

Case Report

## Cytokeratin: a Shortcut to Diagnose Spindle Cell Carcinoma

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### Abstract

A relatively rare subtype of squamous cell carcinoma (SCC) is spindle cell carcinoma (SPCC). It is composed of epithelium-derived spindle cells arranged in sheets with mesenchymal properties and small, hardly detectable regions of SCC, challenging its definite diagnosis. We encountered five cases of SPCC. In case one, chronic inflammation and subepithelial blister with leukoplakia was found 5 years before our examination. And later, exophytic features, keratotic papules and scar with elevated margins was seen on lateral border of the tongue. In case two, three and four, an abnormal soft tissue elevations were examined, and in the fifth case we examined the soft and bony specimen from the posterior aspect of maxillary ridge. We evaluated all of them histologically and immunohistochemically for cytokeratin to reach final diagnosis.

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### Introduction

Spindle cell carcinoma is an uncommon subgroup of squamous cell carcinoma [1]. It is known as sarcomatoid squamous cell carcinoma and polypoid cell carcinoma as well. In fact SPCC is an unusual poorly differentiated tumor composed of spindle epithelial cells and can be mistaken with sarcoma easily because of their similarity and can be diagnosed by ultrastructural and immunohistochemical analysis [2].

The tumor is uncommon and reported in head and

neck, laryngeal, lingual, alveolar ridge and gingival areas [1, 3]. SPCC is a biphasic tumor composing of an insitu and mesenchymal appearance and has high potential to develop metastasis or recurrence; However, the origin of the both parts is the epithelium. Commonly the mesenchymal part is mimicking a fibrosarcoma or malignant histiocytoma [4], so we had to differentiate them to administer proper treatment. Cytokeratin antibody is a key to investigate the cellular originality. Here we describe five cases resembling

sarcomas diagnosed definitely as spindle cell carcinoma by using this marker.

### Cases

In this case study, five known cases of SPCC are presenting which were referred to the Shiraz school of dentistry, department of oral & maxillofacial pathology. First case was a 60 y/o male who came with the chief complaint of a lesion on his tongue with different presentations such as exophytic features, keratotic papules, and scar with elevated margins. During the clinical examinations a mobile submandibular lymph node was detected at the side of the lesions.

5 years ago patient sought consult to another center with a white lesion at the lateral border of the tongue which was diagnosed as chronic inflammation and subepithelial blister consistent with leukoplakia. In the following year the same center reported the lesion as an acanthosis and submucosal chronic inflammation. In the recent consult, two specimens were removed from the indurated and keratotic site. The histopathologic features of the lesion was reported as following:

There are sections of acanthotic oral mucosa showing papillary appearance with atypia in all thickness of epithelium. Connective tissue shows spreading of malignant epithelial cells, and deep fascicles of malignant spindle cells attached to the epithelium. Cellular atypia is prominent with mitotic rate of 8/10 HPF. Severe infiltration of chronic inflammatory cells and invasion to muscular tissue are also seen in the depth of connective tissue. Immunohistochemistry (IHC) reported that the PanCytokeratin (AE1/AE3) was positive in spindle cells.

The other 3 cases were soft tissue masses of maxilla in a 64y/o male, mandibular ridge in a 57 y/o female and mandibular vestibule in a 53 y/o male which were sent to the school of dentistry for pathologic diagnosis. Common histopathologic features of these three were acanthotic parakeratotic stratified squamous epithelium, with intracellular edema and severe exocytosis. Their underlying connective tissue were consistent of oval to spindle shaped malignant cells with nuclear hyperchromatism, prominent nucleoli, and pleomorphism. Clear cells with foamy and vesicu-

lar cytoplasm, mild inflammatory cells infiltration and thick collagen bundles were interspersed through. In some areas, pleomorphic cells were connected to the dysplastic epithelium.

The fifth case was a soft and bony tissue specimen from the posterior aspect of the maxillary ridge of a 32 y/o male which was sent to oral & maxillofacial pathology department. The lesion was diagnosed as epithelial tumor after incisional biopsy in about one year ago, beside ulceration and granulation tissue.

But recent clinical examinations showed a large fast growing lesion in the right side of the maxilla with involvement of the maxillary bone, sinus and right nostril. The microscopic examination showed sheets of loosely arranged malignant spindle and undifferentiated cells which were focally positive for cytokeratin (CK), epithelial membrane antigen (EMA) and had high mitotic rate by Ki-67. This was suggestive of spindle cell carcinoma.

### Discussion

A relatively rare subtype of SCC is spindle cell carcinoma as WHO in 2005 put it into histological class of head and neck tumors. It is composed of epithelium-derived spindle cells arranged in sheets with mesenchymal properties [5-7]. The spindle cells in SPCC share a common pathogenic process in tumorigenesis despite phenotypical divergence. They don't grow as a non-neoplastic mesenchymal reaction and they are not an admixture of malignant epithelial and mesenchymal cells. They are a variant of SCC. The epithelial and spindle components share a common pathway of tumorigenesis despite their conspicuous divergence at the phenotypic level [8]. Alterations in keratin filament expression and network beside lack of cell adhesion molecules such as cadherins lead to this spindle shape of the tumor cells [9]. Many cases of SPCC are reported in the lips and tongue, but its development in the alveolar gingiva is relatively rare when evaluating oral cavity [8-12].

Their prognosis is like poorly differentiated SCC or even poorer as metastasis, particularly to the cervical lymph nodes, lung, and heart is a common feature in many cases of them [13]. Survival rates was reported 27.5% [10] to 36% [4].

**Table 1:** Immunohistochemical profile to distinguish spindle cell carcinoma from other similar lesions.

CD3 (SP1)	Negative	EMA (E29)	Positive (focal & weak)	S100 ( S100p )	Negative
CD20 (L26)	Negative	P63 protein ( 4 A4 )	positive	Keratin HMV	Negative
CD30 (Ber-H2)	Negative	Keratin ( AE1 / AE3 )	Positive	Cytokeratin 20	Negative
CD34 (QEnd-10)	Negative	Vimentin	Positive	Cytokeratin 7	Negative
CD68 (Kp1)	positive	Melan A	Negative	LCA	Negative
SMA : Focal positive (weak )		Ki67 (M1B1 )	High		

Histological studies alone cannot explain the spindle cell components. Investigations suggest that SPCC is formed by mesenchymal differentiation of epithelium-driven cells as spindle cells are positive for epithelial cell markers such as pan-cytokeratin (AE1/AE3) and epithelial membrane antigen (EMA) on IHC staining, and simultaneously in many cases cells are positive for mesenchymal cell marker, vimentin [5-6]. To address the histogenesis of the spindle cells within these tumors and differentiating SPCC with other sarcomatous lesions, we should use the proper profile of Immunohistochemical markers (Table 1) [9, 13]. Upon reviewing the risk factors associated with this lesion, it was concluded that the risk factors of SPCC were similar to that of SCCs' with the prominence of chronic tobacco usage [3].

Clinical appearance of SPCC in the oral cavity varies and most lesions appear as pedunculated and polypoid masses. Ellis and Corio have reviewed many cases and mentioned that the appearance of spindle cell carcinoma predominantly occurred as exophytic large mass that increases in size over a short period of time [14]. However other investigators reported that spindle cell carcinoma sometimes appear as a nodular and fungating mass which may be associated with a non-healing ulcer [13].

In this study AE1/AE3 and EMA markers were positive for all the SCC components and spindle cells. Ellis *et al.* reported similar findings and shown that the neoplastic cells may be of epithelial origin which undergone alteration resulting in loss of desmosomes and cohesiveness [14]. Also we found that the spindle shaped tumor cells were positive for vimentin, which shows true mesenchymal metaplasia in these bizarre fibroblast-like carcinoma cells [4]. In our cases, presence of necrosis, absence of keratin pearls, and large number of mitosis were indicating that clinical behavior of tumor is similar to a poorly differentiated SCC, the finding that is in consistence with histopathological views.

Thus, to summarize, diagnosis of spindle cell variants of head and neck SCCs specially in mucosal sites is challenging because of many similar lesions such as mucosal spindle cell melanoma, Fibrosarcoma, leiomyosarcoma and myoepithelial carcinoma with common histopathological properties. Also it is possible to be confused with sarcomatoid bony lesions like osteosarcoma extending to the mucosa if the radiological view is not taken into consideration.

So, accurate diagnosis of SPCC should be based on clinical behavior and morphological features beside immunohistochemical profile to reach proper patient management.

**Conflict of Interest:** None declared.

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