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Sarcomatoid Carcinoma of the Mandible: A Case Report and Literature Review

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Abstract

Background: Sarcomatoid carcinoma is a rare biphasic malignancy with an epithelial and mesenchymal component. Given its histological particularity, the diagnosis of this tumor still represents a challenge for pathologists and surgeons. Sarcomatoid carcinoma of the mandible is a very rare and aggressive entity. To date, only sporadic cases have been reported in the literature. **Aim:** To report a rare case of aggressive mandibular sarcomatoid carcinoma treated with radical surgery and adjuvant chemoradiation, and discuss the related literature. **Case Report:** We introduce a rare case of mandibular sarcomatoid carcinoma occurring in a 34-year-old woman. Treatment consisted of radical surgery and re-excision for positive margins, adjuvant radiation therapy (66 Gy in 33 fractions in simultaneous integrated boost delivered using Volumetric Modulated Arc Therapy) and Cisplatin-based concurrent chemotherapy. The tumor displayed aggressive behavior and high metastatic potential, causing tumour recurrence and extensive lung metastasis. **Conclusion:** Sarcomatoid carcinoma of the mandible is an extremely rare malignant entity, with a high tendency for local recurrence, distant metastasis. Treatment involves radical surgery and adjuvant chemoradiation, although the outcome and prognosis might be poor.

Keywords

Sarcomatoid Carcinoma, Mandible, Adjuvant Chemoradiation, VMAT

1. Introduction

Sarcomatoid carcinoma is a rare biphasic malignant tumor with both mesenchymal and epithelial components. Given its histological peculiarity, the diagnosis of this tumor always represents a challenge for pathologists and surgeons.

Carcinosarcomas usually occur in the urinary tract and upper respiratory tract in elderly men, and is rarely found in the maxillofacial region. Primary sarcomatoid carcinoma of the mandibular gingiva is extremely rare. Only sporadic cases have been reported so far in the literature, and have mainly focused on the histopathological aspects of this disease. The little data available in the literature have exhibited considerably aggressive clinical behavior, poor prognosis, high rates of recurrence and frequent metastasis. Treatment is primarily surgical resection, though an adjuvant therapy may be necessary [1] [2].

Here, we report a clinically aggressive, recurrent and metastasizing primary sarcomatoid carcinoma of the left mandible in a 34-year-old woman, despite aggressive local treatment with radical surgery and adjuvant chemoradiation. In addition, we present a brief review of the relevant literature and increase our knowledge on this rare entity.

2. Case Report

A 34-year-old female patient presented to a dental office in December 2017 with a complaint of intermittent chin paresthesia and rapidly growing painless mass on the left mandibular gingiva for one month. The patient did not report a habit of smoking or daily drinking of alcoholic beverages. Medical history was not significant. Oral cavity examination showed a 30 mm × 30 mm irregular, indurated, nonmobile tumor in the left mandibular region both on buccal and lingual gingiva. Patient consent was obtained for taking photograph and using it for study and publication purposes (**Figure 1**). Lymphnodes were not palpable. Speech, swallowing and mouth opening were unimpaired. Clinical examination revealed no extraoral pathological findings.

Panoramic radiography revealed irregular osteolytic bone destruction in the left mandible. DentaScan imaging showed heterogeneous lytic lesion of the left mandibular horizontal branch, destroying the cortical bone, extending to soft tissues and reaching the alveolar rim with loss of teeth 34 to 38. An incisional biopsy was performed. The diagnosis was high grade fibrosarcoma of the jaw. Computed tomography scans ruled out metastatic disease.

Figure 1. Clinical examination of the oral cavity at diagnosis showing left mandibular mass lesion.

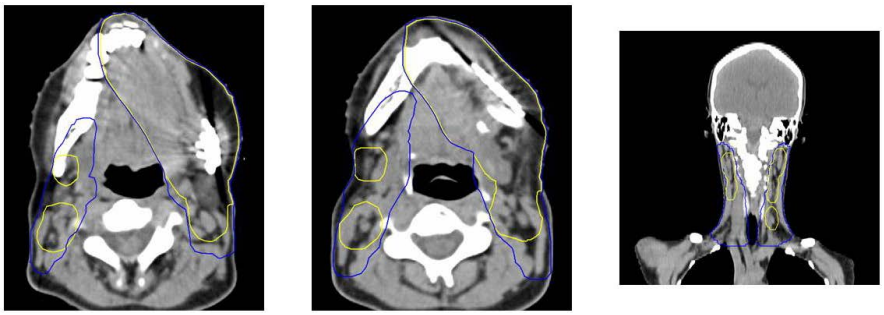
After counseling, detail discussion and consent, the patient underwent complete gross excision of the left mandibular tumor by a left hemi-mandibulectomy and reconstruction with iliac crest bone grafting. Histopathologic examination found spindle cells tumor proliferation, hyperchromatic nuclei, very marked mitotic activity with atypical mitoses, evoking a sarcoma. Anterior, posterior and lateral surgical margins were positive. Immunohistochemistry of the malignant stromal elements exhibited abundant expressions of vimentin and smooth muscle actin. The epithelial component was positive for Epithelial membrane antigen (EMA), AE1/AE3 cytokeratin and p63 protein. Desmin, h-caldesmon, and S100 protein were negative. Based on the histological and immunohistochemical findings, the final diagnosis was corrected to sarcomatoid carcinoma.

Multidisciplinary board considered re-excision. However, during this time interval, the patient experienced subsequent tumor progression very shortly after surgery. Re-excision was performed, although clear margins could not be obtained. Given the aggressive and rapidly evolving behavior of the tumor, with positive surgical margins despite re-excision, multidisciplinary board opted for adjuvant treatment. The patient was sent to radiation oncology department for evaluation and was taken up for concomitant chemoradiation with cisplatin-based chemotherapy.

Simulation was performed using the CT simulator (SOMATOM Sensation Open; Siemens). The patient was immobilized in supine position with a 5-point head neck and shoulder thermoplastic mask. An intra-venous iodine contrast enhanced planning CT with 3-mm slice thick reconstruction was obtained. The CT DICOM images were transferred to the Monaco® treatment planning system Version 5.11 (Elekta, Stockholm, Sweden) for target delineation.

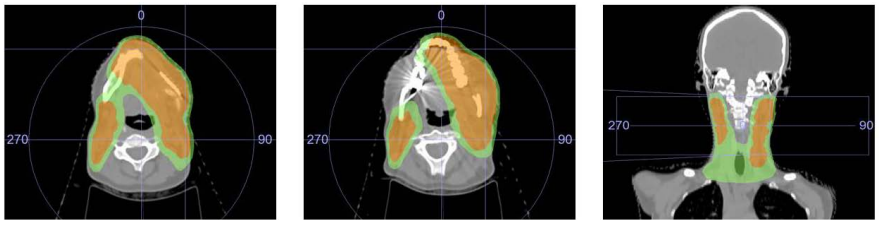
The acquired images were co-registered with diagnostic CT images to contour the preoperative gross tumor volume (GTV-T), with the aim of better selecting the clinical target volume (CTV-T). Multiple suspicious cervical lymph nodes were identified on the planning CT scan, in left level II, III, and IVa and right level II and III. The largest node measured 1.5 cm × 2.2 cm. A 5-mm isotropic margin was given around the preoperative GTV to generate high-risk clinical target volume (CTV-T HR), and was adjusted on the planning CT, including the entire surgical bed to consider the microscopic disease. A 5-mm isotropic margin was given around the nodal gross tumor volume (GTV-N) to generate high-risk clinical target volume (CTV-N HR). A low-risk clinical target volume (CTV-LR) was defined as the CTV-T HR with a 5-mm margin, including the drainage lymph nodes starting 3 mm below the skin. The planning target volume (PTV) was created adding a 5 mm expansion around the corresponding CTV, except in the skin direction (**Figure 2**). Organs at risk were contoured according to the Radiation Therapy Oncology Group (RTOG) atlas for normal tissue contouring.

A dose prescription of 66 Gy in 33 fractions of 2 Gy was given to the PTV-HR and 56 Gy to the PTV-LR (**Figure 3**). Two-arc volumetric modulated arc therapy (VMAT) with simultaneous integrated boost (SIB) technique plan with 6-MV photon beams was set by the medical physicist. Doses were acceptable for all



(a) (b) (c)

Figure 2. Axial (a) (b) and frontal (c) views of the planning CT scan showing the target volumes: PTV-HR and PTV-LR in yellow and blue, respectively.



(a) (b) (c)

Figure 3. Axial (a) (b) and frontal (c) views of the planning CT scan. VMAT was delivered to the region of high risk to doses of 66 Gy and 56 Gy (95% isodose lines in orange and green respectively).

organs at risk with homogenous uniform dose coverage in PTV with 1.09 conformity index. VMAT plan was delivered using Elekta VERSA HD®. Patient set-up was verified weekly by kV cone-beam CT imaging prior to treatment. Six cycles of weekly cisplatin were administered concurrently with radiotherapy. The patient was assessed for treatment-related toxicity once a week by the radiation oncologist. The patient tolerated the treatment well and experienced reversible grade 2 (G2) mucitis, according to Common Terminology Criteria for Adverse Events version 5.0. There were no treatment interruptions.

At a 3-month follow-up visit after chemoradiation, local control of the tumor was achieved. However, the evaluation CT scans revealed a pulmonary metastatic relapse. Multidisciplinary board decided for pulmonary metastasectomy and palliative Adriamycin-Ifosfamide chemotherapy.

Despite 4 cycles of palliative chemotherapy, our patient died from local tumour recurrence and extensive lung metastasis.

3. Discussion

Sarcomatoid carcinoma is an uncommon subgroup of malignant mixed tumors with carcinomatous and sarcomatous components. It consists of proliferation of both sarcomatoid pleomorphic spindle cells and carcinomatous squamous cells [1]. Most of the available literature focuses on morphological and immunohistochemical features of this entity [2] [3]. Since its first description by Virchow in

1864, a variety of terms have been used in the literature, such as carcinosarcoma, spindle cell carcinoma, pseudosarcoma, pleomorphic carcinoma and polypoid carcinoma, reflecting the complexity of its histogenesis [4]. Krompecher in 1900 described the transformation of parenchyma (epithelium) into stroma, a gradual metamorphosis to a spindle cell morphology, and introduced the expression "sarcomatoid carcinoma" [5].

Sarcomatoid carcinoma has a predilection for occurrence in the breast or the urinary, respiratory or digestive tract. It accounts for less than 3% of all head and neck malignancies of epithelial origin.

The most common site of origin in the head and neck region is the glottis and hypopharynx. The extra-laryngeal origin is much less frequent. It is reported to represent less than 1% of all tumors within the oral cavity [1] [6] and occurrence in the mandible is extremely rare. To the best of our knowledge, only seven cases of primary sarcomatoid carcinoma arising from mandibular gingiva have been reported in the literature, and have shown very aggressive clinical behavior, frequent recurrence, and a high incidence of metastasis (**Table 1**) [1] [7]-[12].

With a male-predominance, sarcomatoid carcinomas show a wide range of age of occurrence from 2nd to 8th decade and a mean age during the 5th decade. The origin of this tumor is controversial. Alcohol consumption, tobacco use, poor oral health and radiation are considered to be the possible predisposing factors. Other factors include genetic predisposition, trauma and inflammation

Table 1. Literature review of published sarcomatoid carcinoma of the mandible cases.

References	Case	Age/Sex	Tumor location/size	Treatment	Outcome
Stojadinovic *et al*., 2002	1	67/M	Left mandible 50 × 40 mm	Preoperative irradiation + Hemi-mandibulectomy and bilateral neck dissection	No evidence of disease at 5 years
Park *et al*., 2006	2	55/M	Left mandible 40 × 40 mm	Palliative chemotherapy	Died of metastatic disease
Kwon *et al*., 2010	4	80/M	Right mandible 53 × 32 mm	No treatment	Died of metastatic disease
Shen *et al*., 2014	3	72/M	Left mandible 30 × 30 mm	Partial left mandibulectomy	Died at 8 months of local recurrence and metastatic disease
Mahajan *et al*., 2017	5	51/M	Left mandible 25 × 20 mm	Mandibular resection and reconstruction with recon plates + adjuvant chemotherapy	Not reported
Shah *et al*., 2018	6	65/F	Right mandible 25 × 35 mm	Not reported	Not reported
	7	42/F	Left mandible 20 × 20 mm		

[2] [8]. Our case concerned a 34-year-old female patient with no apparent predisposing factor.

The clinical presentation varies from an exophytic, pedunculated, polypoid mass with an ulcerated surface to a frankly infiltrative ulcer [2] [11].

The main radiographic and CT appearance of mandibular sarcomatoid carcinoma is diffuse, irregular osteolytic bone destruction with a soft tissue mass [3] [13]. However, these imaging appearances are not unique features of this low-incidence neoplasm. The differential diagnosis includes a number of benign and malignant tumors, such as squamous cell carcinoma, fibrosarcoma, malignant fibrous histiocytoma, leiomyosarcoma, rhabdomyosarcoma, malignant peripheral nerve sheath tumor, osteosarcoma, mesenchymal chondrosarcoma, Kaposi's sarcoma, angiosarcoma, synovial sarcoma, malignant melanoma, fibromatosis, leiomyoma, nodular fasciitis and reactive epithelial proliferations [2].

Therefore, the diagnosis of mandibular sarcomatoid carcinoma can be challenging for the pathologist and must depend on histopathological and immunohistochemical examinations.

Epithelial differentiation and staining for one or more epithelial markers supports the diagnosis. In most cases (26% - 62%) Keratin and cytokeratin are commonly found to be positive. Furthermore, positivity to mesenchymal-type markers is also demonstrated. Almost all of the cases show positivity for vimentin and about a third of them for smooth muscle actin [1] [3].

The optimal treatment of sarcomatoid carcinomas of the head and neck region is not based on high level evidence as this is a rare entity and only retrospective reports have been published. It usually follows the same footsteps as that of squamous cell carcinoma of similar stage. Nevertheless, in comparison to squamous cell carcinoma, within the head and neck region, sarcomatoid carcinoma is considered as a more aggressive tumor, with a tendency to recur and metastasize early [3].

Wide surgical excision, with or without radical neck dissection, is the treatment of choice. It is common for the patients to undergo several surgeries, owing to frequent recurrence. Despite wide-margin surgical resection and improved cooperation between ablative and reconstructive surgeons, the outcome continues to be poor. Currently, there is no literature describing the reconstructive strategies for sarcomatoid carcinomas in the head and neck area. However, caution should be exercised when planning reconstruction after resection. The reconstructive surgeon should take into account the poorer prognosis in such cases and avoid complicated procedures that require long operative time and may increase the rate of perioperative complications, prolong the hospital stay, and potentially delay the initiation of adjuvant therapies [14].

The effectiveness of radiotherapy was suggested by Ballo *et al.* in 1998, however, more recent studies did not confirm the impact of radiotherapy on survival [13]. Most authors agree that irradiation is ineffective. Radiation therapy is considered an acceptable alternative for inoperable patients. Adjuvant (che-

mo)radiotherapy is still under debate and might be of benefit in all cases with high risk features *i.e.* stage III and IV, positive or unclear surgical margins, extracapsular spread, vascular/perineural invasion and nodal metastasis. The role of cytotoxic chemotherapy is unclear [5] [15].

4. Conclusions

Sarcomatoid carcinoma is a very rare, aggressive and highly malignant entity with a complex histogenesis making its diagnosis extremely difficult and often misleading and controversial.

The management of sarcomatoid carcinoma remains challenging due to the rarity of this malignancy, high tendency for local recurrence, distant metastasis, and poor outcome. Surgery is considered to be the mainstay in the management of sarcomatoid carcinomas and should be performed as soon as possible with the aim of complete resection. Adjuvant treatment can be of value in high-risk disease, nevertheless the chance for survival might be poor.

Conflicts of Interest

Authors declare having no conflict of interests.

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