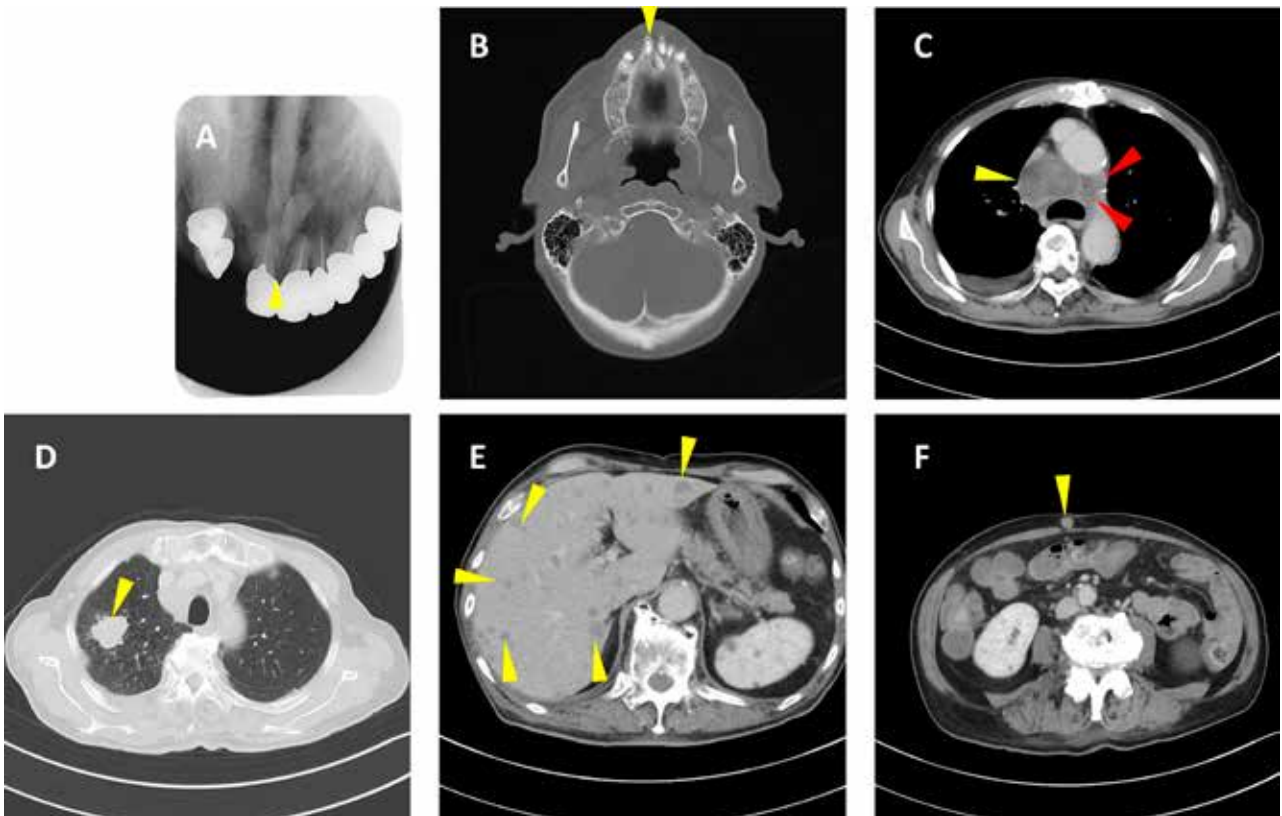


Fig. 2 Diagnostic imaging performed at the first visit.

A) Dental X-ray. B-F) Computed tomography (CT) axial view.

No obvious alveolar bone resorption is observed (A, B). Whole-body CT revealing a mass measuring 72 mm × 54 mm in contact with the mediastinal lymph nodes and right myocardium (C), nodule in the lung (D) and multiple nodules liver (E), and a subcutaneous mass which had been noted for several months before gingival lesions (F). Red arrows indicate lymph node metastases (C).

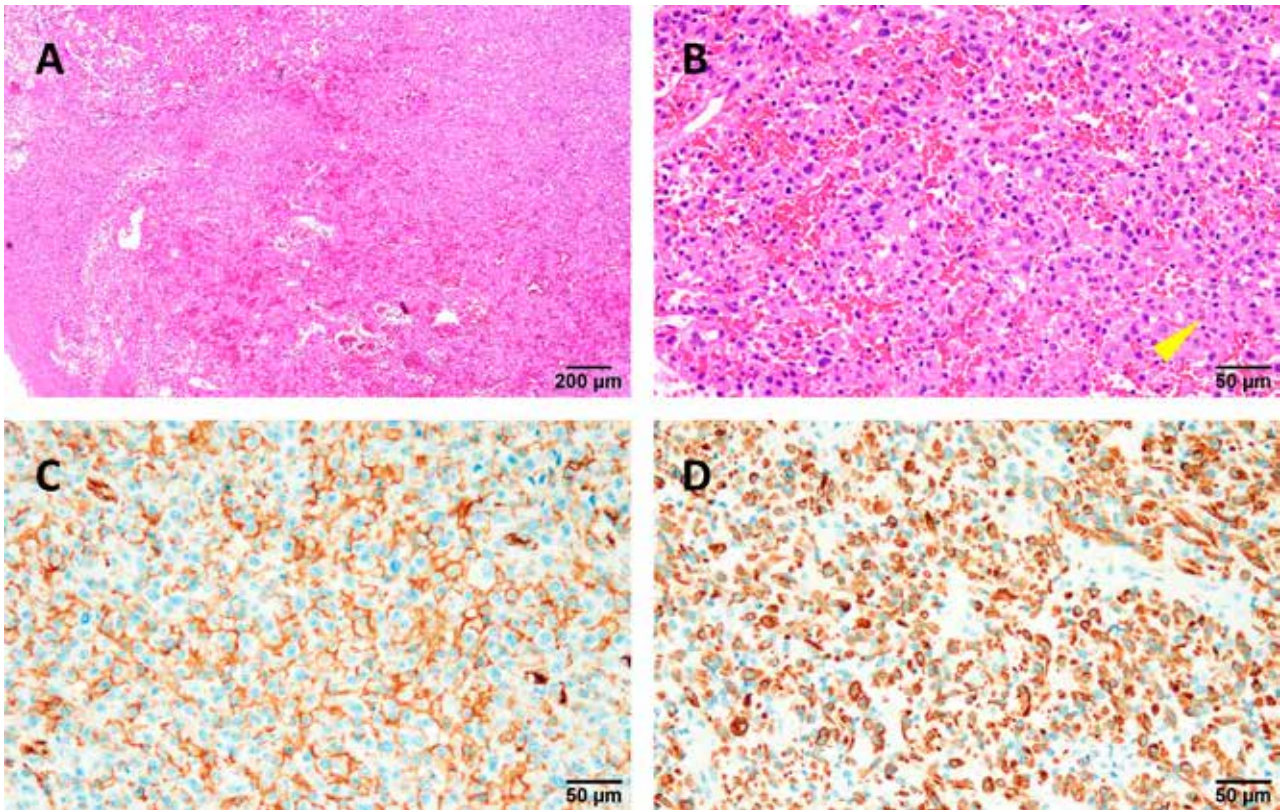


Fig. 3 Histopathological features based on hematoxylin and eosin staining (HE) (A, B) and immunohistochemical features of primary tumor (C, D).

A) Low power field. Scale bar is 200 μm . B) High power field. Scale bar is 50 μm .

HE staining shows short spindle-shaped cells with oval-shaped nuclei and eosinophilic cytoplasm proliferated in bundles and sheets (yellow triangle), and networks with atypical mitosis are also observed within the tumor.

C) CD31 positive. D) CK- AE1/AE3 positive. Scale bars are 50 μm .

The cell membrane of CD31 and the cytoplasm of CK-AE1/AE3 are stained brown by DAB.

eroded, and a small amount of stratified squamous epithelium remained at the margin. Mild inflammatory nucleomegaly was observed in the remaining squamous epithelia. In the lesion, short spindle-shaped cells with oval-shaped nuclei and eosinophilic cytoplasm proliferating in bundles, sheets, and networks with atypical mitosis were also observed within the tumor. Irregularly shaped vascular spaces were filled with erythrocytes and inflammatory cells around the tumor cells (Fig. 3A, B). Immunohistochemical examination revealed that the tumor cells were positive for CD31 and CK-AE1/AE3 (Fig. 3C, D). These histopathological findings confirmed the diagnosis of epithelial angiosarcoma. Since the maxillary gingival lesion was an angiosarcoma, whole-body CT was performed for systemic examination.

It showed a mediastinal mass measuring 72 mm \times 54 mm, multiple mediastinal lymph node, a lung nodule, multiple liver masses, bilateral adrenal enlargement, and a subcutaneous mass (Fig. 2C-F). After consultation with the Department of Diagnostic Imaging, although we could not rule out that the lung lesions were the primary tumor, based on imaging and histopathological findings, the mediastinal lesion was suggested as the primary tumor, and we diagnosed the oral tumor as a metastatic tumor. In addition, angiosarcoma often metastasizes via a hematogenous route, and lymphatic metastasis is rare [9] although, we think that the lesion adjacent to the large mediastinal lesion

(Fig. 2C, red arrows) are metastatic lymph nodes. Therefore, we considered that the mediastinal lesion was not lymph node metastasis.

On follow-up, the patient's general condition rapidly deteriorated. As the tumor had spread throughout his body, palliative therapy was administered. As palliative therapy, home care, including a visiting doctor and home nursing, was provided. Two weeks after the first visit, the patient's general condition worsened further; he was unable to walk on his own, and he spent the entire day in bed. The patient died at home 3 weeks after the first visit.

DISCUSSION

Lahat *et al.* reported that the most common site of primary angiosarcoma was the skin (approximately 49.6%), followed by the breast parenchyma (14.4%), soft tissue (11.2%), heart (6.7%), bone (4.1%), and others (14%) [3]. Approximately 50–60% of cutaneous angiosarcomas arise in the head and neck [2]. Macroscopic observations typically reveal initial signs of erythema, hemorrhage, and purpura with unclear borders. As the disease progresses, necrotic eschars, ulcers, and nodular lesions manifest. In many cases, the lesion is already large at the time of initial diagnosis [10, 11]. Patients with tumors measuring > 5 cm in size have a significantly worse prognosis [1, 12]. The presence of satellite lesions around the primary tumor at diagnosis was also associated with significantly wors-

ened survival [9]. Histologically, most angiosarcomas show complex vessels lined by atypical endothelial cells with an inter-anastomosing pattern and inter-tumoral hemorrhage. In some angiosarcomas, vascular differentiation may be an extremely subtle finding in hematoxylin and eosin-stained sections and requires vascular immunohistochemical markers for recognition [13]. In our case, irregular vascular lumens and hemorrhages were observed within the tumor. Angiosarcoma is predominantly composed of fascicles of spindled cells, with little evidence of vascular differentiation [13]. Cytoplasmic CD31 and CD34 are the most frequently used immunohistochemical markers for angiosarcoma diagnosis; however, CD31 is more specific [14]. As this disease is rare, treatment guidelines supported by high-level evidence have not yet been established. Surgical resection is recommended as the first-line treatment for solitary tumors measuring < 5 cm in maximum diameter [15]. Local therapy, combining surgical resection and radiation therapy, improves survival [16]. Guadagnolo *et al.* demonstrated that the 5-year overall survival rate was higher in surgery and radiation therapy (68%) than in surgery alone (40%) [9]. Because the margin of the angiosarcoma is unclear, the postoperative recurrence rate is high. Postoperative RT of ≥ 50 –60 Gy contributes to the improvement in survival rate [12, 17]. Surgical resection is not suitable for the treatment of distant metastases, and systemic treatment is recommended. The National Comprehensive Cancer Network guidelines in the United States recommend the use of paclitaxel alone for chemotherapy [18]. Previous studies have shown a response rate of 53% (complete response: 13%, partial response: 40%) and increased progression-free survival (approximately 6 months) for scalp angiosarcoma treated with weekly paclitaxel [20]. In addition to paclitaxel, multitargeted tyrosine kinase inhibitors with activity against vascular endothelial growth factors 1, 2, and 3; platelet-derived growth factors; and immune checkpoint inhibitors with activity against programmed cell death protein 1 are expected to emerge as new therapeutic drugs for angiosarcoma [19, 21]. In advanced cases, radical treatment becomes difficult. Angiosarcoma rapidly enlarges as a hemorrhagic lesion, increasing the risk of bleeding and leading to a decline in quality of life. Thus, palliative interventions that focus on preserving patient quality of life, such as palliative radiotherapy for controlling local lesions, are necessary in these cases.

Metastatic tumors in the oral cavity are rare and most commonly arise in the jawbone but can also arise in the oral soft tissues [8]. Due to its rarity, it is often difficult to differentiate it from inflammatory and reactive lesions that are common in this area. In particular, the early stages, gingival metastatic lesions are easily mistaken for benign lesions, such as pyogenic granuloma, hemangioma, giant cell granuloma, and peripheral fibroma, based on their clinical appearance [22, 23]. Most metastatic oral tumors are malignant epithelial tumors [5]. Circulating tumor cells with epithelial–mesenchymal transition is thought to metastasize to the jawbone by infiltrating and progressing through the niche [24, 25]. In our case, we hypothesized that epithelial–mesenchymal-transformed tumor cells might have colonized and metastasized to the gingiva.

Immunohistochemical analyses were positive for epithelial markers, such as CD31 and CK-AE1/AE3.

In oral soft tissues, the attached gingiva is the most common site of metastatic colonization. Inflammation may play a role in attracting metastatic cells to the attached gingiva [26]. Malignant cells may be entrapped by the rich capillary network of the chronically inflamed gingiva [26]. Metastatic lesions in oral soft tissues are easily recognized, in contrast to those in the jawbone. Oral metastatic lesions can be the first sign of undiscovered malignancy. Nevertheless, there are many unknowns related to diagnosis, treatment, and prognosis of angiosarcoma. As angiosarcoma is rare, it is difficult to review many cases at a single institution. Hence, we consider that it is necessary to accumulate cases under the leadership of the academic society at multiple institutions.

CONCLUSION

In our case, a mediastinal lesion was discovered after the diagnosis of gingival lesions. As angiosarcoma is rare, there is an insufficiency in data related to its treatment outcomes and prognosis for radical and palliative treatments. Furthermore, no treatment method supported by high-level evidence has been established. Increasing the number of case reports, such as the one presented here, promotes further understanding and contributes to establishing more effective treatments for angiosarcoma. We believe screening should be required for systemic evaluation when oral lesions have a metastatic appearance, and that oral and maxillofacial surgeons should be aware of angiosarcomas that rarely occur in the oral cavity.

ETHICAL APPROVAL

This article does not contain any study with human participants or animals performed by any of the authors. The treatment of the presented patient was not in any way influenced due to this article.

CONFLICT OF INTEREST

The authors report no declarations of interest.

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CONSENT FOR PUBLICATION

The patient's family provided consent for publication of this case report.

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