Spindle Cell Carcinoma of Oral Cavity: A Rare Aggressive Variant of Squamous Cell Carcinoma

Sajith Babu¹, Anush R², Sithara A³, Aswathy K⁴, Sangeetha Nayanar⁵

¹Associate Professor, Department of Surgical Oncology, Malabar Cancer Centre, Moozhikkara, Kerala India.
²Maxillofacial surgeon, Dental College, Kottayam, Kerala India.
³Assistant Professor, Department of Pathology, Malabar Cancer Centre, Moozhikkara Thalassery, Kerala India.
⁴Assistant Professor, Department of Pathology, Malabar Cancer Centre, Moozhikkara Thalassery, Kerala India.
⁵Professor, Department of Oncopathology, Malabar Cancer Centre, Moozhikkara Thalassery, Kerala India.

*Corresponding author
Dr Sajith Babu TP
Email: drsajith@gmail.com

Abstract: Spindle cell variant of squamous cell carcinoma of oral cavity is a rare but aggressive variant. A case report with review of literature is presented highlighting the importance of good clinical suspicion and correct histopathological diagnosis with the help of immunohistochemistry.

Keywords: Spindle cell, carcinoma, oral cavity

INTRODUCTION

Spindle cell carcinoma (SpCC) is a rare and aggressive variant of squamous cell carcinoma (SCC). Spindle cell carcinomas are most commonly seen in upper aerodigestive system [1], larynx and hypopharynx, particularly in vocal cords, and rare in oral cavity. Though squamous cell carcinoma is the most common type of malignancy in oral cavity, the spindle cell variant is seen occasionally.

SpCC are so named because of the presence of spindle-shaped elongated epithelial cells, thus, mimicking sarcomas. Hence it has been described under many names in literature like pseudosarcoma, carcinosarcoma, sarcomatoid carcinoma. These were earlier considered to be a non-neoplastic variant of squamous cell carcinoma. However, the majority of the spindle cell components are non-diploid, which indicates that they are neoplastic and not reactive. Combined cytokeratin - vimentin positivity reflects that these bizarre fibroblast-like cells are carcinoma cells with true mesenchymal metaplasia. Electron microscopy often shows the presence of junctional complexes between tumor cells, with or without pericellular basal lamina and cytoplasmic skeins of intermediate filaments. The W.H.O. classification of tumors of the oral cavity and oropharynx has placed this disease under malignant epithelial tumors of Squamous Cell Carcinoma (SCC) and labeled it as “Spindle cell carcinoma” (SpCC) [2,3].

Since this is a relatively rare disease and even rarer in oral cavity it creates a diagnostic dilemma [4]. Distinguishing spindle cell variant of squamous cell carcinoma is important because it is aggressive tumor with rapid progression, high incidence of local recurrence and hence, warrants more aggressive management [2].

This tumor has distinct clinical features and behaviour, and the establishment of the correct diagnosis is important for management. Since only a few cases have been reported in the medical and dental literature, we are presenting this unusual case report with its immunohistochemical features.

CASE REPORT

Clinical findings

A 65 year old female patient, with performance status 1(ECOG) reported to our centre with complaints of ulcer and growth in right cheek region of two months. The lesion initiated as a small painless ulcer which gradually increased in size and with associated pain. No ankyloglossia, trismus or bleeding was present. No metastatic symptoms were present. The medical history and family history were unremarkable. Personal history revealed that she was a tobacco chewer for more than 40 years using dried tobacco leaves, betel leaves, arecanut and lime (which is called as pan chewing in Indian subcontinent).

On examination an ulceroproliferative lesion of size 4x3 cm was seen in the right retro molar trigone (RMT) extending onto lower alveolus, gingivo buccal sulcus and buccal mucosa. There was no extension into the floor of mouth or oropharynx. The lymph node at level 1B was palpable, hard non fixed and non-tender in nature. Based on these clinical features a provisional diagnosis of carcinoma was reached.
Investigations:

The routine blood investigations were within normal limits. Computerised tomography of head and neck region was done which showed a soft tissue lesion at RMT extending inferiorly towards origin of medial pterygoid muscle with destruction of cortical bone of mandible at angle region (Figure 1). Nodes at level 1B and level 2 were found to be suggestive of metastatic. Ultrasound scan of abdomen and pelvis was done which ruled out any distant metastasis.

Histopathology and immunohistochemistry (Figure 2)

Microscopically, sections showed tissue lined by stratified squamous epithelium with extensive ulceration of mucosa and an invasive neoplasm diffusely arranged as bundles. Individual cells were spindling shaped and polygonal having moderately pleomorphic vesicular nuclei. Immunohistochemistry showed concurrent presence of malignant epithelial and sarcomatoid spindle cell components by co-expression of cytokeratin (CK) and vimentin. All these features were suggestive of spindle cell carcinoma.

Treatment:

As the patient had stage IV disease, multimodality treatment was planned for her. The patient underwent composite resection with hemimandibulectomy (Figure 3) with modified radical neck dissection on ipsilateral side and the defect was reconstructed with pectoralis major myocutaneous flap. Frozen section was done for margin status which showed clear margins. Histological examination of resected specimen showed spindle cell carcinoma infiltrating the underlying mandible. Focal perineural infiltration was noted with no lymph vascular emboli. One node at level II showed metastasis with spindle cells and no extracapsular extension. All the other 60 nodes at levels I to V showed no metastasis. TNM stage was pT4aN1.

Hence adjuvant radiotherapy, 64 Gy in 30 fractions was given. The patient was on monthly follow up for one year and two monthly for the second year and has been disease free after 18 months.

Fig–1: CT scan of Oral cavity showing malignant lesion in right RMT region with mandible erosion

Fig–2a: Squamous epithelium with underlying malignant cells
Fig 2b: Spindle cells mixed with squamous cells

Fig 2c: Immunohistochemistry showing cytokeratin positive cells

Fig 2d: Immunohistochemistry showing vimentin positive cells
DISCUSSION

SpCC is a rare variant of SCC which has malignant spindle cells of epithelial origin. Spindle cell component is responsible for the mesenchymal appearance and make the diagnosis challenging. SpCC has been described under many names in literature like pseudosarcoma, carcinosarcoma and sarcomatoid carcinoma [5]. These were earlier considered to be a non-neoplastic component of squamous cell carcinoma. However, the majority of the spindle cell components are non-diploid, which indicates that they are neoplastic and not reactive [6].

Three different theories have been proposed to explain histogenic nature of spindle cells. First theory is that spindle cells and epithelial cells are arising simultaneously from separate stem cells deserving the name “collision” tumor. Second theory explains the nature of the spindle cell component as an atypical reactive proliferation of the stroma and hence called “pseudosarcoma”. Finally, according to the last theory, cells of both spindle and epithelial components have the same monoclonal origin, and “dedifferentiation” or “transformation” to spindle cells has been occurred [7-9]. Monoclonal hypothesis is the most widely accepted today.

Gupta et al. described that some of the spindle cells or transient cells with mesenchymal appearance express dual antigen-positivity with both epithelial (cytokeratin) and mesenchymal (vimentin) markers. 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 [10].

The disease has predilection for 6th or 7th decades of life and slight male predilection. Tobacco usage, alcohol consumption and history of radiation are established risk factors for spindle cell carcinoma [11]. Transcriptionally active HPV have been found associated rarely, though not influencing the prognosis [12]. SpCC is a rare disease, mostly seen in head and neck region, with predilection for larynx and hypopharynx. Oral cavity is less frequently involved and lower alveolus is one of the rare sites for involvement of the disease. Laryngeal tumors clinically present as polypoid exophytic masses and exhibit typical symptoms such as hoarseness, voice changes, airway obstruction, and dysphagia. Oral and oropharyngeal tumors may present as a painful or painless masses with non-healing ulcer, dysphagia, or bleeding [13]. These tumors usually grow up rapidly, as was this case.

Histological diagnosis is based on identification of malignant spindle cell component along with conventional SCC, which may be scantily represented. “Streaming” or “dropping off” of spindle cells from the overlying epithelium is a characteristic feature. Focal osteoblastic / chondroblastic differentiation may be seen [14]. Metastatic deposits and recurrences may exhibit conventional SCC or SpCC or both.

Sarcomas like fibrosarcoma and leiomyosarcoma and other spindle cell lesions like inflammatory myofibroblastic tumor can be differentiated from SpCC by identification of uninvolved epithelium in sarcoma, whereas epithelium is involved in SpCC [15]. Mucosal melanomas and myoepithelial carcinomas can be differentiated by IHC (S100, HMB 45 positive in the former and myoepithelial markers like SMA, GFAP, CD10, calponin in the latter). SpCC shows double labeling with cytokeratins 1/18/ AE1/ AE3/EMA and vimentin. Myogenic markers are often positive. p63, MOC 1 and TTF 1 has recently been reported as a useful marker.
It has been reported that epithelial marker expression decreases as the degree of epithelial differentiation decreases and may be lost entirely [17]. Electron microscopy shows desmosomes or tonofilaments in spindle cells.

The factors influencing overall survival are tumor grade, lymph nodes, metastasis, stage, vascular invasion and distant recurrence. A high local recurrence rate (73.3%) and distant metastasis rate (33.3%) were observed [2]. Spindle cell carcinomas should be treated aggressively with both surgery and radiation, with a 2 cm margin [2]. Neck dissection should be done as for squamous cell carcinoma. For advanced stage III & IV disease multi-modality treatment is advocated. Salvage surgery has been advocated and shown benefit for the recurrences [2]. Although spindle cell carcinoma has many similar clinical and histopathological features with SCC, its biological behavior is more aggressive than conventional SCC, with glottis tumors showing better prognosis than other sites in head and neck [18].

CONCLUSION

A rare case of spindle cell carcinoma arising from the retromandibular trigone (RMT) is presented. Based on the limited number of studies in literature, its exact pathogenesis, clinical behavior, and long term prognosis have not been well understood yet. Moreover aggressive nature and tendency to recur warrant early detection and aggressive management of the disease. Clinical features and history along with HPE and IHC could prove vital. Spindle cell carcinoma should be always considered as a differential diagnosis during evaluation of the ulceroproliferative lesions of head and neck region containing spindle cells.

REFERENCES


Available Online: http://saspjournals.com/sjmcr
SV. Sarcomatoid (spindle cell) carcinoma of the head and neck mucosal region: a clinicopathologic review of 103 cases from a tertiary referral cancer centre. Head and neck pathology. 2010 Dec 1;4(4):265-75.