



## Carcinosarcoma of the Oropharynx: A Case Report and Review of Literature

Authors

**Dr Shobana Vallabhaneni<sup>1</sup>, Dr Kanika Sharma<sup>2</sup>, Dr Amar Bhatnagar<sup>3</sup>,  
Dr Hemamalini Aiyer<sup>4</sup>, Dr Garima Rawat<sup>5</sup>**

<sup>1</sup>DNB Resident, Radiation Oncology, Dharamshila Narayana Superspecialty Hospital, Delhi, India

<sup>2</sup>Senior Consultant, Radiation Oncology, Dharamshila Narayana Superspecialty Hospital, Delhi, India

<sup>3</sup>Senior Consultant, Surgical Oncology, Dharamshila Narayana Superspecialty Hospital, Delhi, India

<sup>4</sup>Senior Consultant, Pathology, Dharamshila Narayana Superspecialty Hospital, Delhi, India

<sup>5</sup>Senior Resident, Pathology, Dharamshila Narayana Superspecialty Hospital, Delhi, India

### Abstract

*The co-existence of carcinoma and sarcoma within the same tumor, termed as carcinosarcoma is an exceedingly rare condition which requires skilled oncopathologists to make the accurate diagnosis with the aid of histopathology combined with immunohistochemistry. The literature on the management of this entity is extremely sparse that it requires prospective studies to understand its etiopathogenesis, clinical course and ideal management techniques. The present knowledge inclines towards surgery as a primary treatment option with or without adjuvant radiotherapy depending upon the adverse features. We describe here a case of a 62-year-old gentleman who presented with complaints of dysphagia for a short duration with histopathology revealing carcinosarcoma of the oropharynx and immunohistochemistry depicting spindle cell squamous cell carcinoma with heterologous chondrosarcomatous and osteosarcomatous differentiation.*

### Introduction

Carcinosarcoma is a rare biphasic malignant tumor consisting of components of epithelial and mesenchymal origin. The term carcinosarcoma was first used by Virchow in 1864<sup>(1)(3)</sup>. Carcinosarcoma is a common entity in the upper aerodigestive tract, respiratory tract, and urogenital tract. Among the head and neck malignancies, oral cavity (63%) is a much more common site than larynx (17.5%) and oropharynx or hypopharynx (11.7%). The precise histogenesis of carcinosarcoma has not been elucidated yet. However, there are several hypotheses postulated in the literature for the possible cellular origin

amongst which the monoclonal hypothesis is widely accepted<sup>(2)</sup>.

### Case Report

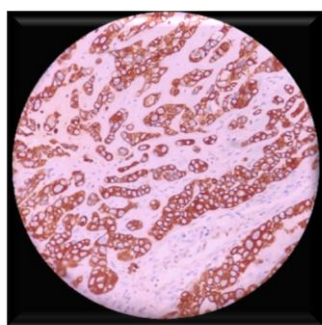
A 62-year-old gentleman presented to the oncology outpatient department with complaints of acute onset of dysphagia for solids of 15 days duration. He did not have any complaints of pain while swallowing, vomiting, regurgitation of food, halitosis, swelling in the neck, or voice changes. He did not complain of any weight loss. On examination, the patient was an average built adult with Eastern Cooperative Oncology Group (ECOG) performance status 0. Examination of the

oral cavity was grossly normal. General physical examination did not reveal any other abnormal findings. A Flexible Naso-Laryngo Pharyngoscopy revealed an ulceroproliferative growth over the lingual surface of epiglottis extending into the right vallecula. Base of tongue, bilateral tonsillar fossae, aryepiglottic folds, arytenoids, pyriform fossae, and vocal cords appeared normal. Histopathologic examination performed elsewhere showed a malignant tumor with mixed epithelial and chondroid

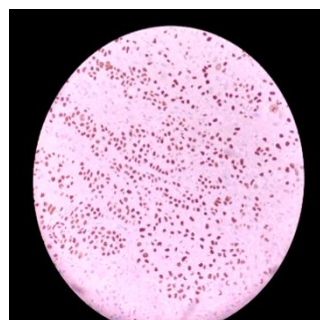
differentiation, suggestive of carcinosarcoma. Further, immunohistochemistry was performed which revealed spindle cell squamous cell carcinoma with heterologous chondrosarcomatous and osteosarcomatous differentiation. The tumor cells were immunoreactive for cytokeratin (CK-AE1/AE3), p40 & p63. S100, Vimentin & CD-99 were immunoreactive in the cartilaginous component. (Table 1 – IHC) (Immunohistochemistry {IHC} Images 1-8).

**Table 1 – IHC**

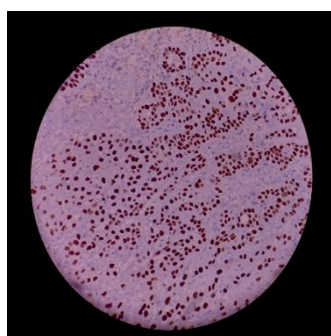
ANTIBODY	INTERPRETATION
CK	Immunoreactive score 4+ in neoplastic cells
P40	Immunoreactive score 4+ in neoplastic cells
P63	Immunoreactive score 4+ in neoplastic cells
S100	Immunoreactive score 3+ in cartilaginous component
Vimentin	Immunoreactive score 3+ in cartilaginous component
CD99	Immunoreactive score 3+ in cartilaginous component
Ki-67	Immunoreactive score 3+ in neoplastic cells (40%)



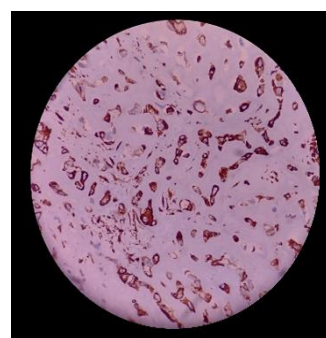
**Image 1 - IHC positive for CK**



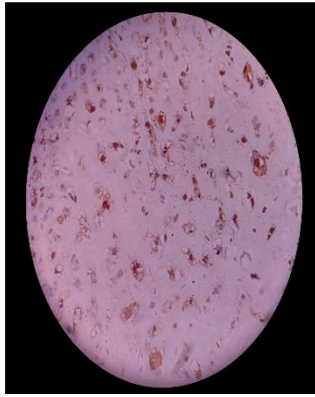
**Image 2 - IHC positive for p40**



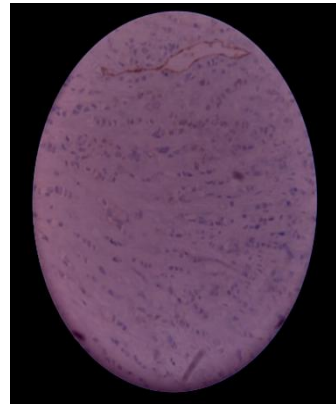
**Image 3 – IHC positive for S100**



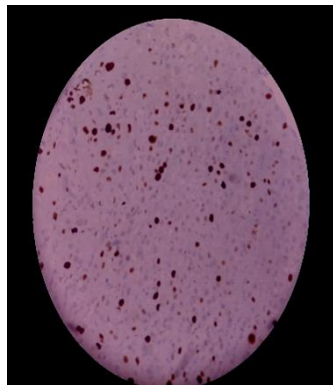
**Image 4 – IHC positive for Vimentin**



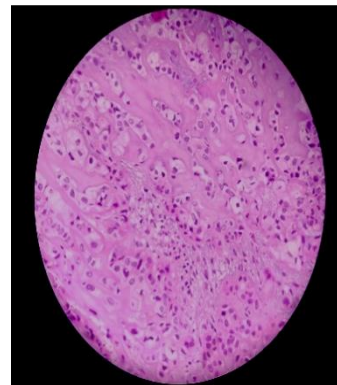
**Image 5 – IHC positive for S100**



**Image 6 – IHC positive for CD99**



**Image 7 – IHC positive for Ki 67**



**Image 8 – IHC positive for osteosarcomatous component**

Further, a contrast enhanced computed tomography (CECT) scan suggested a heterogeneously enhancing ill-defined soft tissue density mass measuring 20 x 16 x 9 mm in the right half of epiglottis with irregular border on the lingual surface causing partial obliteration of the right vallecula. No involvement of hyoid, pre epiglottic space, para glottic space, pyriform fossae, or the aryepiglottic folds was noted. Few sub centimetric right level II lymph nodes were noted and categorized as reactive nodes radiologically. He was advised for robotic surgery which he underwent successfully. Histopathology report did not warrant any adjuvant radiotherapy. He is now asymptomatic and continues to be on regular follow up.

### Discussion

Carcinosarcoma is a rare entity in the oropharynx. There is one case report in the literature and very

few cases included in case series of carcinosarcoma in the head and neck. Though the histopathological diagnosis of carcinosarcoma is commonly identified in some sub sites of head and neck like oral cavity and larynx, its rare presentation in oropharynx lead to paucity in the literature for adopting a standard course of management.

Carcinosarcoma is a biphasic aggressive malignant tumor which is composed of epithelial and mesenchymal elements<sup>(2)</sup>. The precise origin and histogenesis of carcinosarcoma is unknown. There are several hypotheses proposed enumerating the possibilities of such a development<sup>(1)(5)(14)</sup> –

1. Collision tumor hypothesis suggests that carcinosarcoma might be because of two independent tumors colliding resulting in a single neoplasm<sup>(13)</sup>.

2. Combination theory suggests that both the components are derived from a single stem cell which undergoes divergent differentiation early in the evolution of the tumor.
3. Conversion theory states the possibility of sarcomatous elements derived from the carcinoma during tumor evolution.
4. Composition theory suggests that the presence of spindle cells is a pseudosarcomatous stromal reaction to the presence of carcinoma.

Collision tumors are entirely different from multiphenotypic or metaplastic tumors that are monoclonal in origin<sup>(13)(14)</sup>. Multiphenotypic tumors fit into the hypothesis of combination or conversion theory<sup>(14)</sup>. The case reported in this article shows spindle cell squamous cell carcinoma with heterologous (sarcomatous components not belonging to the primary tissue of origin) chondrosarcomatous and osteosarcomatous differentiation on immunohistochemistry which is a multiphenotypic tumor<sup>(14)(15)</sup>.

After the first case identified by Virchow in 1864, a landmark study by Batsakis et al. categorized the tumor into three types<sup>(3)</sup> – Pleomorphic (Spindle Cell) carcinoma, Carcinoma with pseudosarcomatous stroma and Carcinosarcoma. Two antithetical hypotheses have also been proposed explaining the origin of carcinosarcoma, the multiclonal and the monoclonal hypothesis. But the recent immunohistochemical and molecular studies strongly favor monoclonality in carcinosarcoma, a process where a single pluripotent stem cell can differentiate into mesenchymal and epithelial elements, thus, confirming the monoclonal hypothesis<sup>(2)(10)(12)</sup>.

Within the sarcomatous differentiation, the most common histology among the heterologous elements is chondrosarcoma, osteosarcoma and fibrosarcoma in the same order. Moderate to poorly differentiated adenocarcinoma (not otherwise specified) or undifferentiated carcinoma is the most common carcinomatous component.

Risk factors associated with the development of carcinosarcoma of head and neck most commonly include smoking and alcohol consumption, advanced age, male gender, and a previous history of radiation to head and neck<sup>(7)</sup>.

Diagnosis of a metaplastic tumor is a daunting challenge as the mesenchymal portion must be differentiated from desmoplastic reaction and spindle cell squamous cell carcinoma<sup>(1)(11)</sup>. Immunohistochemistry for specific antibodies is useful for definite typing<sup>(1)(3)</sup>. Antibodies to CK, p40, S100, vimentin, p63 & CD 99 are some of the commonly tested ones. A thorough immunohistochemistry is imperative for the diagnosis of carcinosarcoma as it is an aggressive tumor which requires accurate diagnosis for early management and for employing the correct treatment modality<sup>(6)</sup>.

In a study conducted by Tarun K. et al, 11 Indian patients of carcinosarcoma in upper aerodigestive tract were analyzed<sup>(3)</sup>. The study demonstrated oral cavity as the most common site among the Indian population in contrast to the glottis which is a common site in the West along with a lower age group susceptibility (average age is 58.8 years vs 70 years), and higher incidence of nodal metastases (81.8% vs 24%) in comparison to the Western population studies<sup>(3)(4)</sup>. 7/11 patients were treated with surgery as a primary treatment followed by adjuvant radiotherapy. 1 out of these 7 patients received neoadjuvant chemotherapy for T4a disease. 3/11 patients had disease in the oropharynx (base of tongue – 2 & soft plate – 1) and 1/11 patients had disease in the supraglottis. These patients were treated with definitive radiotherapy and surgery reserved for salvage. 2 patients treated with definitive radiotherapy and 1 patient treated with definitive surgery had recurrence. They identified surgery followed by adjuvant radiotherapy as the best available option in the current setting for management of carcinosarcoma of upper aerodigestive tract. However, definitive radiotherapy can be given to patients with inoperable disease with reasonably good outcomes.



In a study conducted by Berthlet et al on 17 patients of carcinosarcoma, it was identified that surgery was superior to radiotherapy as a primary treatment of carcinosarcoma. Patients diagnosed with early stage extra laryngeal disease who underwent surgery as a primary treatment had an overall survival advantage<sup>(4)</sup>. Adjuvant treatment with radiotherapy was offered in the presence of adverse features like close/positive margins, lymph node involvement, extra nodal extension, perineural invasion and higher depth of invasion<sup>(4)</sup>. Close/positive margins were addressed via surgical re excision first or via adjuvant radiotherapy when re excision is not feasible<sup>(3)(4)</sup>. However, a study conducted by Ballo et al on 28 patients with T1-T2 N0 sarcomatoid carcinoma of vocal cords identified that radiation delivered to similar volume disease of the more conventional histology of squamous cell carcinoma had similar outcomes with 5 year local control rates of 94% & 54% for T1& T2 lesions, respectively. The 10-year disease specific and overall survival was 92% & 63% respectively. A median dose of 65 Gy was delivered with the median field size of 20cm<sup>2</sup> in this study population<sup>(7)(8)</sup>. This study questioned the old but consistently validated concept of radioresistance exhibited by these tumors. Many other studies conducted by Dubal et al and Thompson et al also revealed that surgery alone or followed by post-operative radiotherapy delivered better results in terms of local recurrence and survival. These studies could not make a valid comment upon on treatment with definitive radiotherapy as all the patient population treated with radiotherapy alone had an advanced stage disease that is associated with a poor outcome<sup>(7)(9)</sup>. It was also interesting to identify 17 patients of the total study population of 187 in the study conducted by Thompson et al had a previous history of irradiation to larynx thus, making accurate interpretations difficult<sup>(7)</sup>. Most of these studies are retrospective studies which analyzed data from database and cancer registries. Therefore, randomized prospective trials are needed to understand the course of the

disease and for establishing guidelines for the precise management of carcinosarcoma in the future. However, owing to the relative rarity of the disease in head and neck malignancies, a prospective trial would be exceedingly difficult to accomplish. A detailed histopathological examination and a thorough immunohistochemistry will help in establishing the precise diagnosis and might bring a few more cases into light<sup>(11)</sup>.

### Conclusion

With the rarity of the diagnosis in head and neck malignancies, there are no fixed guidelines as of today for the management of carcinosarcoma. Precise diagnosis is possible with an experienced pathologist examining the specimen and immunohistochemistry to characterize the tumor. From the existing knowledge using the meager number of case reports and case series published and the retrospective database analyses, it can be agreed upon that the primary treatment of carcinosarcoma of head and neck is surgery followed by adjuvant radiotherapy, if adverse features are present in histopathology. Prognosis mainly depends upon the initial stage of the disease, extent of the carcinoma component, depth of invasion, treatment modality and extent of excision. Due to the aggressive nature of the disease, characterized by high rates of recurrences, metastases, and mortality, it is important to monitor the patients strictly and keep them under close follow up<sup>(2)</sup>. Whether definitive radiotherapy is an alternative to surgery and is radioresistance of these tumors truly valid needs to be answered in the future with more prospective studies comparing arms of definitive radiotherapy versus surgery.

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