

Sarcomatoid (Spindle Cell) Neoplasm of the Head and Neck Mucosal Region:-A Clinicopathologic Review of Case Series

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Abstract:- Spindle cell neoplasms are defined as neoplasms that consist of spindle-shaped cells in the histopathology. Spindle cell neoplasms can affect the oral cavity. In the oral cavity, the origin of the spindle cell neoplasms may be traced to epithelial, mesenchymal and odontogenic components. It has a more aggressive behavior as compared to classical squamous cell carcinoma warranting surgical interventions with wider surgical margins. This article aims to report two cases of spindle cell neoplasm of maxilla along with review the spindle cell neoplasms of the oral cavity with emphasis on histopathology, immunohistochemistry and treatment options.

Keyword:- SCSC = spindle cell squamous carcinoma, SPCC= spindle cell carcinoma, SOHND= supra omohyoid neck dissection

I. Introduction

Spindle cell carcinoma of head and neck, a subtype of squamous cell carcinoma is a unique and rare neoplasm, composed of both malignant epithelial and mesenchymal components.¹Spindle cell squamous carcinoma (SCSC) is a rare and peculiar biphasic malignant neoplasm that occurs mainly in the upper aerodigestive tract.² They are unusual variants of squamous carcinoma commonly reported in larynx but also described in other mucosal sites such as gingiva,tongue,hypopharynx, and nasal cavity.³ It consists of sarcomatoid proliferation of pleomorphic spindle shaped cells and squamous cell carcinoma. The diagnosis of SCSC is often difficult to arrive at, especially when the carcinomatous component is not included in the biopsy specimen. Although the findings of histologic, ultrastructural, immunohistochemical, and, more recently, molecular studies support the epithelial nature of the sarcomatoid component, this view is not yet unanimously accepted, and, as a consequence, there is no clear consensus as to prognosis and optimum treatment.² The mean age of diagnosis is in the sixth decades of life.

It has male predilection.The predisposing factors are the same as squamous cell carcinoma, including alcohol abuse, cigarette smoking, poor oral hygiene and previous radiotherapy. Growth is usually exophytic polypoid or pedunculated and can cause obstructive symptoms. It is potentially aggressive and have a propensity for recurrence and metastases.⁴ This tumor has specific clinical features and behavior, and the establishment of the correct diagnosis has important implications for management.⁵ Surgery is considered to be the mainstay in the management of SpCC. The effectiveness of radiotherapy was suggested by Ballo *et al* in 1998, however, more recent studies did not confirm the impact of radiotherapy on survival. The role of cytotoxic chemotherapy is unclear.⁶ Only a few cases have been reported in the medical literature. Therefore, in this unusual case report with its immunohistochemical features are highlighted and a review of the literature was carried out.⁵

II. Case Report

In February ,2016, a 15yrs old male patient came to the Dept of Oral and Maxillofacial surgery, Guru Nanak Institute Of Dental Sciences & research , with a chief complaint of swelling on left side of palate, left upper jaw for last 1 month. There was occasional oral bleed . Patient gives history of rapidly enlarging lesion on the left side of the palate for last 7 days with no h/o pain, no nasal discharge or discharge from eye (fig. 1). Patient was asymptomatic one month ago. There was no h/o fever, wt loss, or any swelling over body.There was no such relevant medical history.



Fig. 1 Clinical view showing the polypoid mass involving the left side of palate

On examining the patient it was notified that mouth opening was adequate there was a soft to firm large mass involving the left upper alveolus extending from the incisors till the left maxillary second molar, crossing the midline on the palate. There was bulge on the floor of the nasal cavity. No paresthesia present. The overlying mucosa was intact with a traumatic ulcer due to trauma from lower teeth. No exophthalmos present and pupillary light reflex and orbital movements was within normal limits. No lymph node was palpable. Left maxillary molars were mobile. On taking the OPG (fig. 2) it revealed a radiolucent lesion on the left maxillary antrum with root resorption of upper left molars.

CECT(fig. 2) of face was showing large heterogeneous growth involving the left maxilla and causing destruction of hard palate. Retroantral space was involved. Pterygoid base was involved, at the origin of the temporalis and medial pterygoid muscle. Pterygomaxillary fissure, PPF and SPF were involved. Floor of the orbit was eroded, lateral wall of nasal cavity was eroded.

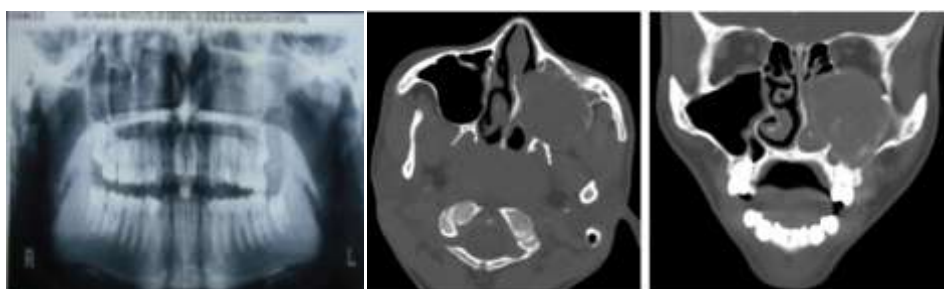


FIG 2. OPG and Computed tomography scan showing the extension of the lesion

On 18th February, Incisional Biopsy was taken from the palatal lesion and sent for histopathological (H/P) and immunohistochemical (IHC) evaluation. H/P impression was “**Malignant spindle cell Neoplasm**”, Immunohistochemistry impression is suggestive of “**Spindle cell sarcoma most consistent with fibrosarcoma**”. After that we refer the patient for further treatment and possibility of chemoradiation.

NaF18 PET CT was done and increased tracer activity was noted at the left maxilla at the primary site. No evidence of distant metastases was noted as well as no lung nodules.

Mri Of Pns and Orbit was done , and it showed large well defined peripherally sclerotic lesion of left maxillary sinus of approximate 4.7 x 4.3 x 6.8 cm. there was erosion of medial wall of maxillary sinus, the lesion was extending into left nasal cavity. The lesion was involving maxillary alveolar ridge, palatal and buccal surface of hard palate. There was superior displacement of floor of orbit without invasion of extraocular muscles or intra or extraconal spaces of orbit.

Total maxillectomy of left side, with supraomohyoid neck dissection and reconstructed the defect with free fibula osseocutaneous flap along with split thickness skin graft and was referred for EBRT to tumour bed with margins to a dose of 64.8Gy/36#/7 weeks using conformal technique.

The post operative 5 months check up was uneventful and patient is presently doing well (fig. 3).



Fig. 3. Post-operative 5 months photograph.

III. Case Report 2

In June 2016, a 52 years old male patient walked in to the Dept of Oral and Maxillofacial Surgery, Gnidrs, Kolkata with a chief complaint of swelling inside his mouth on right side for last 5 days. On taking the detail history, the patient was apparently alright one month ago. After that he noticed a blockage of right nostril alongwith pain in the right back teeth region. There was history of epiphora from right eye. Gradually a swelling appears at the right cheek region, then inside the mouth on the rt side a small swelling appeared, which bleed occasionally. There was history of episodic fever for last 5 days.

Extraorally the swelling was firm, non tendered, fixed to the underlying structure with local rise of temperature, overlying skin was fixed. There was no discharging sinus, no infraorbital paraesthesia. Facial nerve functions are normal. Right level IB palpable, firm, non tendered, free from the skin, free from the underlying structure.

Intraorally the growth was soft, non pulsatile, non tendered, pedunculated, lobulated surface, without surface ulceration and situated in the mucobuccal fold region in relation to rt maxillary first and second molar. The growth was erythematous and bleeds on provocation (fig.4).



Fig. 4. Clinical view showing- extra-oral -firm swelling, fixed to the underlying structure with local rise of temperature, overlying skin was fixed. Intraoral -the growth was soft, pedunculated, lobulated surface, without surface ulceration and situated in the mucobuccal fold region in relation to rt maxillary first and second molar.

37 degree occipitomenal view showed diffuse radioopacity of right maxillary antrum. cect of face, showed a large heterogeneously enhancing mass filling the right maxillary sinus. Medial wall of right maxilla was destroyed with extension of mass into the nasal cavity which is blocked by the lesion. There was destruction of the maxillary alveolar process and floor of the maxilla, superior wall was not destroyed and there was infraorbital extension of the growth. Lateral wall (inferior part) was destroyed by the lesion with mass into the cheek and posterior wall (inferior part) was also destroyed with extension of the mass into the infratemporal fossa. Medial pterygoid plate was destroyed, along with involvement of masticator space. Pterygoid muscles were involved. Pterygomaxillary fissure and sphenopalatine foramen were also infiltrated. Base of the skull was normal and there was no intracranial extension(fig. 5).

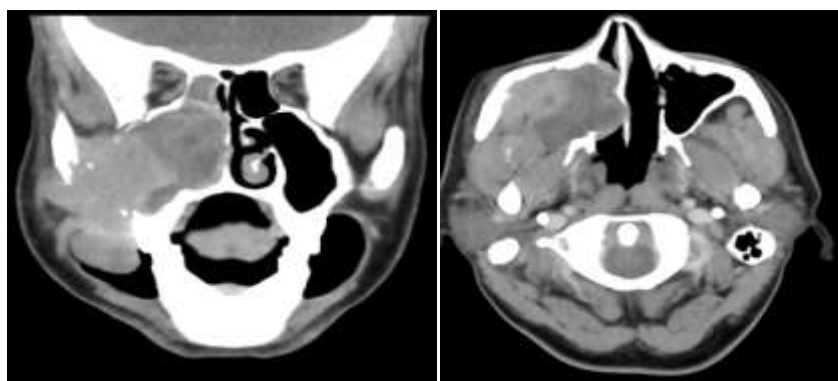


FIG. 5.Computed tomography scan showing the extension of the lesion

Chest radiograph (PA view) appeared normal.

We did excisional biopsy from the exophytic growth which obliterate the mucobuccal fold and did incisional biopsy from the right maxillary sinus from buccal corridor to get some cheesy, grayish, myxoid, fat like lobulated mass and sent them for histopathologic evaluation. The pre operative h/p evaluation showed a

lesion composed of spindle shaped cell lying in a myxoid stroma. The h/p evaluation was suggestive of **spindle cell neoplasm**, immunohistochemistry was necessary to know the exact categorization(fig. 6).

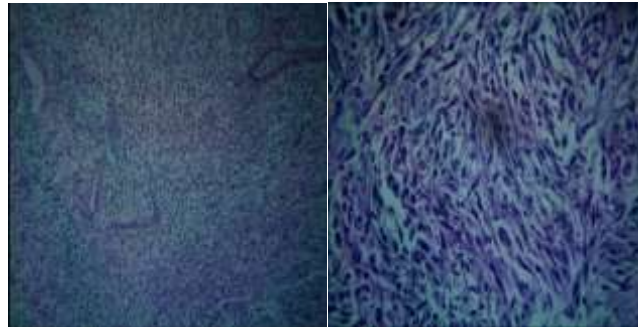


Fig. 6. Photomicrograph showing sarcomatoid proliferation of spindle-shaped epithelial cells in the deeper portions of the tumor (H&E staining, original magnification --10 X and 40X)

We planned for total maxillectomy with wide local excision of lesion (keeping 2 cm safe margin all over), and SOHND. So, we gave lateral rhinotomy incision with lynch incision and lip split, did total maxillectomy of right side with wide local excision of lesion , ethmoid and right frontal sinus obliteration with abdominal fat graft, did supraomohyoid neck dissection. Obturator was placed. The primary defect was reconstructed by rt lateral forehead flap and secondary defect was reconstructed by split thickness skin graft(fig. 7). We sent the specimen for h/p and IHC evaluation. The post operative h/p evaluation from right sided maxilla with lesion and skin was suggestive of Sarcomatoid carcinoma of maxilla. The h/p evaluation from soft tissue mass from ethmoid was free of any tumour cells. H/p from lymph nodes from rt sided, level IA, IB, IIA, IIB, III was free of tumour infiltration.





Fig.7.Per-operative surgical photographs—neck dissection,wide local resection,reconstruction with abdominal dermis graft and lateral forehead flap---the final closure. IHC of the maxillary growth was done, and was immunoreactive (score 2+in neoplastic cells) for S-100 IHC marker and negative for other markers like CD34, CD99, HMB 45 etc. the IHC report was suggestive of **Spindle Cell Sarcoma with features favouring MPNST (Malignant Peripheral Nerve Sheath Tumour).**

We did the post op follow up for 1 month(fig. 8), and preparing the patient for further chemoradiation but within 2 month interval the patient succumbed to his illness 5 months following the onset of symptoms(fig. 9).

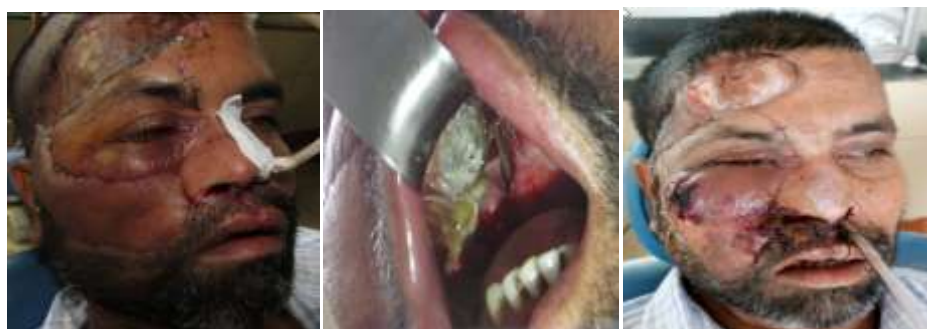


Fig.8. Post-operative- 1 month view --- 1 and ½and months with recurrence



FIG.9. Post-operative 2 months photograph with massive recurrence

IV. Discussion

Sarcomatoid (spindle cell) carcinomas are unusual variants of squamous carcinoma reported to account for less than 1% of all tumours of oral regions³ and 3% of all squamous carcinomas in the head and neck region.³ Occurrence of carcinosarcoma in maxillary sinus is very rare, with only 11 cases reported since 1957¹³. It is considered a biphasic malignant tumour, as it has spindled or pleomorphic tumor cells which simulate a true sarcoma but of epithelial origin.⁴ About one third are monophasic spindled or pleomorphic histologically, making the diagnosis more challenging.⁴ Both the sarcomatoid as well as conventional squamous carcinoma components have now been proven to arise monoclonally from a single stem cell, and there is further evidence to prove that the sarcomatoid component represents a dedifferentiation and suggests molecular progression of the conventional component.³ The initial description of this type of entity was given by Virchow in 1864. It is also known as pseudosarcoma, carcinosarcoma, sarcomatoid squamous cell carcinoma or polypoid squamous cell carcinoma.¹ WHO classification has placed this tumour under a highly malignant variant of squamous cell carcinoma and labelled it spindle cell carcinoma.⁴ Spindle cell carcinoma has been thought to be a collision

tumour, combination tumour or composition tumours. There was a great confusion on whether it is carcinoma or sarcoma, and benign or malignant.⁴ It was later when studies of the morphologic, immune histochemical, ultra structural and molecular features of spindle cell carcinoma have been established, that this tumour is recognized as a carcinoma that has surface epithelial changes and an underlying spindle-shaped neoplastic proliferation.⁴ This tumour occurs mainly in upper aerodigestive tract. The larynx, particularly the glottis in 70% of cases is the commonest primary site.^{1,4} The second commonest site is the oral cavity, which may arise from the tongue, floor of the mouth, alveolar ridge, gingivae or lower lip. It may also occur in other sites of body such as head and neck skin, in the soft tissues of the scalp and orbit. The mean age of diagnosis is in the sixth decades of life, but it can be diagnosed in younger age group and older age group (range 29 -93).⁴ Some authors have reported male predilection with ratio of 12:1.⁴ However, it is becoming more common in females. The predisposing factors are the same as squamous cell carcinoma, including alcohol abuse, cigarette smoking, poor oral hygiene and previous irradiation site.⁴

Growth of this tumour is exophytic polypoid or pedunculated in 98.9% of cases. It can also be sessile, nodular or endophytic.⁴ The lesion usually has an extensive surface ulceration with friable, fibrinoid necrosis of variable thickness or shaggy exudates.⁷ This tumour has tendency to cause obstructive symptoms especially when it occurs in larynx.^{1,3,4} Patients may present with cough, voice change, and hoarseness of voice, dyspnea or stridor. Tumours of oral cavity and oropharynx typically present with just complaint of a mass or with painful, non healing ulcer or bleeding.⁴

Spindle cell carcinomas are staged according to the TMN classification of American Joint Committee on Cancer staging, based on their size and the presence or absence of metastases to local lymph nodes or other parts of the body.⁴ Clinically they tend to present at an advanced stage, with most tumours being T3 or T4 at presentation and pursuing an aggressive course.⁸ Neck node involvement, which is uncommon in squamous cell carcinomas of maxilla, may be present. Leventon et al, have proposed depth of invasion by the tumour to be the most important prognostic criterion, with deeper infiltration indicating a poorer survival.⁸

Two hypotheses for origin have been proposed. While the convergence hypothesis suggests origin from two stem cell lines, the divergence hypothesis suggests origin from a single stem cell differentiating into epithelial and sarcoma elements. It has been shown that the expression patterns of K-ras gene, p53 gene and X-chromosome inactivation are similar in both the epithelial and sarcomatous components giving support to origin from a single stem cell.⁸

Histologically, Spindle cell carcinoma exhibits both epithelial cell component and sarcomatoid or spindle cell component.⁴ The spindle cell component may demonstrate varied histological appearance ranging from benign reactive lesion to malignant lesions. The most common ones are pleomorphic (malignant histiocytoma like) and spindle cell sarcoma (fibrosarcoma like). While spindled component usually predominates, the squamous component is either focal dysplasia, carcinoma in situ or invasive SCC.⁴ Histological and immune histochemistry demonstration of both squamous cell component and the spindle cells with sarcomatous appearance is essential in establishing the diagnosis. Differential diagnosis includes a number of benign and malignant tumours, such as fibromatosis, nodular fasciitis, reactive epithelial proliferations, squamous cell carcinoma, fibrosarcoma, malignant fibrous histiocytoma, leiomyosarcoma, rhabdomyosarcoma, malignant peripheral nerve sheath tumour, mesenchymal chondrosarcoma and malignant melanoma.⁷ Histologically, routine light microscopic analysis after hematoxylin-eosin staining showed a biphasic appearance. The dominant component of the tumor was irregular spindle-shaped cells with scant cytoplasm and hyperchromatic spindle-shaped nuclei. These cells showed diffuse proliferation with squamous differentiation. However, the tumor cells exhibited very little interstitial fibrillar collagen and minimal storiform or whorl patterns, although myxoid stromal elements were seen. Abnormal mitotic figures were present in each microscopic field. These characteristics were indicative of SpCC.⁹

Immunohistochemical studies are useful to know the histogenesis of the spindle cells within these tumours and nature of SpCC.⁴ There are numerous histogenetic hypothesis have been proposed over the years, with 3 principal theories,^{4,7} including: 1) it is a collision tumour or a carcinosarcoma; whereby a separate epithelial and mesenchymal cell have each become malignant; 2) it is a spindle cell carcinoma or sarcomatoid carcinoma – an epithelial cell that differentiates into spindle cell component; or 3) it is pseudosarcoma – a squamous cell carcinoma that undergoes benign reactive stromal.^{4,7}

Immunohistochemical characterization of tumour cells using antibodies to keratin, vimentin, and S-100 protein is very helpful in differentiating SpCC from true spindle cell sarcoma, melanoma and malignant myoepithelioma.⁷ Epithelial markers include keratin (AE1/AE3, CK 1,8,9), epithelial membrane antigens, KI, and K18. The most sensitive and reliable ones are keratin and epithelial membrane antigen. They are helpful in differential diagnosis from other sarcomatous lesions.⁴ In the IHC, it is important to remember that SpCC should not be ruled out of the differential diagnosis by a positive reaction for vimentin in sarcomatoid tumour cells.⁷ Absence of staining for keratin in the sarcomatoid tumour cells does not always exclude SpCC because some SpCC show immunoreactivity of keratin in their sarcomatoid components only with some anti-keratin

antibodies. Different kinds of anti-keratin antibodies should be applied in the differential diagnosis of SpCC.⁷ IHC analysis of our second case showed immunoreactive to S-100 IHC markers (score 2+ in neoplastic cells). This S-100 is present in the nucleus and cytoplasm of glial and Schwann cells, melanocytes, chondrocytes, adipocytes and myoepithelial cells. All tumours derived from these cells are positive for S100. Its main use is in the evaluation of peripheral nerve sheath and melanocytic series. IHC analysis of our first case showed cytokeratin, and CD 34 positivity.

Su et al¹⁴ found a 3-year overall survival of 27.5% and a local recurrence and distant metastasis rate of 73.3% and 33.3%, respectively. Ellis and Corio¹⁵ reported an overall survival of 31%. The mean survival for those who died of disease was less than 2 years. Oral cavity tumors appear to behave more aggressively than other subsites.

The treatment option in Spindle cell neoplasm has been debated. Some authors are of the opinion that wide radical resection alone is sufficient while some prefer surgery with radiotherapy. The best long term outcome for patient is surgery followed by radiotherapy.⁴ Traditionally, surgery is considered as the mainstay treatment of the SpCC. This fact is explainable by the location and natural history of the disease.⁶ The majority (70%) of the SpCC are located in the glottic region and present with symptoms of hoarseness, dyspnoea and cough, appearing as polypoidal and pedunculated masses, usually less than 2 cm in size. In this situation, a wide local excision is a radical treatment as the underlying stroma is not involved by the tumour.⁶ The outcome of surgery alone for early SpCC is excellent. More advanced disease requires combined treatment with adjuvant radiotherapy. SpCC were traditionally believed to be aggressive, radioresistant tumours, and radiotherapy was considered to have a limited role.⁶ Radiotherapy is considered an acceptable choice for inoperable patients and useful in case with surgical margin positive or extensive nodal disease.^{4,7} Unfortunately 30% of all oral cases, most cases were ending fatally within one year. This is similar in connection with the high grade SCC.⁷ Presence of metastasis signals a poor prognosis as per study conducted by Ellis and Corio and this applicable in cases of oral cavity.⁷

Ballo *et al* reviewed 28 cases of early sarcomatoid carcinoma of the larynx (21 were classified as T1N0M0 and 7 as T2N0M0) treated with radical radiotherapy (mean dose 65 Gy). With the median follow-up of ten years (range from 1.5 to 24 years) only four patients recurred and were salvaged with radical laryngectomy.⁶ The study concluded that there was no difference in outcome of radiotherapy between SCC and SpCC- and that the histologic diagnosis of sarcomatoid carcinoma by itself should not influence the decision to treat a patient with early stage glottic disease with irradiation.⁶

Thompson *et al* reviewed 187 cases of laryngeal SpCC. Seventeen patients (9%) had a history of a prior radiation of the larynx. All patients were managed by surgery (excisional biopsy only in 24 patients, excisional biopsy followed by radical surgery in 66 patients and surgery followed by adjuvant radiotherapy in 97 patients). This study, as most of the literature focused on diagnostic controversies (histopathological features) and clinical aspects were not reported in detail. The dose of radiation ranged from 2–72Gy (incomplete treatment course to full treatment). The authors relied on the records of the Data Oncology Services (cancer registry) of referring departments. They also reported a lower percentage of patients who died of their disease in the surgery only group (18.5%) compared with the surgery and radiation group (42.3%), although the survival was longer in the radiation group (3.6 years) compared to those in the surgery only group (1.9 years). There was no significant difference in length of survival between the patients managed by radiation alone (no salvage, mean survival 3.9 years) versus patients who had radiation and a salvage procedure (mean survival 3.9 years). The authors conclude that patients who were managed with surgery alone had a better outcome than patients managed with surgery and postoperative radiation. However, the authors admitted that they were unable to make a specific comment about the possibility that radiation therapy was used only in the more clinically advanced cases. It is not possible to draw any conclusion concerning the role of radiotherapy, and also it is not possible to recommend the dosage of radiotherapy or the volume to be treated.¹⁰

Reys *et al* reported two cases of SpCC of the tongue. Both patients presented with locally advanced disease (T4N2M0 and T4aN1M0) and were managed with a combined modality treatment i.e. radical surgery followed by adjuvant chemoradiotherapy. Pulmonary metastasis developed in first patient in five months after surgery while the second patient was disease-free two months after surgery.¹¹

Bice *et al*, who found survival of SpCC of the oral cavity and oropharynx worse than survival of conventional SCC. At the same time, there was no difference in the outcome for larynx or hypopharynx site. In his large study analysing 118 patients he identified in multivariate analysis only age, tumour size, and M (metastatic) stage as variables significantly affecting the survival with SpCC.¹²

In our cases we also went for radical surgery followed by chemoradiation, but in second case though we did the surgery successfully, but we lost the patient even before sending him for radiotherapy. The first case is still doing well after undergoing surgery and radiotherapy.

In a study by H H SU et al, out of total 15 patients of SpCC of oral cavity and oropharynx receiving surgery, recurrence rate was 73.3% and metastasis rate 33.3% was reported. In another study by Anupam Sharma et al the overall recurrence rate was found to be 71.4% and metastasis rate of 21.4%.⁷

V. Conclusion

spcc is a neoplasm of epithelial origin and considered to be a variant of SCC. It mimics other connective tissue sarcomas and spindle cell malignancies under light microscopy. Immunohistochemistry is helpful to know the histogenesis and nature of SpCC. Sarcomatoid carcinoma of maxilla is a rare aggressive tumour with poor prognosis. Surgery and radiotherapy form the mainstay of treatment. Exploration of the role of chemotherapy and novel targeted therapy agents is warranted in order to improve treatment details. Prognosis of the disease is always poor and distant metastasis is always more than the conventional SCC. There is no clear consensus as regards to prognosis and optimum treatment.

Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflicts of interest: None

Acknowledgement: Dr . P . Sinha (anesthesiologist)

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