Scholars Journal of Medical Case Reports **ISSN 2347-6559 (Online)**
Sch J Med Case Rep 2017; 5(8):467-472 **ISSN 2347-9507 (Print)**

(An International Publisher for Academic and Scientific Resources) DOI: 10.36347/sjmcr.2017.v05i08.005

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

Sajith Babu[1], Anush R[2], Sithara A[3], Aswathy K[4], Sangeetha Nayanar[5]
[1]Associate Professor, Department of Surgical Oncology, Malabar Cancer Centre, Moozhikkara, Kerala India.
[2]Maxillofacial surgeon, Dental College, Kottayam, Kerala India.
[3]Assistant Professor, Department of Pathology, Malabar Cancer Centre, Moozhikkara Thalassery, Kerala India.
[4]Assistant Professor, Department of Pathology, Malabar Cancer Centre, Moozhikkara Thalassery, Kerala India.
[5]Professor, 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, ginigvo 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.

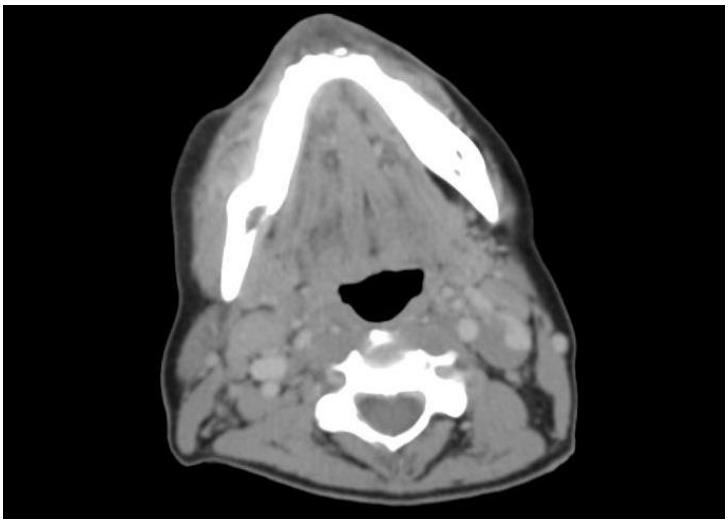
Histopathology and immunohistochemistry (Figure 2)

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.

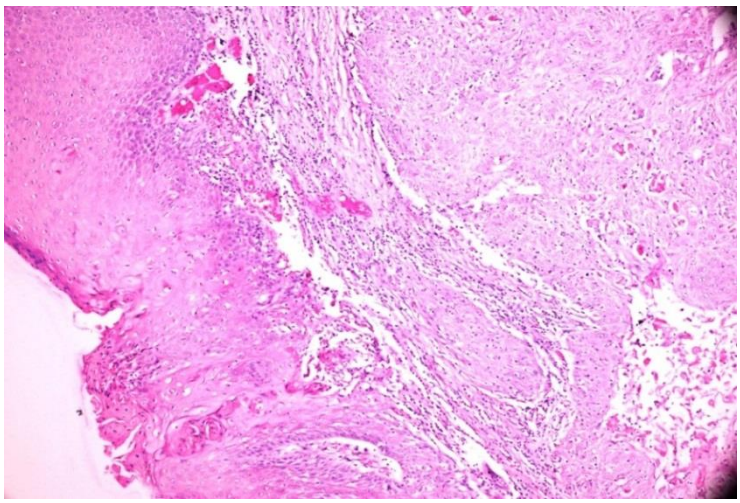
Treatment:

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.

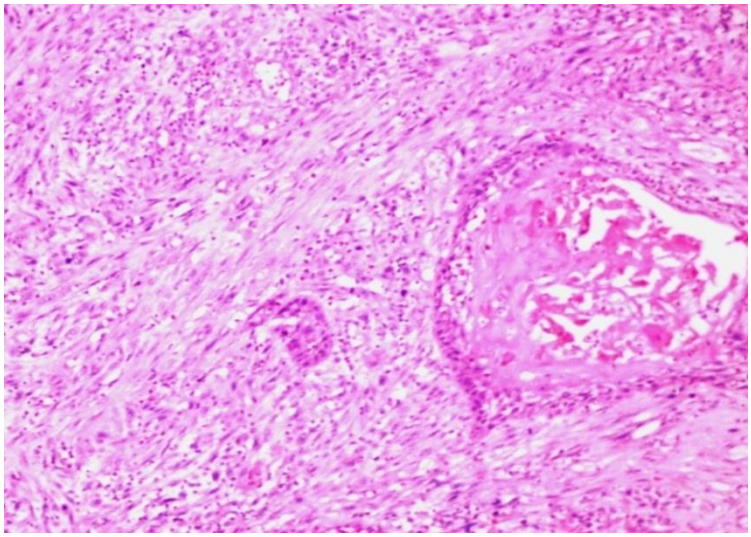
Hence adjuvant radiotherapy, 64 Gy in 30 fractions was given. The patient was on monthly follow up for one year and two monthly for the second year and has been disease free after 18 months.



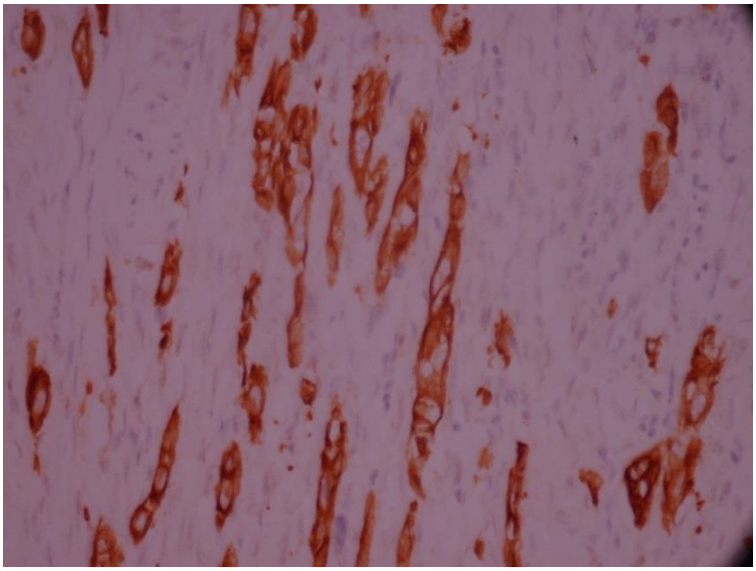
Fig–1: CT scan of Oral cavity showing malignant lesion in right RMT region with mandible erosion



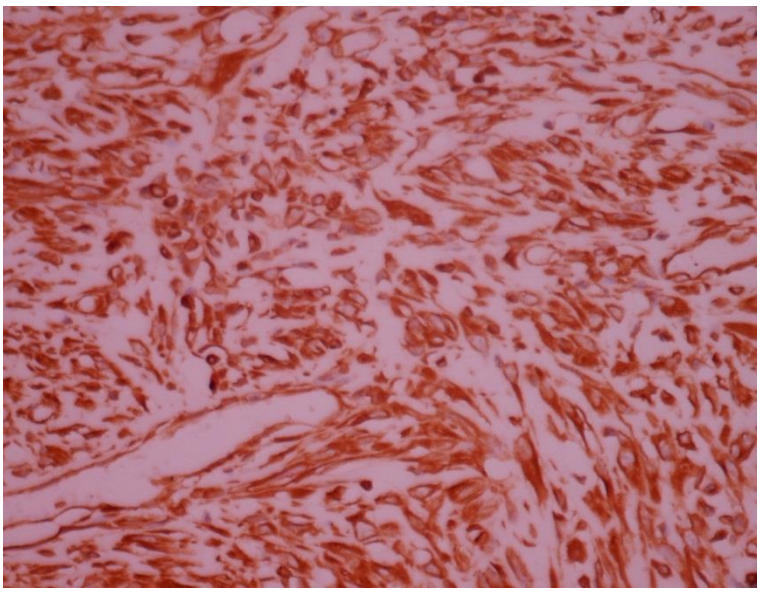
Fig–2a: Squamous epithelium with underlying malignant cells



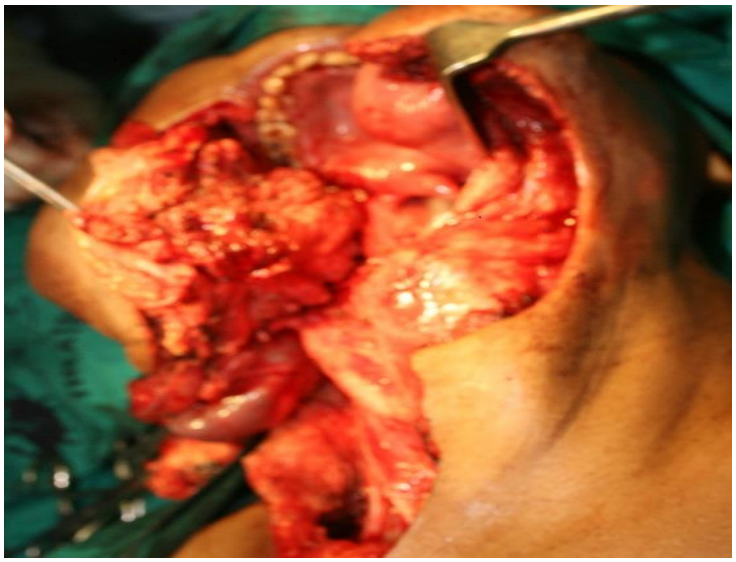
Fig–2b: Spindle cells mixed with squamous cells



Fig–2c: Immunohistochemistry showing cytokeratin positive cells



Fig–2d: Immunohistochemistry showing vimentin positive cells



Fig–3: Surgical resection of the spindle cell carcinoma of RMT with mandible

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 representated. "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

[16]. 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

1. Kudo Y, Ogawa I, Kitagawa M, Kitajima S, Samadarani Siriwardena BS, Aobara N, Matsuda C, Miyauchi M, Takata T. Establishment and characterization of a spindle cell squamous carcinoma cell line. Journal of oral pathology & medicine. 2006 Sep 1;35(8):479-83.
2. Su HH, Chu ST, Hou YY, Chang KP, Chen CJ. Spindle cell carcinoma of the oral cavity and oropharynx: factors affecting outcome. Journal of the Chinese Medical Association. 2006 Oct 1;69(10):478-83.
3. Barnes L, Eveson JW, Reichart P, Sidransky D. World Health Organization classification of tumours: pathology and genetics of head and neck tumours. Word Health Organization Classification of Tumours: Pathology and genetics of head and neck tumors. 2005.
4. Oktay M, Kokenek-Unal TD, Ocal B, Saylam G, Korkmaz MH, Alper M. Spindle cell carcinoma of the tongue: a rare tumor in an unusual location. Pathology research international. 2011 Feb 20;2011.
5. Batsakis JG, Tumors of head and neck 2nd edition. 1979: 150: 217-19.
6. Lewis JE, Olsen KD, Sebo TJ. Spindle cell carcinoma of the larynx: review of 26 cases including DNA content and immunohistochemistry. Human pathology. 1997 Jun 1;28(6):664-73.
7. Shibuya Y, Umeda M, Yokoo S, Komori T. Lubsen H. Spindle cell carcinoma of the oral Spindle cell squamous carcinoma of the maxilla: cavity and larynx. J Cranio- Mac- Fac.surg Report of a case with immunohistochemical analysis. J oral Maxillofac surg 2000
8. Battifora H. Spindle cell carcinoma ultrastructural evidence of squamous origin and collagen production by tumour cells. Cancer 1976;37: 2275-82.
9. Oktay M, Kokenek-Unal TD, Ocal B, Saylam G, Korkmaz MH, Alper M. Spindle cell carcinoma of the tongue: a rare tumor in an unusual location. Pathology research international. 2011 Feb 20;2011.
10. Prakash N, Harish Kumar MS, Sharada P, Pradeep GL. Spindle cell carcinoma of the oral cavity: a case report of a rare entity and review of literature. World Journal of Dentistry. 2010 Jun 25;1(1):55-8.
11. Leventon GS, Evans HL. Sarcomatoid squamous cell carcinoma of the mucous membranes of the head and neck: a clinicopathologic study of 20 cases. Cancer. 1981 Aug 15;48(4):994-1003.
12. Watson RF, Chernock RD, Wang X, Liu W, Ma XJ, Luo Y, Wang H, El-Mofty SK, Lewis JS. Spindle cell carcinomas of the head and neck rarely harbor transcriptionally-active human papillomavirus. Head and neck pathology. 2013 Sep 1;7(3):250-7.
13. Romanach MJ, Azevedo RS, Carlos R, De Almeida OP, Pires FR. Clinicopathological and immunohistochemical features of oral spindle cell carcinoma. Journal of oral pathology & medicine. 2010 Apr 1;39(4):335-41.
14. Katase N, Tamamura R, Gunduz M, Murakami J, Asaumi JI, Tsukamoto G, Sasaki A, Nagatsuka H. A spindle cell carcinoma presenting with osseous metaplasia in the gingiva: a case report with immunohistochemical analysis. Head & face medicine. 2008 Dec 1;4(1):28.
15. Völker HU, Scheich M, Höller S, Ströbel P, Hagen R, Müller-Hermelink HK, Eck M. Differential diagnosis of laryngeal spindle cell carcinoma and inflammatory myofibroblastic tumor–report of two cases with similar morphology. Diagnostic pathology. 2007 Jan 9;2(1):1.
16. Lewis JS, Ritter JH, El-Mofty S. Alternative epithelial markers in sarcomatoid carcinomas of the head and neck, lung, and bladder--p63, MOC-31, and TTF-1. Modern Pathology. 2005 Nov 1;18(11):1471.
17. Viswanathan S, Rahman K, Pallavi S, Sachin J, Patil A, Chaturvedi P, D'Cruz A, Agarwal J, Kane

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.

18. Samdhani S, Choudhary A, Mahanta VR, Srivastava SP. Spindle cell sarcoma of larynx. Indian Journal of Otolaryngology and Head and Neck Surgery. 2006 Jul 1;58(3):305-6.