Case Report

Lesion of Dual Nature - Carcinoma or Sarcoma: A Histopathologic Dilemma

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ABSTRACT

Sarcomatoid carcinomas are biphasic tumors proven to be monoclonal dedifferentiated forms of conventional squamous carcinomas. It is a variant of squamous cell carcinoma (SCC) which has spindled tumor cells, which simulate a true sarcoma, but are epithelial in origin. They are extremely uncommon in the head and neck region. Only 10 cases have been discussed in the literature. When compared to SCC of maxilla, this variant is associated with poor diagnosis and advanced disease at presentation as is demonstrated in the case presented. Diagnosis of sarcomatoid squamous carcinoma is challenging because of overlapping histopathological features with other spindle-cell tumors. Understanding their clinicopathologic characteristics facilitates their diagnosis and appropriate clinical management. Surgery and radiotherapy form the mainstays of treatment. We report a rare case of spindle-cell carcinoma involving the mandible.

Key words: Cytokeratin, sarcomatoid, spindle-cell lesion, squamous cell carcinoma, vimentin

INTRODUCTION

Spindle-cell squamous cell carcinoma (SCC), also known as sarcomatoid SCC, is a rare variant of squamous cell affecting the upper aerodigestive tract. It was first described by Martin and Stewart in 1935. Spindle-cell carcinoma (SpCC) is a relatively rare malignancy.[1] It comprises up to 3% of all variants of oral SCC (OSCC).[2] The most common site of origin in head and neck region is larynx (particularly vocal cords) and hypopharynx. Usually, oral cavity is not affected.[1] It is a poorly differentiated variant of SCC with a more aggressive behavior.[3] This biphasic tumor is composed of both malignant epithelial and malignant mesenchymal components. There is a wide spectrum of nomenclature for this tumor type such as the carcinosarcoma, pseudosarcoma (Lane 1957), sarcomatoid carcinoma, collision tumor, and pseudosarcomatous carcinoma.[3] The World Health Organization classification of tumor has placed this entity under malignant epithelial tumors of squamous cell and labeled it SpCC.[4] This is a rare entity with only 18 cases reported in the oral cavity. We hereby present before you another case of SpCC.

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CASE REPORT

A 60-year-old male patient visited the outpatient department of Sharad Pawar Dental College and Hospital with the chief complaint of an ulcerative lesion in the lower front region of the jaw since 3 months. He was apparently alright 3 months back then he noticed a small ulcerative lesion in the lower back region of the jaw. The lesion gradually increased to the present size of (4 cm × 3 cm). It was associated with dull aching pain, which was continuous in nature. Patient also gives a history of burning sensation in the same region, which preceded the ulceration. Patient has a habit of chewing tobacco with lime since 15–20 years, 3–4 times/day. He places the quid in the lower lingual vestibule. The general condition of the patient was fair. He gives no history of any systemic illness nor does he give a history of similar treated or untreated lesion in the past or elsewhere on the body.

The extra oral examination revealed a single left submandibular lymph node of size (2 cm × 3 cm)

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approximately palpable. It was oval, firm, tender and fixed to the underlying structures.

The intraoral examination revealed a single linear ulcerated lesion of size (4 cm × 1 cm) app, pinkish in color with irregular surface, everted edges, diffused margins and indurated base. The lesion extended superoinferiorly from crest of the alveolar ridge till the depth of the buccal vestibule and anteroposteriorly from mesial of lower left canine to distal of lower left first molar.

The orthopantamograph of the patient revealed an irregular radiolucency extending from of lower left lateral incisor to lower left first molar region. It extended superoinferiorly from the crest of the ridge till the lower border of the mandible. Floating tooth appearance was seen with lower left second premolar region.

A provisional diagnosis of malignancy was made, and incisional biopsy was carried out after the routine hematological investigation.

Microscopic examination of the incised specimen showed that the tumor consisted of malignant epithelial and mesenchymal components. The bulk of the tumor was mainly composed of bizarre, basophilic, hyperchromatic, pleomorphic spindle-cells accompanying small areas of neoplastic epithelial cells arranged in sheets and islands suggestive of SCC. Invasive spindle-shape cells with frequent and prominent mitotic figures, arranged irregularly with fascicle pattern in some areas and resembling fibrosarcoma were observed [Figure 1]. Spindle-shaped cells revealed pleomorphism, hyperchromatism, and abnormal mitotic figures. Atypical mitoses were abundant [Figure 2]. Together with the spindle-shaped tumor cells, proliferation of polygonal epithelial cells was also seen.

Immunohistochemistry using pancytokeratin was performed. Immunohistochemistry revealed that polygonal lesional cells were strongly positive for cytokeratin. The spindle-cells were focally positive for cytokeratin. Moreover, the spindle-cell component was strongly positive for vimentin [Figure 3].

With this, the final diagnosis of spindle-cell variant of OSCC was made.

However, the patient did not return to the center for further treatment.

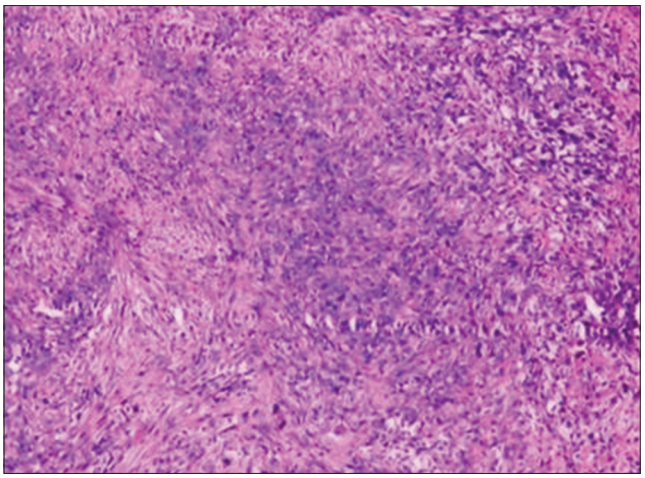

Figure 1: Low power view showing islands of neoplastic epithelial cells

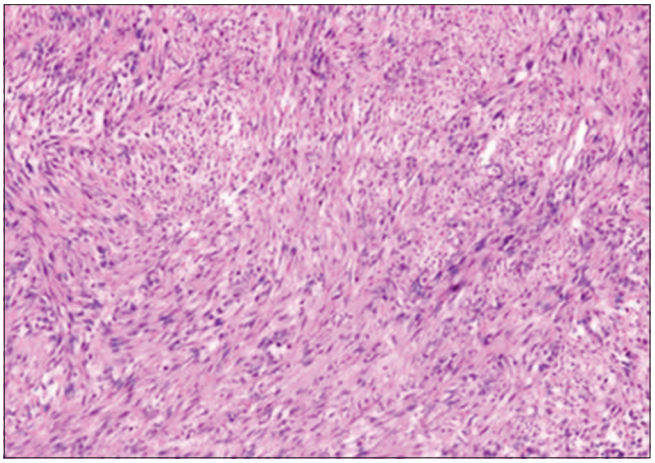

Figure 2: Low power view showing islands of neoplastic epithelial cells along with neoplastic spindle-cell arranged in storiform pattern

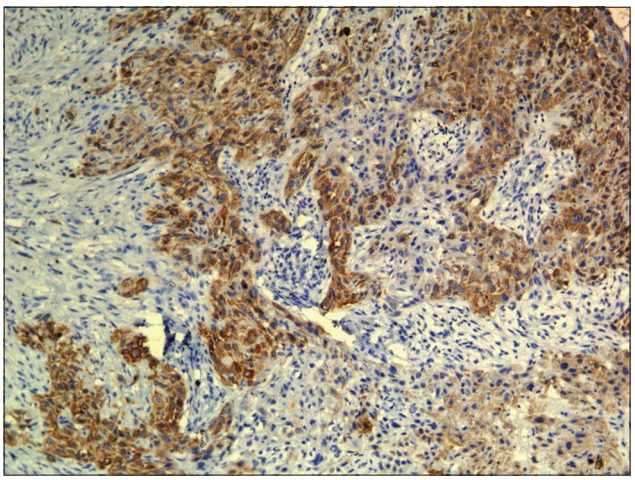

Figure 3: Pan-cytokeratin staining with SCC cells showing strong positivity and focal positivity of spindle-cell reflecting their epithelial origin

DISCUSSION

Squamous cell carcinoma is the most commonly occurring oral malignancy. SpCC is an unusual form of poorly differentiated SCC consisting of elongated (spindle) epithelial cells that resemble a sarcoma.[5] This rare variant of SCC has both malignant squamous cells and spindle-cells component.[3]

Spindle-cell carcinoma is considered to be a biphasic tumor composed of a SCC either *in situ* or invasive and SpCC.[6] It is a monoclonal epithelial neoplasm with the sarcomatous component derived from squamous epithelium with divergent mesenchymal differentiation.[15]

There has been confusion over the basic nature of the sarcomatoid element: whether it is benign or malignant, and mesenchymal or epithelial in origin.[7] Thus, to establish the correct diagnosis, any clue of the epithelial component should be carefully sought in suspected lesions.[5]

Mainly three theories have been proposed to explain the histogenesis of spindle-cells. First theory states that the spindle-cells and epithelial cells arise simultaneously from separate stem cells. Thus, the tumor deserving the name of a "collision" tumor. Second theory explains the nature of the spindle-cell component as an atypical reactive proliferation of the stroma and hence the tumor being called "pseudosarcoma." According to the last theory, both spindle and epithelial components have the same monoclonal origin, and "dedifferentiation" or "transformation" of epithelial cells to spindle-cells has occurred.[3,6,19]

The third theory is greatly supported these days by the evidences that: (1) they occur in the sites that normally have squamous epithelium and a preponderance of SCC rather than sarcomas. (2) A polypoid or the ulcerated appearance similar to SCC. (3) A direct continuity and smooth transition of the spindle-cells with areas of squamous epithelium. (4) Immunoreactivity with epithelial antigens. (5) A dual expression of epithelial and mesenchymal differentiation with double labeling techniques in some neoplastic spindle-cells.[8] The spindle-shape of the tumor cells has been considered to be caused by the lack of expression of cell adhesion molecule such as cadherins and the consequent alteration of keratin filament network.[9] It has been suggested that development of the spindle-cell phenotype involves functional loss of genes that control epithelial differentiation and that conversion to spindle morphology is a recessive entry.[10] Battifora reported the actual transformation of epithelial cells into mesenchymal cells.[5] Tonofilaments have some effect as intracytoplasmic support struts and assist the cell in resisting deformation from external pressures. The relatively rapid loss of desmosomes and tonofilaments which occur in the cells of spindle squamous tumors render them more susceptible to molding from the surrounding stroma. The cells lying between dense bundles of collagen get squeezed into spindle-cells.[19] Alonso *et al*. found that SpCC demonstrated prominent local invasiveness and high angiogenic response. It is known that in the inflammatory state, epitheloid cell might change in shape into spindle morphology to aid in migration. These facts suggest that the spindle-cell pattern might be linked with invasiveness and metastasis.[5]

Although the exact cause of SpCC is not known, it is strongly associated with a history of tobacco intake, cigarette smoking and alcohol abuse as found in our case. It has also been suggested that SpCC is associated with radiation exposure and some authors considering it to be a prerequisite or risk factor for SpCC.[1-3,17] However, as seen in our case, certain other authors have also presented the data opposing the same.[17,18] As in a recent study on 103 cases by Seethalakshmi *et al*. no cases had a prior history of radiation. This discrepancy could be attributed to the fact that, the treatment of choice for primary OSCC is surgery, as against that for the laryngeal carcinomas, where SpCC is mostly seen. SpCC is more predominant in men compared to females (1.2:1 ratio) in the fifth to seventh decade of life at the time of diagnosis. However, the lesion is becoming more common in females.[3,4] The similar findings are seen in our case also.

The subsite distribution in the oral cavity showed that the most common site involved was buccal mucosa and gingivobuccal sulcus, followed by upper or lower alveolus, tongue, hard palate and lip.[1,2,5,17]

The tumors usually grow up rapidly. Although rapid growth was not the case in our patient, the lesion expressed classical polypoid and occasionally the ulcerated appearance.[16] This is in accordance with our case.

The diagnosis of SpCC requires histological demonstration of both the squamous cell component and the spindle-shape cells with sarcomatous appearances. Histopathology shows the presence of SCC at the surface or deeper within the tumor. Although this is rare, especially in the oral cavity tumors, where the surface is ulcerated or denuded. Lesion shows a blending of squamous cells and spindle-cells which can be differentiated by their different arrangement which includes storiform, solid, and fascicular appearance in about half of cases there is also a desmoplastic stromal fibrosis, and because the epithelial cells are capable of transforming into sarcomatoid spindle-cells.[15,17] The typical histopathological features were seen in our case.

In addition to histological studies, immunohistochemical studies of epithelial and mesenchymal markers are used to diagnose a tumor. Epithelial markers include keratin (AE1/AE3, CK1, 8, 9), epithelial membrane antigens, KI, and K18. Mesenchymal markers include vimentin, desmin, S-100, Osteopontin, and bone morphogenetic protein (2, 4).[5, 15] For SpCCs with poorly differentiated epithelial tumor components Lewis *et al*. have shown that p53, a transcription factor that is important for epithelial

proliferation and differentiation, is particularly useful for diagnosing SpCC of the head and neck region.[5,19]

These cases are difficult to differentiate histologically from other spindle-cell lesions, especially atypical fibroxanthoma (AFX). The neoplastic cells of AFX are highly atypical and are variably fusiform or pleomorphic with few bizarre multinucleated cells. The predominant cells in AFX are plump, spindle-shaped, and occur in poorly arranged fascicles. The cells have a prominent nucleus which is often vesicular. Mitotic activity is usually brisk. Typically AFX cells shade off at the periphery to blend with the surrounding dermal fibroblasts; this feature when present can help make this diagnosis.

The differential diagnosis includes a number of benign and malignant tumors, such as SCC, 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.[9,12]

Spindle cell carcinoma in the oral cavity and oropharynx is potentially aggressive and seems to recur easily and to metastasize.[5] The primary treatment modality for sarcomatoid carcinoma should be the same as for SCC, and surgical excision is the preferred treatment.[12] Poor prognosis has been reported in patients treated with radiotherapy, which is considered to be ineffective, although adjuvant irradiation may be beneficial in patients who have positive surgical margins or who have nodal metastasis at the time of diagnosis.[13] The role of chemotherapy has not been established, but it may decrease the incidence of recurrence or metastasis of primarily sarcomatous tissue.[14]

CONCLUSION

Spindle-cell carcinoma shows plump spindle-cells in transition from SCC, and thus may be considered to arise as a sarcomatous transformation of SCC. This transformation may explain the increased aggressiveness seen in SpCC.

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