SPINDLE CELL CARCINOMA OF MAXILLA:CASE REPORT OF A RARE ENTITY AND REVIEW OF LITERATURE

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Abstract

Spindle cell Carcinoma is a rare biphasic neoplasm consisting of epithelial and mesenchymal components and accounts for less than 1% of all tumours of oral region. It is a rare aggressive variant of squamous cell carcinoma which frequently recurs and metastasizes with poor prognosis compared to classical squamous cell carcinoma. The biologic behaviour is comparable to poorly differentiated Squamous Cell Carcinoma. The 5 year disease free survival rate is approximately 30% for all Oral Tumors. The variants of squamous cell carcinoma frequently arise in mucosa of upper aerodigestive tract. The most common site in head and neck region is in larynx and hypopharynx; the oral cavity being rarely affected. This biphasic malignant neoplasm often assumes a sarcomatous appearance and may present diagnostic difficulty. Hence careful histopathologic analysis is warranted. We report a rare case of spindle cell carcinoma in unusual location with immunohistochemical findings and review of the literature.

Key words: Spindle cell carcinoma, Maxilla, Pancytokeratin, Vimentin

Introduction

Spindle cell carcinoma is rare variant of squamous cell carcinoma. It is important to understand their microscopic peculiarities for correct diaganosis & proper treatment. It occurs mainly in upper aerodigestive tract [(1)]. They may be encountered frequently in larynx, nasal cavity, hypopharynx, oral cavities, esophagus, trachea, skin & breast. The tumour is designated by variety of terms because of their microscopic pecularity and the various terms include carcinosarcoma, pseudosarcoma, sarcomotoid squamous cell carcinoma, pleomorphic carcinoma & polypoid carcinoma. The WHO classification of tumour has placed this entity under malignant epithelial tumours of squamous cell carcinoma and labeled it spindle cell carcinoma [(2)]

Spindle cell carcinoma is an unusual aggressive variant of squamous cell carcinoma that frequently recurs & metastasizes and hence the importance of correct diagnosis & proper treatment [(1)]. Only few cases reported in the medical literature hence the purpose of this case report; and a review of literature was carried out.

Case Report

A female patient aged 60 years reported to dental OP with complaint of swelling of gums and mobility of teeth in upper right posterior region since 4-5 months. Intra oral examination revealed exophytic mass showing irregular to poorly defined margins with surface ulceration of size 4x3 cm (Fig. 1). Lesion extending anteriorly to upper right canine, Posteriorly to right maxillary tuberosity, medially to midpalatine raphe. On palpation lesion was indurated and tender. Routine lab investigation carried out & found to be within normal limits. CT PNS and neck (Fig. 2) revealed heterogenous

enhancing soft tissue lesion noted in right maxilla and oral cavity. Superiorly it is eroding the right maxilla and floor of the right maxillary sinus and invading into sinus cavity. Posteriorly it is extending to lateral pterygoid plates & is closely related to right parotid gland with clear planes of separation. Anteriorly lesion is seen extending to anterior aspect of right maxilla till canine region. The lesion measures 39x25 mm with density difference of 40 HU causing destruction of right maxilla and alveolar process. Evidence of soft tissue density of fluid level noted in right maxillary sinus. Rest of frontal sinuses and maxillary sinus normal. There is evidence of multiple enlarged and small lymph nodes noted in right submandibular, cervical region along jugular vesels. Features suggestive of malignant process.

Incisional biopsy was taken from right upper molar region. Histopathological examination revealed dysplastic epithelium with islands of neoplastic epithelial cells invading underlying connective tissue & diagnosis of moderately differentiated squamous cell carcinoma was made.

The treatment undertaken was hemimaxillectomy and supraomohyoid lymph node neck dissection. On histopathological examination the given tissue section consisted predominantly of spindle cell component which showed hypercellular and hypocellular area with variable collagen. On high power view anaplasitc pleomorphic cells showing frequent mitosis (Fig. 3 and 4). On serial section few cells with squamoid features seen which constituted a minor component of tumour section (Fig. 5). It presented with diagnostic difficult. On the basis of histopathology differential diagnosis suggested was poorly differentiated squamous cell carcinoma, malignant mesenchymal neoplasm, spindle cell variant of melanoma.

The sarcomatoid like appearance predominated & hence to ascertain the true nature of spindle cell component Immunohistochemical analysis was undertaken. Immunohistochemistry revealed that spindle cells showed immunoreactivity for pancytokeratin, vimentin (Figure 6 and 7), no immunoreactivity for desmin. Spindle cells showing positivity for pancytokeratin suggested its epithelial origin and hence a diagnosis of spindle cell carcinoma was made.

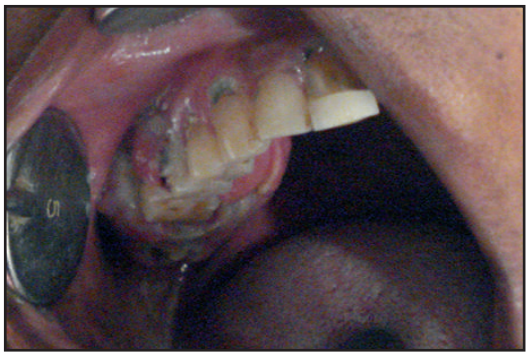

Fig. 1 : Exophytic lesion with poorly defined margins showing surface

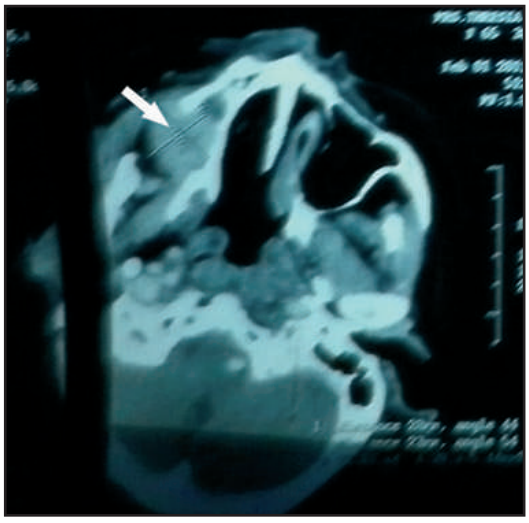

Fig. 2 : CT PNS & Neck suggestive of malignant process

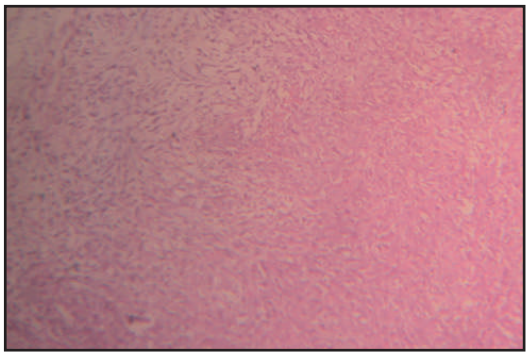

Fig. 3 : Neoplastic spindle ceslls in diffuse pattern in variable collagenous stroma (H&E stain 10x)

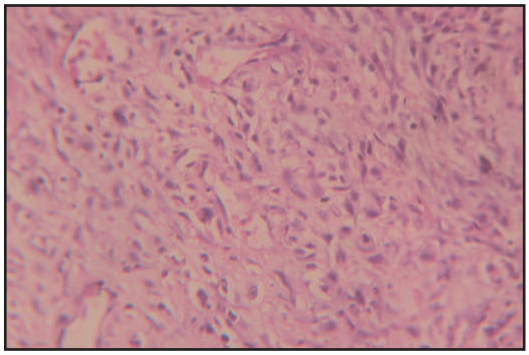

Fig. 4 : Anaplastic spindle cells with hyperchromatism, pleomorphism, prominent mitosis (H &E stain 40 x)

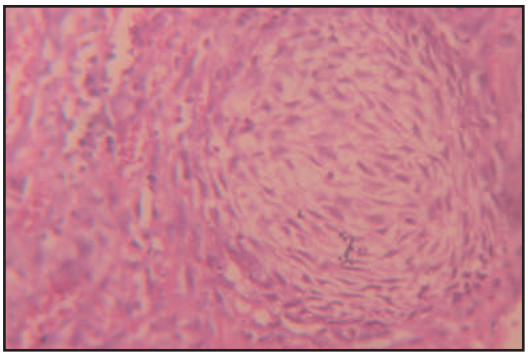

Fig. 5 : High power view showing squamoid feature (H&E stain 40x)

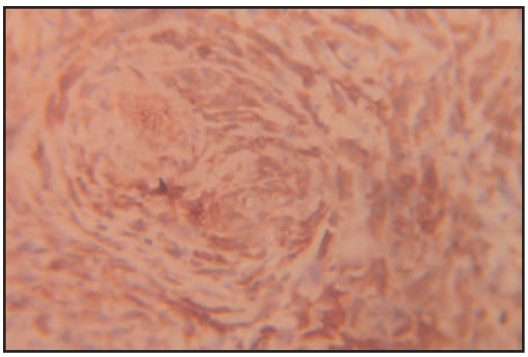

Fig. 6 : Spindle cells positive for pancytokeratin

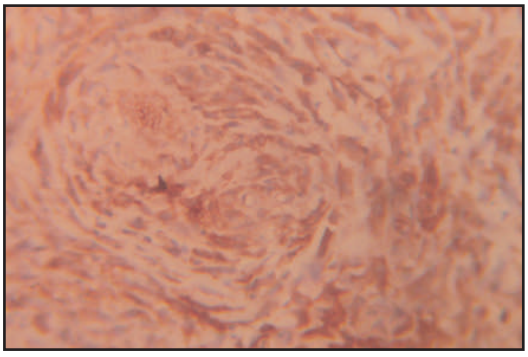

Fig. 7 : Spindle cells positive for vimentin

Discussion

Spindle cell carcinoma account for less than 1% of all tumours of oral regions[3]. It is biphasic malignant neoplasm with confusion ever the basic nature of sarcomatoid element whether it is benign or malignant,and mesenchymal or epithelial in origin. The sarcomatoid cells thought to be derived from squamous cells and the epithelial nature of the sarcomatoid component of spindle cell carcinoma was revealed by combination of immuno histochemical staining for keratins and electron microscopic demonstration of tonofilament / or desmesome like structure[2].

The age at the time of diagnosis range from 47 to 88 yrs with mean age of 65.7 yrs and shows predilection of male patient [2]. The clinical presentation vary from exophytic ulcerated mass, polypoid nodule infiltrative ulcerated lesion [4]. The present case showed exophytic ulcerated mass. Four factors considered to be possibly predisposing for this disease - tobacco, alcohol, poor oral health, previous irradiation to area of tumour. Some author emphasized that radiation or trauma induces spindle cell carcinoma [6]. The present case was female aged 60years with history of paan chewing.

The tumour shows the presence of two distinct, epithelial derived components and sarcomatoid or dysplastic spindle cell component. The spindle cell component may assume various histological patterns. The most common ones are pleomorphic (malignant histiocytoma like) and spindle cell sarcoma (fibroscaroma like) [2]. The spindle cell component may present diagnostic challenge especially when squamous cell component is not obvious. The spindle cell component may resemble lesions ranging from benign reactive lesion like radiation induced granulation tissue to malignant lesions like fibrosarcoma. Three different theories proposed to explain histogenetic nature of spindle cells. First theory states that spindle cells & epithelial cells arise from separate stem cells & hence the name collision tumour. Second theory explain spindle cell

component as an atypical reactive proliferation of the stroma & hence the term pseudosarcoma. Finally last theory states cells of both spindle & epithelial components have same monoclonal origin & dedifferentiation or transformation to spindle cells occurred. Several studies revealed that spindle cells have similar characteristic feature of squamous cells in immunohistochemical, ultrastructural, molecular & genetic aspects[5,11,16]. The carcinomatous portion comprise very minor portion and hence the diagnostic difficulty encountered in the present case.

Histological studies alone cannot explain the spindle cell components. Recent IHC studies attempted to explain histogenesis of the spindle cells within these tumours and the concept that spindle cell elements are epithelial in origin is now proven by positive keratin immunostaining and demonstrating of desmosomes and tonofilaments in the cells strongly supported[5]. Immuno histochemically most sensitive and reliable epithelial markers for demonstration of epithelial phenotype are keratin and epithelial membrane antigen which is useful in differential diagnosis from other sarcomatous lesions. The vimentin positivity reflects that these bizarre fibroblast like cells are carcinoma cells with true mesenchymal metaplasia. The results indicate that these cells have acquired mesenchymcal properties both morpholgically and functionally through meteplastic changes and simply correlated to the concept of a malignant epithelial cell undergoing alterations, resulting in loss of keratin and acquiring vimentin as cytoskeletal protein. The double labeling with keratin and vimentin in spindle cells illustrating the versatility of the interemediate filament phenotype. It has been suggested that development of spindle cell phenotype involves functional loss of genes that control epithelial differentiation and that conversion to spindle morphology in a recessive entry. P63 has been reported as useful marker for spindle cell carcinoma[2].

Although the spindle cell component forms the bulk of the tumour definitive squamous differentiation usually is seen, sometimes at the advancing front or within invaginations at surface where epithelium is not ulcerated or denuded[13,16]. In the present case we could see few squamous cells at the advancing front. The tumour may be hypocellular or hypercellular with obvious malignant pleomorphism with typical & atypical mitotic figures. The cellular arrangement may appear storiform, herringbone, fasicular, loose or even hypocellular with dense collagen[16]. The cells were pleomorphic with large, oval-round, vesicular nuclei. Bizarre cells, frequent mitotic figures observed in sarcomatous component. The absence of keratin pearls, large number of mitosis indicate that the clinical behaviour might be close to that of poorly differentiated squamous cell carcinoma.

The importance of IHC undertaken in the present case to make a diagnosis because bulk of the tumour composed of anaplastic cells and on repeated serial sections could make out only few cells with squamoid features. Several studies regarding their intermediate filament pattern has been published. The spindle cells invariably express vimentin reactivity, keratin expression being more variable.

Kudo et al found that spindle cell squamous carcinoma cells expressed wnt-5a and vimentin mRNA at high levels, but did not express E-cadherin mRNA. This expression pattern was similar to that of fibroblast, not of oral squamous carcinoma cells. Their findings suggest that nature of spindle cell squamous carcinoma cells may be similar to mesenchymal cells & the positvity for cytokeratin showed epithelial nature of spindle cell squamous carcinoma cells[1]

According to shibuya *et al* there was notable difference in immunostaining pattern between squamous cell carcinoma and spindle cell carcinoma. The positive immunoreactivity for cytokeratin, α-cat and β cat shown everywhere in squamous cell carcinoma tumour but only in some foci in spindle cell component. Keratin expression decreases whereas vimentin expression

increases in spindle cell of spindle cell carcinoma[5]. There was severely reduced expression of E-cad & the heterogenous expression of α cat or β cat are responsible for morphologic shift from converntional squamous cell carcinoma to sarcomatoid component in spindle cell carcinoma. According to shibuya etal the expression of cadherin- catenin complex was regarded as hall mark of epithelial cell. It is believed that dysfunctional cadherin catenin complex causes cells to shift in morphology from squamoid to a more spindled type and permits a more infiltrative & diffuse pattern of growth[5].

The concept that sarcomatous portion arises from transformation of squamous cells was proposed as early as 1900 by krompecher[6] and was later supported by other light microscopists. Battifora[11] has reported that sarcomatous portion of these tumours represent actual mesenchmyal metaplasia[11]. The malignant epithelial cell undergoing alteration resulting in loss of keratin and acquiring vimentin as the cytoskeletal protein.

Spindle cell carcinoma in the oral cavity and oropharynx is potentially aggressive and seems to recur easily and to metastasize. It is difficult to predict biologic behaviour in every case, patients whose tumour are deeply invasive tend to have poor prognosis, whereas those with early stage tumours usually have excellent prognosis[8].Unfortunately 5year disease free survival rate is ~30% for all oral tumours.[17]

Some authors are of the opinion that wide radical resection alone is the best mode of treatment while some others are of the opinion that surgery with radiotherapy required. Many authors are of the opinion radiotherapy &chemotherapy is ineffective. The treatment option of surgery followed by radiotherapy was found to yield best long term patient outcome similar to conventional squamous cell carcinoma.[13]

Distant metastases and depth of tumour invasian into underlying structures were found to be reliable prognostic features, together with their polypoid configuration. Thus metastases usually contain squamous cell carcinoma or squamous cell carcinoma and spindle cell component and rarely only just spindle cell component.

Genetically, the sarcomatoid & epithelial components of spindle cell carcinoma harbor similar mutations and have concordant ploidy. P53 overexpressed in both components. The tumour shows LOH frequencies similar to those of poorly differentiated squamous cell carcinoma. A specific marker on the short arm of chromosome 4 was shown to be more commonly lost in these tumours than in other squamous cell carcinoma variants[14]

Summary

Spindle cell carcinoma is biphasic malignant tumour & considered to be variant of squamous cell carcinoma. The interesting aspect of this tumour is that it mimics other connective tissue sarcomas & spindle cell malignancies at light microscopic level. In the past the nature of spindle cell & their histogenesis was strongly debated. Immunohistochemical & electron microscopic studies have contributed to solve the diagnostic difficulty & their epithelial origin. Spindle cell carcinoma is aggressive tumour & tend to recur easily & metastasize. The prognosis depends on depth of tumour invasion. It is difficult to predict the biologic behaviour but tumours deeply invasive tend to have poor prognosis.

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