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Case Report

Dentistry Section

Fallacious Carcinoma-Spindle Cell Variant of Squamous Cell Carcinoma

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ABSTRACT

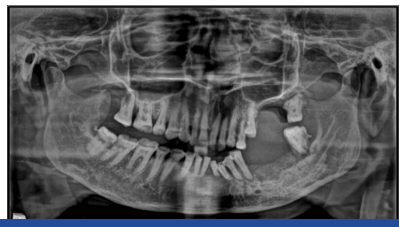
Spindle cell carcinoma is a unique, rare and peculiar biphasic tumour of head and neck which is not frequently observed in the oral cavity. This variant of squamous cell carcinoma although of monophasic epithelial origin, simulates a sarcoma and is an aggressive carcinoma with high frequency of recurrence and metastasis. A correct and timely diagnosis is of paramount importance. Most of the tumours require an Immunohistochemistry (IHC) panel for confirmation or diagnosis. We report a case of spindle cell carcinoma with varied histopathological morphology and clinical presentation in a middle aged female with a brief review of literature.

Keywords: Alveolar ridge-(mandible), Biphasic histopathology, Carcinosacoma, Lane's tumour

CASE REPORT

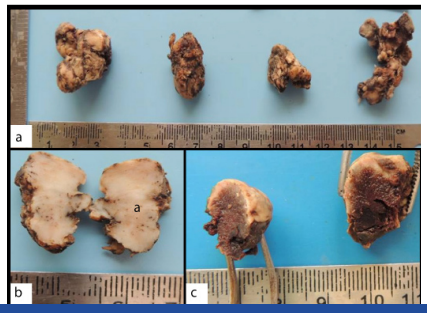
A 60-year-old female reported to the clinic with a large intraoral mass. Patient complained of inability to eat, swallow and breathe comfortably. She gave a history of growth, over a span of 1 year. A positive habit history of 30 years was present for tobacco (chewable form). The patient was symptomatic for last 10-11 months, mainly complaining of inability to swallow, breathe and talk because of the obstructive mass. Inspection and palpation revealed an 8cm × 6cm mass on the left mandibular alveolar ridge. The mass formed a large bosselated swelling covered by a thin epithelium [Table/Fig-1]. The lesional mass involving the lingual vestibule showed areas of ulceration. It appeared firm and non tender in nature. Level II lymphnodes were palpable and were firm and nontender.

An extra-oral roentgenograph revealed a lytic lesion extending from distal aspect of 34 to mesial aspect of 38 and involved the retromolar area. Erosion of the bone with irregular jagged edges was seen involving the alveolus and underlying bone of the mandible extending from 34 to 38 without the involvement of inferior alveolar canal [Table/Fig-2].



[Table/Fig-1]: Intra oral photograph showing a large bosselated mass on the left alveolar ridge extending from the region of 33 till the retromolar area and involving both buccal and lingual vestibule.
[Table/Fig-2]: Orthopantomograph showing irregular lytic lesion with jagged edges in left mandible extending from distal aspect of 34 to mesial aspect of 38 involving the retromolar area. The soft tissue shadow is seen extending uptill the maxillary molar region.

An incisional biopsy was done and it was reported as malignant spindle cell lesion of aggressive nature. The tumour mass was excised with radical neck dissection under general anaesthesia. The tumour mass was highly friable and haemorrhagic in nature. It crumbled into many bits while it was being excised. The excised specimen was firm to rubbery in consistency, was homogenous in some areas and haemorrhagic in other sites [Table/Fig-3]. Multiple areas of necrosis were also noted.



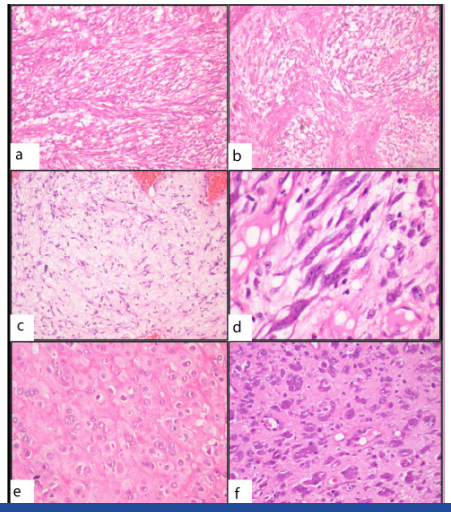
[Table/Fig-3a-c]: a- Grossing specimen showing multiple friable soft tissue bits.
b- Cut surface showing homogenous areas.
c- Cut surface showing haemorrhagic areas.

On histopathology, the tumour showed spindle cells arranged in various patterns. Some areas showed hypercellularity with spindle cells arranged in fascicles, storiform-like pattern and were admixed with mixed inflammatory cells [Table/Fig-4a&b]. Hypocellular areas were seen which showed few dysplastic spindle cells laid in a stroma which was rich in extracellular matrix, hyalinization and granulation tissue [Table/Fig-4c&d]. In one area subepithelial area showed chondroid differentiation [Table/Fig-4e]. Epitheliod cells were also seen in small nests and islands in stroma rich in eosinophilic hypocellular areas [Table/Fig-4f]. Superficial areas showed complete loss of epithelium with ulceration. Underlying tumour showed fibrinoid necrosis and numerous small capillaries and granulation tissue. Deeper areas revealed dysplastic epithelium invading the connective tissue [Table/Fig-5a&b]. The squamous dysplastic cells showed normal and abnormal mitotic figures [Table/Fig-5c]. Areas of necrosis and haemorrhage were also seen.

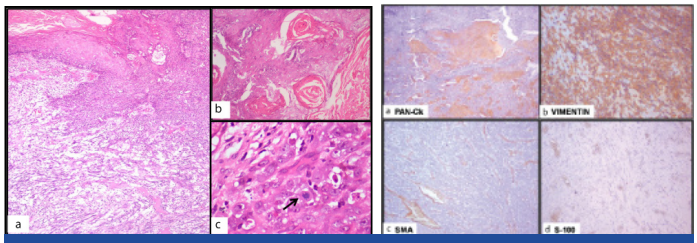
A diagnosis of Spindle cell carcinoma was made and IHC markers were used for confirmation. Pan-Cytokeratin (PanCK), vimentin, SMA, S-100, Ki-67 and p63 were done.

The cells showed positive expression for pancytokeratin in the epitheloid cells in the cytoplasmic domain [Table/Fig-6a]. Almost all the spindle cells stained deeply with vimentin [Table/Fig-6b] which was patchy in the epithelium.

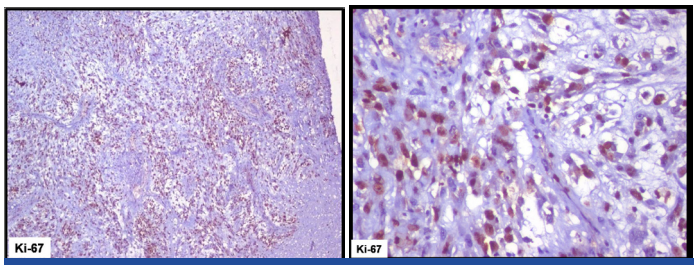
SMA was negative and was positive only in the cells lining the capillaries [Table/Fig-6c] and a patchy S-100 positivity was seen [Table/Fig-6 d]. Ki-67 showed 70% activity [Table/Fig-7,8] and P63 was negative [Table/Fig-9].



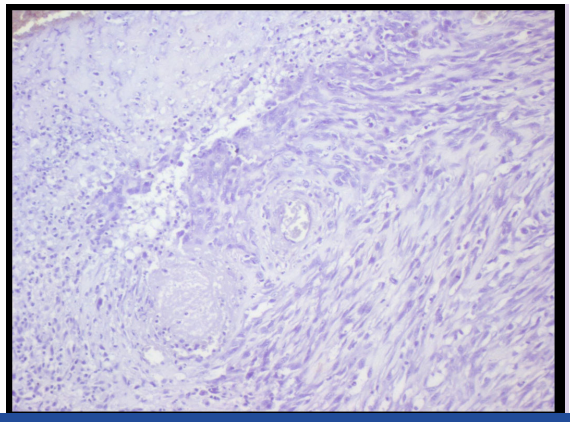
[Table/Fig-4a-f]: a) Malignant spindle shaped cells arranged in streaming fascicles (H&E stain, x100).
b) Malignant spindle shaped cells arranged in storiform -like pattern (H&E stain, x100).
c) Bizarre spindle shaped cells seen in hypocellular areas on myxoid background. (H&E stain, x40).
d) Dysplastic spindle shaped cells showing celluar and nuclear pleomorphism. The spindle cells show binucleation with prominent nucleoli. (H&E stain, x400).
e) Connective tissue stroma showing areas of chondroid differentiation. (H&E stain, x200).
f) Connective tissue stroma showing epitheloid cells arranged in small nests. (H&E stain, x200).



[Table/Fig-5a-c]: a) The overlying dysplastic epithelium invading underlying connective tissue stroma (H&E stain, x40).
b) Dysplastic epithelium showing keratin pearls. (H&E stain, x100).
c) Dysplastic epithelial cells showing mitotic figures. (H&E stain, x400).
[Table/Fig-6a-d]: a) Epithelium and nests of tumours cells showing positivity for PAN-CK (IHC stain, x40).
b) Spindle cells showing positivity for vimentin. (IHC stain x40).
c) Tumour cells were negative for SMA. The blood vessels showed positivity for SMA (IHC stain x40).
d) The tumour cells showed patchy positivity for S-100. (IHC stain, x40)



[Table/Fig-7]: More than 70% of tumour cells were positive for Ki67 antigen (IHC stain, x40).
[Table/Fig-8]: Tumour cells showing positivity for Ki67 antigen (IHC stain, x400).



[Table/Fig-9]: Tumour cells were negative for P63 (IHC stain, x100).

A confirmatory diagnosis of spindle cell carcinoma was given. Positive lymph nodes at level II, were also confirmed histopathologically. On follow up, within a span of 10 months to 1 year, the patient had developed multiple metastasis to the lungs and the patient eventually died due to the disease process.

DISCUSSION

Spindle cell carcinoma is a biphasic tumour with epitheloid and spindle shaped neoplastic proliferation of cells accounting for 3% of squamous cell carcinomas. Biphasic morphology is a cardinal rule to call a tumour carcinosarcoma. It also derives various names because of this -carcinosarcoma, pleomorphic carcinoma, Lane's tumour, malignant mixed Mullerian tumour, pseudocarcinoma, pseudosarcoma, sarcomatoid carcinoma [1].

The first description of this tumour was given by Virchow (1864). The name accepted by WHO, proposed by Shervin et al., is spindle cell carcinoma [2]. A tumour that is predisposed by factors like tobacco, alcohol, poor oral health and irradiation. Commonly a polypoid exophytic mass with hyper and hypocellular areas seen histologically, predominant in spindle cell morphology [3]. It is a carcinoma with conflicting theories of histogenesis. Irrespective of variable names and theories spindle cell carcinoma is treated and staged as conventional squamous cell carcinoma.

Spindle cell carcinoma accounts for 1% of all tumours of oral region [4]. It is commonly encountered in larynx, hypopharynx, oesophagus, nasal cavity and trachea. It is rare tumour in the oral cavity [4,5]. A tumour called by various names is ideally called as spindle cell carcinoma as approved by WHO as a variant of squamous cell carcinoma. The tumour is frequently a polypoidal, sessile, soft tissue mass with surface ulceration. It is firm to rubbery in consistency and non tender in nature, sometimes giving a false picture of benign/ reactive growth. Our case showed a bosselated firm mass with a fast growth rate.

Similar cases of spindle cell carcinoma in the oral cavity affecting the alveolar ridge were reported by Prakash N et al., in a 65-year-old female involving socket region irt 47 and by Parikh N et al., in a 65-year-old male involving left maxillary alveolar ridge [2,6].

Spindle cell carcinoma is common in 6-7th decade of life with a profound male domination (M: F-11:1) [7]. The present case was in a 60-year-old female with a history of an expansive mass in the oral cavity since 1 year. The tumour is generally exophytic, polypoidal mass, firm and non-tender [3]. The duration of symptom is less than 1 year in 95% of patients [5]. Our case showed a large 8cm × 6cm exophytic soft tissue mass in the left alveolar region extending into the pharynx and retromolar area. It was polypoidal mass which was asymptomatic and appeared creamish white in colour interspersed with erythematous areas. Spindle cell carcinoma is said to be predisposed by factors like tobacco habit, alcohol, irradiation exposure, poor oral hygiene [3,4]. In our case, the patient had a history of chewable form tobacco consumption since 30 years. The histogenesis of this tumour is quite intriguing, there are many theories proposed. The first theory states that it's a collision tumour which is defined as two separate neoplastic clones combined in the same lesion [8]. The Second theory states that it is due to the atypical reactive stroma which gives a pseudosarcoma picture. The Third theory states that the tumour is of epithelial origin which has undergone de-differentiation. There is enough support for this tumour to be of single cell origin as the tumour shows monoclonal origin from stem cells [3,9].

The epithelial and spindle components share a common pathway of tumorigenesis despite their conspicuous divergence at the phenotypic level. The concept was advanced by Kettle and Krompecker who stated that the epithelial cells could assume the morphologic characteristics of mesenchymal cells. Saphir and Vass concluded that most of the lesions were actually carcinomas with spindling features supporting the monoclonal origin [2].

There is also strong evidence that the transformation of the epithelial cells into spindle cells are envisaged to be a part of Epithelial-Mesenchymal Transition (EMT) showing phenotypic plasticity at the microscopic and IHC level [4,5].

EMT is the process by which epithelial cells adopt a mesenchymal phenotype or fibroblast-like properties. The epithelial cells undergoing EMT involve reorganizing their cytoskeleton, stretching out and breaking connections with their neighbors [10].

At microscopic level, the morphology of the cancer cells undergoing EMT switch their epithelial characteristics (cobblestone-like, nonmotile and noninvasive) to their mesenchymal elongated, motile, and invasive characteristics [10]. In our case, a transition of the non-motile polygonal shaped epithelial cells to spindle cells with invasion of the cells into underlying connective tissue was noted as shown in [Table/Fig-5a].

In general, cells proceeding towards EMT exhibit down-regulation of many epithelial markers, including E-cadherin, desmoplakin, cytokeratins, claudins, occludins, and beta-catenin and up-regulation of mesenchymal markers, including N-cadherin, vimentin, fibronectin, and Snail-1/2. The process of EMT can be assessed at IHC level using selected markers which show concurrent presence of malignant epithelial and sarcomatoid spindle cell components by co-expression of cytokeratin (CK) and vimentin [10]. This assessment was carried out by Sarma et al., who analysed 40 cases of Spindle cell carcinoma and found concurrent presence of CK and vimentin to various degrees in the tumour cells [11]. Gui-Young Kwon et al., in their case report did show that the tumour cells were immunoreactive for both pancytokeratin and vimentin, supporting the diagnosis of spindle cell carcinoma [9]. In our case, both CK and vimentin were positive in tumour cells confirming the diagnosis of spindle cell carcinoma.

HISTOPATHOLOGY

The tumour shows hypo and hypercellular areas [3] where the mesenchymal component is more frequently observed with very little epithelial component. The mesenchymal cells are classically spindle cells in different patterns, the common ones being that of malignant fibrous histiocytoma and fibrosarcoma [2,6]. The mesenchymal differentiation can include cartilage formation, bone like calcification, stromal metaplasia [1,5,12]. In instances, the tumour cells show relation to extensive inflammation and granulation tissue simulating inflammatory reactive lesions. The mesenchymal part may show myxoid areas and variable amount of intervening matrix. The presence of numerous sarcomatoid component in various patterns makes it to mimic a mesenchymal malignancy.

The sarcomatoid component is divided into 3 grades [5].

Grade 1-Mild anaplasia
Grade 2-Moderate anaplasia
Grade 3-Severe anaplasia

The epithelial component is not seen frequently for evaluation as most of the tumours show ulceration and fibrinoid necrosis [5]. Depending on the amount of epithelium seen the tumours are divided into 3 groups.

Group I- Frank epithelial differentiation at light microscopic level

(Dysplasia, carcinoma-in situ, squamous nests, lymph node metastasis).

Group II- Epithelial differentiation at IHC level (cytokeratin, AE1/AE3, CK5/6, EMA).

Group III- No evidence of epithelial differentiation.

In 60-70% cases, the epithelial differentiation is seen at the stalk of the polypoidal mass at the deepest part of the advancing front [7]. The squamous component is generally intricately mixed with the spindle cells and show a moderate to poor differentiation, mitotic figures both normal and atypical are frequent finding [1,5].

The present case showed a mesenchymal component which formed most of the tumour mass made of spindle cells in fascicles and storiform pattern with a variable amount of stroma of collagen and extra cellular matrix. An area of chondroid differentiation was seen close to the epithelium. Hypo and hypercellular areas with areas of dense inflammatory response and granulation tissue was a frequent finding. The carcinomatous component was seen as dysplastic epithelium invading into the connective tissue stroma with formation of bizarre spindle cells at the advancing front. Multiple mitosis, normal and abnormal were cited. All in accordance to the references cited. The tumour fell in group I as epithelial differentiation was seen and confirmed at light microscopic level and grade III as the sarcomatous element showed severe dysplasia, as pleomorphism and mitosis was noted in these cells.

A large panel of IHC markers are used in the diagnosis of spindle cell carcinoma depending on the variability of the carcinomatous and sarcomatous component. Commonly used ones being CK, Epitheial Membrane Antigen (EMA), High Molecular Weight CK (HMWCK), vimentin, calponin, P63, CD31 and 34, S-100 and Human Melanoma Black (HMB)-45. In some instances CD10 and CK5/6 are also used. Most of the markers are used to show positive epithelial differentiation to rule off mesenchymal malignancy like angiosarcoma (CD31,34), leiomyosarcoma (calponin), malignant melanomas (HMB45) and malignant fibrous histiocytomas [2,5].

Our case showed a marked CK positivity in epithelial component and vimentin in spindle cell population, S-100 was patchy and SMA, P63 were negative. Ki-67 activity was more than 70%. Confirming a diagnosis of spindle cell carcinoma showing a poorer differentiation.

A differential diagnosis of mesenchymal sarcomas like leiomyosarcoma, fibrosarcoma, angiosarcoma and melanoma is frequently considered because of variable patterns seen in histopathology [1]. A detailed clinical data with a detailed scanning of different areas of tumour histopathology along with a good IHC panel should generally help to diagnose the tumour as was seen in the present case. The staging of spindle cell carcinoma is the same as for conventional Squamous Cell Carcinoma (SCC) [3].

The surgical staging of tumour is very important as it is characterized by recurrence and metastasis [3].

The tumour has 26-75% metastatic rate to the lymphnodes. Some authors state that if metastatic rate is as high as 36%, 2 year survival rate is 55%. [5,6] It has a high recurrence rate [3] with 5% rate of distant metastasis and lung being the frequent site of metastases.

Mortality rate is 14-47% in head and neck tumours [1,13]. Most of the cases are treated with surgery and radiation. The present case was treated with surgery and radiation regime and was under regular observation.

CONCLUSION

The common presentation of Oral Squamous Cell Carcinoma (OSCC) is in the form of a verrucous, verruco-proliferative or ulcerated lesion. In the histopathology also it presents as a well differentiated tumour with squamous differentiation frequently, whereas Spindle cell carcinomas are always deceptive. In our case, clinically the appearance of the lesion was polypoid soft tissue growth resembling that of soft tissue tumours. On histopathology also tumour cells show wide variations masking the epithelial features and pointing more towards a mesenchymal differentiation. The presentation is diverse with areas mimicking fibrosarcoma, chondrosarcoma, angiosarcoma and Leiomyosarcoma as seen in our case. These features give us a wide spectrum of differentials that has to be ruled out with ancillary techniques like immunohistochemistry. These features emphasize that the tumour can be rightly called as Fallacious Carcinoma.

It is important to know the clinical and histopathological variation in spindle cell carcinoma as it is infrequently seen. The timely diagnosis is paramount as it is a more aggressive and poorly differentiated variant of squamous cell carcinoma. It has a higher rate of metastasis to lymphnode and other sites.

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