

# Sarcomatoid squamous cell carcinoma of mandible: A report of two cases

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## Abstract

Spindle cell neoplasms comprise a diverse collection of benign and malignant tumors. These tumors are uncommon in the oral cavity, accounting for <1% of all tumors of oral region. Sarcomatoid squamous cell carcinoma (SSCC), also known as spindle cell carcinoma or Lane's tumor, is a rare and peculiar biphasic malignant neoplasm that occurs mainly in the upper aerodigestive tract. It is a variant of squamous cell carcinoma which has spindled or pleomorphic tumor cells which simulate a true sarcoma, but are epithelial in origin. It is an unusual aggressive variant that frequently recurs and metastasizes, reinforcing the importance of its correct diagnosis. We report two cases of SSCC with immunohistochemical findings.

**Keywords:** Biphasic, immunohistochemistry, keratin, spindle cell carcinoma, vimentin

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**Received:** 20.09.2018, **Accepted:** 28.12.2018

## INTRODUCTION

Sarcomatoid squamous cell carcinoma (SSCC) is an unusual form of malignant epithelial neoplasm that exhibits prominent spindle cell morphology. In the literature, a variety of terms are used to designate SSCC including carcinosarcoma, pseudosarcoma, spindle cell carcinoma, pleomorphic carcinoma and polypoid carcinoma. This reflects the divergent interpretation of the sarcomatoid component as reactive or neoplastic, mesenchymal, or epithelial.<sup>[1]</sup> However, the WHO classification of tumors of the oral cavity and oropharynx has placed this disease entity under malignant epithelial tumors of squamous cell carcinoma (SCC).<sup>[2]</sup> Their clinical course is considered aggressive with a high incidence of metastasis.<sup>[1]</sup>

Although they are relatively rare, they consistently pose a significant diagnostic challenge to pathologists. In this

article, we describe two cases of SSCC involving the mandible with special emphasis on histogenesis.

## CASE REPORTS

### Case 1

A 65-year-old female patient presented with pain and discomfort due to a growth on right mandibular gingiva for 15–20 days, which was rapidly increasing in size [Figure 1]. She had a history of tobacco chewing 4–5 times per day for 30 years. Medical history was not significant. Extraorally, slight bulging was noted on lower right side of the face near the corner of the mouth. Lymph nodes were not palpable. Intraorally, a polypoid, pedunculated, reddish-pink growth of approximately 2.5 cm × 3.5 cm was seen on gingiva and extending into the alveolar mucosa on buccal surface in 43–45 region [Figure 1]. It was firm in

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**How to cite this article:** Shah BJ, Tupkari JV, Joy T. Sarcomatoid squamous cell carcinoma of mandible: A report of two cases. J Oral Maxillofac Pathol 2019;23:163.

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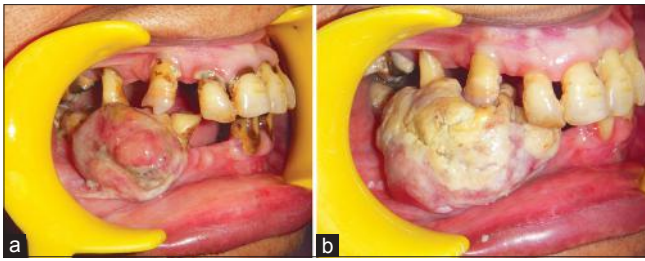


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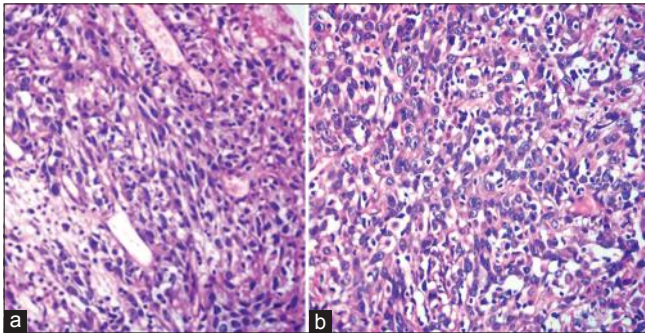
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#### DOI:

10.4103/jomfp.JOMFP\_237\_18



**Figure 1:** (a) Intraorally: Polypoid, pedunculated growth on gingiva, approximately 2.5 cm x 3.5 cm in size and extending on buccal surface in 43–45 region with Grade III mobility of 43, 44. (b) Intraorally: After 15 days, showing increased size of growth with necrotic slough



**Figure 3:** (a) Spindle-shaped cells and epithelial cells (H&E, x40) (b) Pleomorphic epithelial cells with vesicular nuclei and prominent nucleoli (H&E, x40)

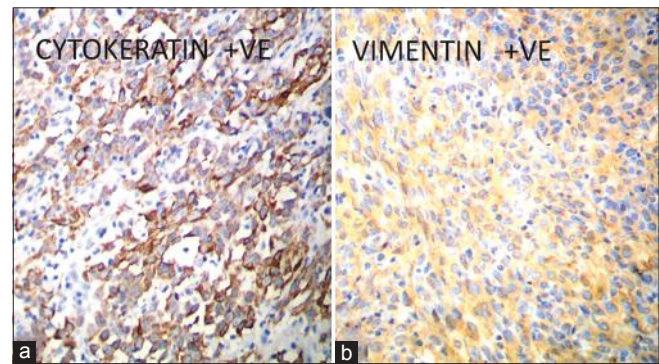
consistency and covered by necrotic slough. The associated teeth – 43 and 44 – were Grade III mobile. Indentations of opposing teeth were seen on the surface of the growth. Intraoral periapical radiograph of 43–44 region showed widening of lamina dura with mild displacement of 43 and horizontal bone loss [Figure 2]. Based on the clinical and radiographic findings, provisional diagnosis of malignant neoplasm with probability of SCC was given.

### Histopathology

Hematoxylin and eosin (H and E) stained slides showed highly cellular polypoidal connective tissue with hemorrhagic and necrotic areas. Two types of cells were seen: one type was of pleomorphic cells with dense hyperchromatic nuclei and dense eosinophilic cytoplasm suggestive of epithelial cells [Figure 3a] and the second type of cells was round to spindle shaped with pale open faced nuclei and prominent nucleoli [Figure 3b]. Abnormal mitotic figures were observed. Mild chronic inflammatory cell infiltrate was seen distributed throughout the stroma. Overall features were suggestive of “high-grade epithelial malignancy.” The tumor cells were immunopositive for cytokeratin [Figure 4a] and vimentin [Figure 4b] and were immunonegative for epithelial membrane antigen [Figure 5a], HMB-45 [Figure 5b], CD-34 [Figure 5c] and



**Figure 2:** Intraoral periapical radiograph of 43–44 region showing horizontal bone loss. Widening of lamina dura and mild displacement of 43



**Figure 4:** (a) Immunohistochemistry: Cytokeratin positive (b) Immunohistochemistry: Vimentin positive

S-100 protein [Figure 5d]. Based on the histopathological and immunohistochemistry (IHC) findings, final diagnosis of SSCC was made.

### Case 2

A 42-year-old female patient reported with a complaint of pain and rapidly growing mass on the left mandibular gingiva for 20–25 days. She had a history of tobacco chewing 2–3 times per day for 15 years. Medical history was not significant. On extraoral examination, slight bulging was seen on the left side of the face. Submandibular lymph nodes on the left side were palpable, tender and mobile. Intraorally, an irregular, localized growth was seen both on buccal and lingual gingiva with ulceration extending from 34 to 36 region of approximately 2 cm x 2 cm in size, reddish pink in color [Figure 6]. It was soft in consistency, tender on palpation and bleed on provocation. Grade I mobility was seen with 35, 36. Radiographically, there was severe interdental and inter-radicular bone loss in the region of 35, 36 [Figure 7]. Based on the clinical and radiographic findings, provisional diagnosis of malignant neoplasm most probably SCC was given.



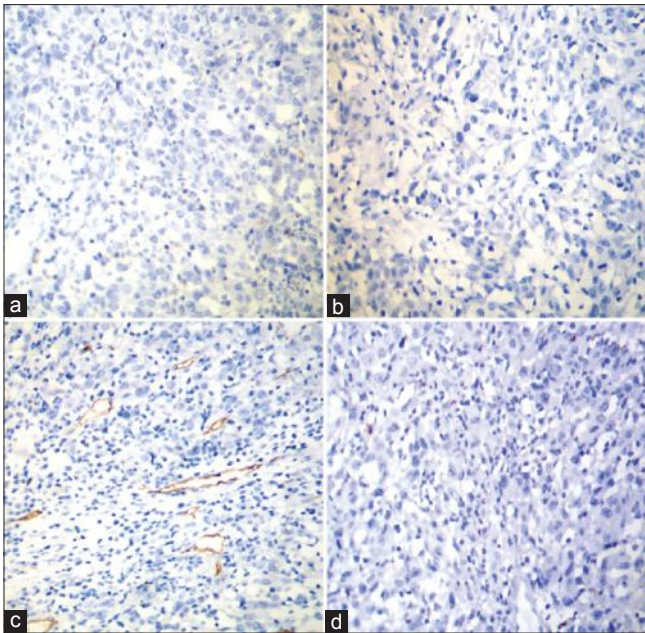


Figure 5: (a) Immunohistochemistry: Epithelial membrane antigen - negative (b) Immunohistochemistry: HMB-45 - negative (c) Immunohistochemistry: CD-34 - negative (d) Immunohistochemistry: S-100 - negative

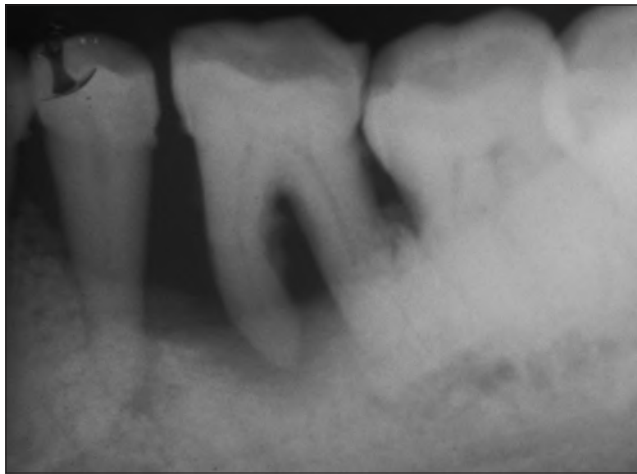


Figure 7: Intraoral periapical radiograph shows severe interdental and inter-radicular bone loss in the region of 35, 36

### Histopathology

It showed highly cellular and vascular connective tissue with necrotic areas at periphery on routine H&E [Figure 8a]. The cellular areas comprised large, pleomorphic cells with dense hyperchromatic nuclei and eosinophilic cytoplasm resembling epithelial cells [Figure 8b]. Cells with pale open faced nuclei and prominent nucleoli were also seen. Abnormal mitotic figures were observed. Mild-to-moderate chronic inflammatory cell infiltrate was seen throughout the connective tissue. Overall features were suggestive of “high-grade epithelial malignancy.” The tumor cells were immunopositive for



Figure 6: Intraorally, an irregular, localized growth seen on gingiva extending from 34 to 36 region of approximately 2 cm x 2 cm in size, reddish pink in color, soft in consistency, tender on palpation and bleeding on provocation. 35, 36 – Grade I mobile

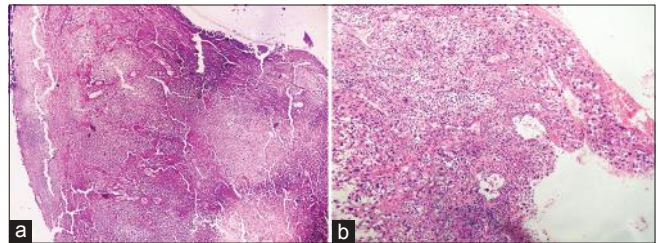
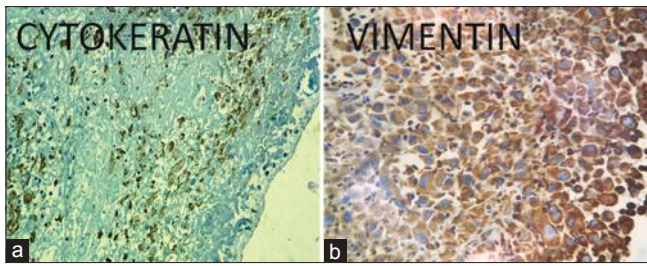


Figure 8: (a) Highly cellular and vascular tissue with necrotic areas (H&E, x4) (b) Large, pleomorphic cells with hyperchromatic nuclei at periphery and central area of lesion (H&E, x10)

cytokeratin [Figure 9a] with proportionately large number of cells showed vimentin positivity [Figure 9b]. The cells were immunonegative for CD-34 and S-100 protein. Based on the histopathological and IHC findings, final diagnosis of sarcomatoid squamous carcinoma was given.

### DISCUSSION

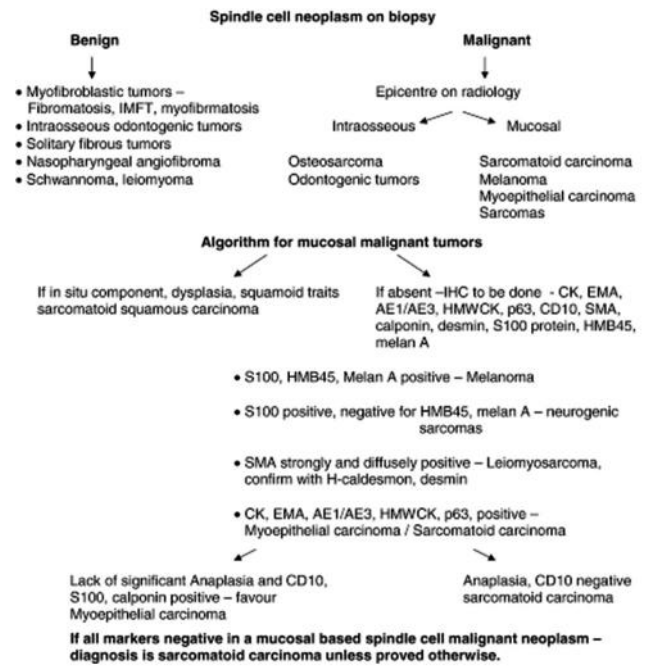
SSCC is a rare, biphasic malignant epithelial neoplasm. It is an unusual variant of squamous carcinoma reported to account for 3% of all SCCs in the head and neck region.<sup>[3]</sup> It consists of proliferation of both sarcomatoid pleomorphic spindle cells and carcinomatous squamous cells.<sup>[2]</sup> Different terms used to designate SSCC are carcinosarcoma, pseudosarcoma, spindle cell carcinoma, pleomorphic carcinoma, polypoid carcinoma, pseudosarcomatous carcinoma, metaplastic carcinoma and Lane’s tumor.<sup>[4,5,2,6]</sup> The initial description of this type of malignancy was reported in 1864 by Virchow, who labeled it as carcinosarcoma.<sup>[7,8]</sup> However, Krompecher is credited with proposing the theory that carcinoma cells can undergo sarcomatous transformation.<sup>[9]</sup> However, the term “spindle cell carcinoma” was first applied by Shervin *et al.*<sup>[11]</sup>



**Figure 9:** (a) Immunohistochemistry: Cytokeratin positive (b) Immunohistochemistry: Vimentin positive

Patient's age at the time of diagnosis ranges from 47 to 88 years, with a mean age of 65.7 years and has more predilection for males.<sup>[2]</sup> The reported cases were present in a 65-year-old and a 42-year-old female patient. Although relatively common in other sites in the body, it is uncommon in the oral cavity, reported to account for <1% of all tumors of oral regions.<sup>[1]</sup> In the oral cavity, the frequent sites involved are lower lip (42%), tongue (20%), alveolar ridge or gingiva (19%).<sup>[10]</sup> The clinical presentation varies from an exophytic, pedunculated, polypoid mass with an ulcerated surface to a frankly infiltrative ulcer.<sup>[2,11]</sup> Alcohol, tobacco, poor oral health and radiation are considered to be the possible predisposing factors.<sup>[2,4,12]</sup> Other factors include genetic predisposition, injury and inflammation in patients.<sup>[13]</sup> In both our cases, the patients had significant history of tobacco chewing. Clinically, polypoid growth with ulcerated surface, covered with necrotic slough involving mandibular alveolar ridge was noticed in both the cases. With radiation as predisposing factor, the time interval from radiation to diagnosis of the tumor ranged from 1.5 to 10 years with a mean of about 7 years.<sup>[10]</sup>

Histopathologically, SSCC shows the presence of two distinct epithelial-derived components: a carcinomatous or SCC component and a sarcomatoid or dysplastic spindle cell component.<sup>[2]</sup> Whenever the surface epithelium is not ulcerated, areas of squamous differentiation are most consistently identified at the base of polypoid lesion, at advancing margins, or within invaginations at the surface.<sup>[2]</sup> The squamous component may be represented by dysplasia, carcinoma *in situ* or frank invasive carcinoma.<sup>[2,13]</sup> SSCC will often present with little invasion into the underlying stroma, as it is polypoid. The carcinomatous and sarcomatoid components will abut directly against one another, with areas of barely perceptible blending and continuity between them. At times, the area of elongation and spindling seems to arise from the basal epithelial cells, making any demarcation indistinct.<sup>[14]</sup> The spindle cell component may assume various histological patterns. The most common ones are pleomorphic (malignant histiocytoma-like) and spindle cell sarcoma (fibrosarcoma-like).<sup>[2]</sup>



**Figure 10:** Approach to the diagnosis of spindle cell neoplasms from mucosal-based sites in the head and neck on biopsy material

Tumors are generally hypercellular, although hypocellular tumors are also recognized. There is no maturation phenomenon. Pleomorphism is often mild to moderate, without a severe degree of anaplasia. The tumor cells are plump fusiform, although they can be rounded and epithelioid. Opacified, dense, eosinophilic cytoplasm, give a hint of squamous differentiation, but is difficult to quantify or qualify accurately. Giant cells of variable types can be seen dispersed throughout the neoplasm. Numerous abnormal mitotic figures are usually observed whereas true tumor necrosis is rare. As would be expected with an infiltrative neoplasm, chronic inflammatory cells can be seen at the base.<sup>[14]</sup> Rarely, metaplastic or frank neoplastic cartilage or bone can be seen.<sup>[14,15]</sup>

The majority of the spindle cell components are nondiploid, which indicates that they are neoplastic and not reactive. The epithelial and spindle components share a common pathway of tumorigenesis despite their conspicuous divergence at the phenotypic level.<sup>[2,16]</sup>

Histological studies alone cannot explain the spindle cell components. The concept that spindle cell elements are epithelial in origin is now proven by positive keratin immunostaining and electron microscopic demonstration of desmosomes and tonofilaments.<sup>[2]</sup> Cells have acquired mesenchymal properties both morphologically and functionally through metaplastic changes. Based on the immunohistochemical studies, it is hypothesized that a



dysfunctional cadherin–catenin complex important for intercellular adhesion causes the tumor cells to shift from a squamous to spindled type, with increased infiltrative behavior. It shows dedifferentiation. The vimentin positivity reflects that these bizarre fibroblast-like cells are carcinoma cells with true mesenchymal metaplasia. The results may be correlated to the concept of a malignant epithelial cell undergoing alterations, resulting in a loss of keratin and acquiring vimentin as the cytoskeleton protein.<sup>[2]</sup> The presence of junctional complexes between tumor cells, with or without pericellular basal lamina and cytoplasmic skeins of intermediate filament, has been demonstrated.<sup>[1,2,16]</sup> Alonso *et al.* found that spindle cell carcinoma demonstrated prominent local invasiveness and high angiogenic response.

Numerous hypotheses regarding the histogenesis of this type of tumor have been proposed. Three dominant pathogenetic theories are that the tumor (1) represents a “collision tumor” (carcinosarcoma), (2) is a SCC with an atypical reactive stroma (pseudosarcoma) or (3) is of epithelial origin, with “de-differentiation” or transformation to a spindle cell morphology (sarcomatoid carcinoma).<sup>[7,8,17]</sup> Recently, the third hypothesis has been supported by following evidences: occurrence in sites that normally have squamous epithelium and preponderance of carcinomas than sarcomas; superficial location; polypoid appearance; direct continuity and smooth transition of spindle cells with areas of squamous epithelium; immunoreactivity with epithelial antigens; dual expression of epithelial and mesenchymal differentiation with double labeling techniques in some neoplastic spindle cells; and the presence of only epithelial, only sarcomatous or a duality of expression in metastatic deposits from laryngeal sarcomatoid carcinoma.<sup>[7,8]</sup>

Furthermore, recent molecular studies have shown evidence of a monoclonal origin from a stem cell capable of divergent differentiation.<sup>[8]</sup> While the convergence hypothesis suggests origin from two stem cell lines, the divergence hypothesis suggests origin from a single stem cell differentiating into epithelial and sarcoma elements. It has been shown that the expression patterns of K-ras gene, p53 gene and X-chromosome inactivation are similar in both the epithelial and sarcomatous components giving support to origin from a single stem cell.<sup>[18]</sup> The tumours are poorly differentiated and show LOH frequencies similar to those of other poorly differentiated SCC's of the upper aerodigestive tract.<sup>[19]</sup>

SSCC in the oral cavity and oropharynx is potentially aggressive and seems to metastasize and recur easily. Although it is difficult to predict biologic behavior in every case, patients whose tumors are deeply invasive tend

to have a poor prognosis, whereas those with early-stage tumors usually have an excellent prognosis.<sup>[2,16]</sup> Distant metastases and depth of tumor invasion into underlying structures were found to be reliable prognostic features, together with their polypoid configuration. Thus, metastatic tumors usually contain squamous cell component or both squamous and spindle cell component and rarely only just the spindle cell component. Treatment includes radical surgery along with neck dissection. Usually, surgery followed by radiation therapy seems to have a better prognosis, similar to conventional SCC.<sup>[14]</sup>

Differential diagnosis includes a number of benign and malignant tumors such as fibromatosis, nodular fasciitis, reactive epithelial proliferations, SCC, fibrosarcoma, malignant fibrous histiocytoma, leiomyosarcoma, rhabdomyosarcoma, malignant peripheral nerve sheath tumor, mesenchymal chondrosarcoma and malignant melanoma.<sup>[7,8,14]</sup>

Immunohistochemical characterization of tumor cells using antibodies to keratin, vimentin and S-100 protein is very helpful in differentiating SSCC from true spindle cell sarcoma, melanoma and malignant myoepithelioma [Figure 10].<sup>[3]</sup> In the IHC, it is important to remember that SSCC should not be ruled out of the differential diagnosis by a positive reaction for vimentin in sarcomatoid tumor cells. The absence of staining for keratin in the sarcomatoid tumor cells does not always exclude SSCC because and some SSCCs show immunoreactivity of keratin only with some anti-keratin antibodies and hence different kinds of anti-keratin antibodies should be applied.<sup>[17,20]</sup> The epithelial marker expression decreases as the degree of epithelial differentiation decreases and may be lost entirely; hence, a negative result does not rule out the diagnosis of sarcomatoid carcinoma.<sup>[9]</sup>

## CONCLUSION

Sarcomatoid squamous carcinoma is an unusual aggressive variant of SCC, which mimics other connective tissue sarcomas and spindle cell malignancies under light microscopy. It frequently recurs and metastasizes, affecting its prognosis. These factors reinforce the importance for correct diagnosis.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will

not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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