CASE REPORT

Spindle Cell Carcinoma: A Confirmatory Diagnostic Analysis by Immunohistochemical Studies

Sumit Majumdar, B. Alekhya, V. Sushma, M. Ravindra

Abstract

Introduction: WHO defines it as a "carcinoma within which there are some elements resembling a squamous cell carcinoma that are admixed with a spindle cell component. Spindle cell carcinoma is an uncommon poorly differentiated type of SCC comprising up to 3% of SCC and it is also known as sarcomatoid carcinoma which is a rare biphasic malignant neoplasm. .

Case Report: A 20 year old female patient complains of pain and growth in lower front teeth region since 3 months and gave a history of growth 2yrs back in the front teeth region for which she has been operated but it has recurred again.

Discussion: The histological features mimicked other connective tissue sarcomas & spindle cell malignancies at light microscopic level. Hence, after undergoing immunohistochemistryA careful study based on clinical, radiological and histopathological and immunohistochemical examination was done and a final diagnosis of spindle cell carcinoma was given.

Keywords: Biphasic, collision tumor and sarcomatoid carcimona.

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Introduction

Spindle cell carcinoma (SpCC), is a fascinating tumor with many controversy's and speculations. This is primarily as a result of bimorphic nature of the lesion, which is squamous cell carcinoma (SCC) and severe dysplasia with a bizarre spindle cell /mesenchymal –type proliferation reminiscent of a sarcoma[1-3].

Due to its bimorphic nature of the lesion several terms and theories of histogenesis were proposed such as spindle cell carcinomacollision tumor, squamous cell carcinoma with sarcoma like stroma, pseudosarcoma, and sarcomatoid carcimona. The cells that represent both non-neoplastic bizarre stromal areas and metaplastically altered SCC cells, or cells of a separate mesenchymal neoplasm that forms a collision tumor with the SCC component, for which the term carcinosarcoma is employed[4-6].

Molecular pathology has recently provided convincing proof of an evolution of the sarcomatoid component from the conventional one. Metastasised cervical lymph nodes may exhibit features of conventional SCC, SpCC, or both together

Most common site of occurrence is upper respiratory tract, tumor also occurs in oesophagus, lungs and oral cavity. SpCC has typically been regarded as a more aggressive neoplasm than conventional SCCs of the head and neck, with higher rates of recurrence and metastasis, and poorer survival rates[7-8].

Case Report

A 20 year old female patient reported to outpatient clinic with a chief complaint of pain and growth in lower front teeth region since 3 months. Patient gives the history of growth 2yrs back in the front teeth region for which she has been operated but it has recurred again.

On extra oral examination face is asymmetrically symmetrical with no TMJ abnormalities, also no abnormalities detected in the jaws; mild incompetency is seen in the lips. Lymph nodes are not palpable. On intraoral examination asessile solitary lobular exophytic erythematous intraoral swelling is observed in relation to 32 to 42 region with obliteration of labial vestibule as shown in (figure 1).On palpation mild tenderness present, surface was Smooth and soft to firm in consistency. Based on clinical features and examination a provisional diagnosis of sarcomatous lesion was given. For the confirmatory diagnosis patient was advised for further radiological investigations.

In Orthopantomogram aggressive destruction of mandible in symphysial and para symphysial region from 33 to 43 was observed (figure 2). In Cone beam computed tomography. A soft tissue density lesion is seen anterior to the symphysis region of the mandible with erosion of adjacent cortical outline of the anterior cortex of the mandible. Epicenter of the lesion was towards mucosal surface impression as peripheral non ossifying fibroma (figure 3).

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Biopsy was done and sends for the histopathological examination final diagnosis. On macroscopic examination Received 28 bits of soft tissue specimen and 8 bits of hard tissue (teeth). Soft tissue bits are brownish in colour, soft to firm in consistency (A,B,C,D,E,F). Hard tissues consists of teeth 42,41,31,32,33,34,35,36 (figure 4).

The Haematoxylin and Eosin stained soft tissue section exhibits proliferation of pleomorphic tumor cells in the form of bundles and fascicles. The spindle cells are arranged in herring bone pattern with cellular & nuclear pleomorphism. Individual tumor cells are oval to spindle shaped having mild eosinophilic cytoplasm with indistinct cytoplasmic border and spindle shaped nuclei. Few of the cells are epithelioid having large hyperchromatic nucleus with inconspicuous nucleoli. The stroma was collagenized with telangiectatic blood vessels with areas of calcification within the tumor tissue and bone trabeculae are filled with plump osteocytes. Tissue section also exhibits myxomatous stroma with few mitotic figures, areas of necrosis and proliferation of blood capillaries (figure 5-8).

Immunohistochemistry

Tumour cells express vimentin(diffuse & strong), Pancytokeratin (focal & strong), EMA (weak & patchy), p63 (very few tumour cells are positive), S-100 protein (few cells are positive), bcl-2 (focal), desmin (focal) (figure 9). Hence based on clinical, radiological, histopathological and immunohistochemical examination a final diagnosis of spindle cell carcinoma was given.

Patient was referred to oncology center for further treatment. Patient had undergone symphysial segmental resection with radiation therapy (figure 10).

Discussion

Spindle cell lesions may be benign or malignant type; and occurs rarely which accounts less than 1% in oral cavity. In 1864, Virchow first described spindle cell carcinoma as a biphasic tumor mainly characterized by various areas of Squamous cell carcinoma in association with proliferation of sarcomatoid spindle cells. Sherwin et al. proposed the term spindle cell carcinoma and acknowledged by the World Health Organisation under the most malignant epithelial tumors of squamous cell carcinoma[9]. WHO defines it as a "carcinoma in which there are some components similar to SCC that are admixed with spindle cell element[10]. OSCC has various variants like basaloid SCC, verrucous carcinoma, adenosquamous carcinoma, spindle cell carcinoma, acantholytic SCC, papillary SCC[11].

Spindle cell carcinoma is an uncommon poorly differentiated type of squamous cell carcinoma accounting nearly 3% of SCC. Other synonym was sarcomatoid carcinoma, a rare biphasic malignant tumor. It is well accepted that this biphasic tumor is composed of SCC and sarcomatous spindle cell carcinoma. It has been also known as collision, combination or composition tumors.

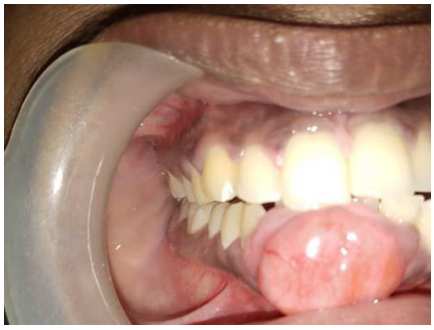

Fig. 1: Solitary lobular exophytic erythematous intraoral swelling is observed in relation to 32 to 42 region with obliteration of labial vestibule

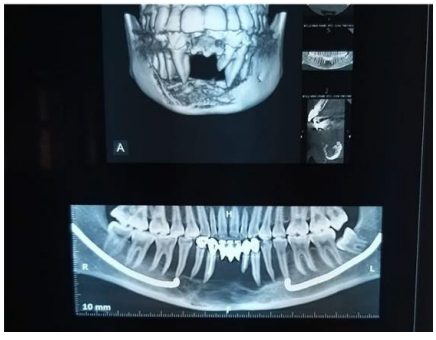

Fig. 2: Orthopantomogram showing aggressive destruction of mandible in symphysial and para symphysial region from 33 to 43 was observed

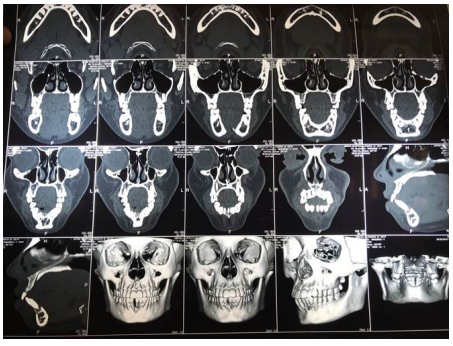

Fig. 3: Cone beam computed tomography :A soft tissue density lesion is seen anterior to the symphysis region of the mandible with erosion of anterior cortex of the mandible.

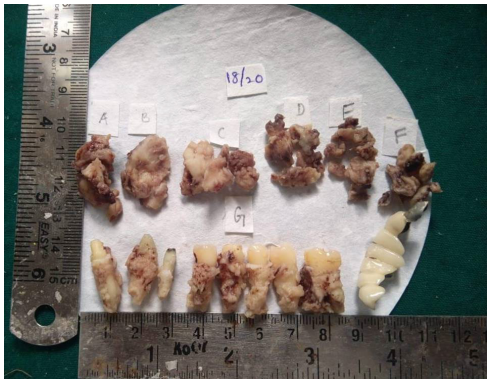

Fig. 4: 28 bits of soft tissue specimen and 8 bits of hard tissue (teeth)

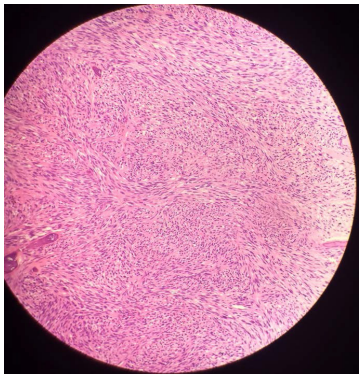

Fig. 5: Proliferation of pleomorphic tumor cells in the form of bundles and fascicles (H and E)

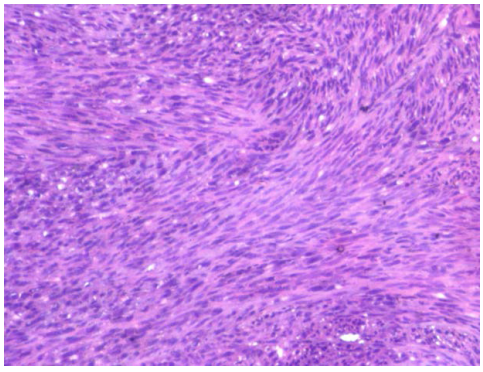

Fig. 6: Spindle cells arranged in herring bone pattern with cellular & nuclear pleomorphism. (H and E)

After the morphologic, immune histochemical, ultra-structural studies and molecular features of spindle cell carcinoma (Spcc), it was recognized as a carcinoma that has changes in the surface epithelium and underlying proliferation of spindle-shaped neoplastic cells. Because of its peculiar histopathological appearance, it has various names like carcinosarcoma, pseudosarcoma, pleomorphic carcinoma, sarcomatoid carcinoma and polypoid carcinoma. Potential, predisposing risk factors were of: smoking, alcohol intake, poor oral hygiene and previous exposure to radiation[12].

Theories that suggest the origin of spindle cells are either growth pattern of variant of SCC, the association of malignant epithelial and mesenchymal cells or the reactive non neoplastic phenomena. The proposed hypothesis and the three theories of spindle cell carcinoma regarding the histogenesis includes[13]:-

(1) it signifies a collision tumor (carcino-sarcoma)
(2) it represents a SCC with an atypical stroma (pseudosarcoma)
(3) it is of epithelial origin, with 'de-differentiation' to a morphology of spindle cell (sarcomatoid carcinoma).

Recently, the third theory holds up the monoclonal hypothesis which states that they have undergone "dedifferentiation" and originates from the same stem cells. It was supported by electron microscopy, immunohistochemical findings and modern techniques.

It occurs mainly in the upper aerodigestive tract; the commonest primary site is particularly the glottis region in the larynx which is about 70% of cases. Oral cavity is the second most common site, which arises from the tongue, alveolar ridge, and floor of the mouth, lower lip or gingiva. It also occurs in other sites such as skin of the head and neck and soft tissues of the orbit and scalp.

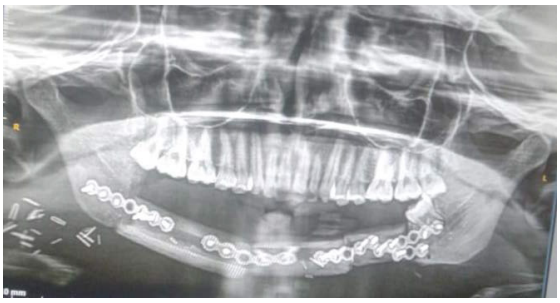

Fig. 7: The Haematoxylin and Eosin stained soft tissue section shows Individual tumor cells are oval to spindle shaped having mild eosinophilic cytoplasm with indistinct cytoplasmic border and spindle shaped nuclei.

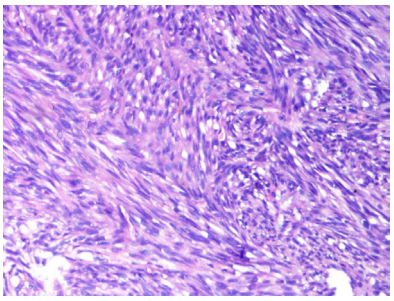

Fig. 8: Few cells are epithelioid having large hyperchromatic nucleus with inconspicuous nucleoli.(H and E)

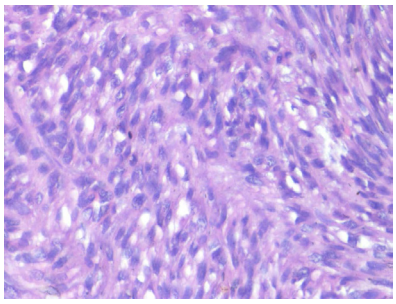

Fig. 9: Tumour cells express diffuse& strong for vimentin ,Pancytokeratin is focal & strong (IHC,)

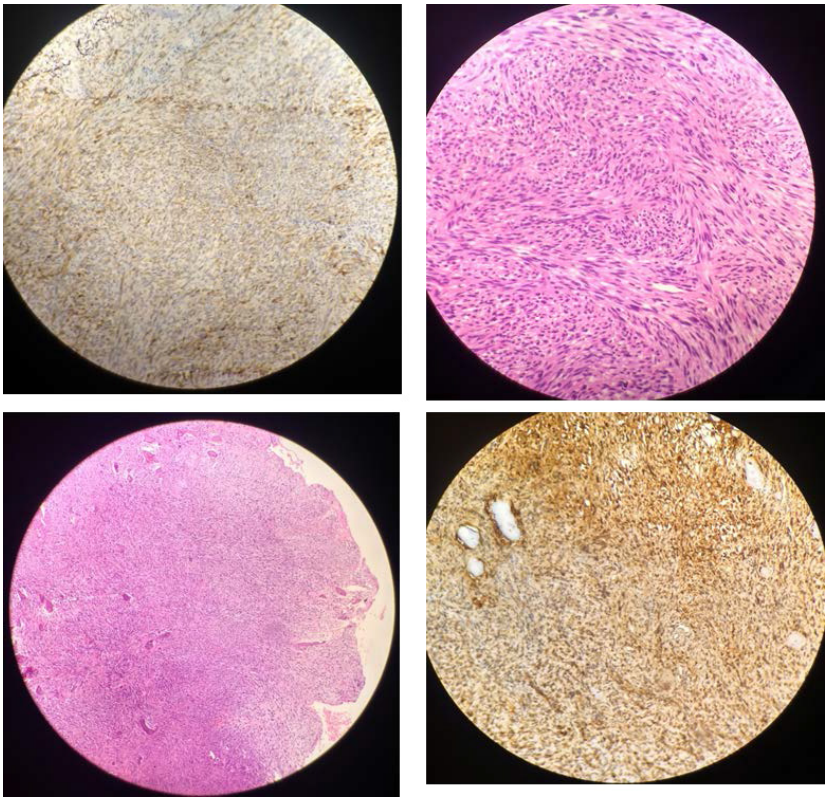

Fig. 10: Post-surgical radiograph showing symphysial segmental resection with radiation therapy.

The mean age is around sixth to seventh decade individuals, but it can be diagnosed in age group in the range of 29-93 years with male predominance. It mainly appears as polypoid exophytic mass or least commonly as ulcerated plaque and somewhat rarely as flat lesion[14].

Histopathologically, it comprises the ulceration of the overlying epithelium exhibits mild dysplasia to invasive carcinoma features and atypical connective tissue stroma consists of fusiform cells resembling fibrosarcoma-like appearance. The epithelial section forms a minor portion of the tumor mass and is usually found within the periphery of the lesion. Sometimes, there will be transition and proliferation of surface basillar cells to sarcomatous spindle cell components. It usually forms the bulk of the lesion and is composed of plumped spindle cells, which can also be epithelioid and rounded in some areas[15].

It usually appears as a fasciculated pattern which consists of hypercellular areas with bipolar cells which are elongated and are arranged in a parallel and interwoven arrangement. The areas of Squamous cell carcinoma intermixed with some areas of pleomorphic spindle cells can also be seen. A transition with the squamous cell carcinoma cells dropping from epithelial nests into the spindle cell regions can also be seen. Rarely, streaming or myxomatous patterns can also be seen, in which the cells were more pleomorphic and stellate with clear areas of intercellular spaces.

Differential diagnoses includes:- fibrosarcoma, malignant fibrous histiocytoma, angiosarcoma, malignant melanoma, leiomyosarcoma, Kaposi sarcoma, malignant peripheral nerve sheath tumor, synovial sarcoma, osteosarcoma, leiomyoma, mesenchymal chondrosarcoma.

Immunohistochemical (IHC) analysis is used to confirm the final diagnosis of Spindle cell carcinoma. Epithelial markers which include cytokeratins (CK 1, 8, 9, AE1/AE3), K1, K18 and epithelial membrane antigens can be used. The most reliable and sensitive markers are cytokeratins and epithelial membrane antigen. AE1⁄AE3 is generally positive for the squamous areas. To confirm the diagnosis, the expression of mesenchymal marker is helpful. Vimentin and pan-actin are usually positive in the spindle cell areas; S-100, α-smooth muscle actin (SMA) and desmin are positive but almost absent in the squamous areas.

The treatment of choice is surgical resection with neck dissection which should be treated like squamous cell carcinomas and the survival and prognosis rate of spindle cell carcinoma is poorer than SCC due to the aggressive nature of spindle cell carcinoma.

Conclusion

We report a case of spindle cell carcinoma which simulates other malignancies of spindle cells and connective tissue sarcoma lesions. Hence, after undergoing immunohistochemistry (IHC), it helped us to know the nature and histogenesis of this lesion. It is rare to occur in oral cavity and its nature is more aggressive which has a more chance of recurrence and to metastasize. A typical histopathological features makes the diagnosis of this lesion extremely complicated and controversial. Patients with early-stage tumors have an excellent prognosis, whereas deeply invasive tumors have poor prognosis.

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