Carcinosarcoma of the Submandibular Gland with a Rhabdomyosarcoma Component: A Case Report and Review of the Literature

Suma M. Narayana, Smrita Singh, Rekha V. Kumar

Department of Pathology, Kidwai Memorial Institute of Oncology, Bengaluru, Karnataka, India

Abstract

Carcinosarcoma of the salivary gland is a rare and aggressive malignancy with a poor prognosis. These neoplasms are composed of malignant epithelial and mesenchymal elements. This report describes a new case of carcinosarcoma arising in the submandibular gland, which had a rhabdomyosarcoma component, without clinical or histological evidence of a preexisting pleomorphic adenoma. Till date, only two case reports have described the occurrence of carcinosarcoma with a rhabdomyosarcoma component in the salivary gland, to the best of our knowledge. Histological and immunohistochemical results are presented. The literature is reviewed, and the possible histogenesis and pathogenesis of carcinosarcoma (true malignant mixed tumor) of the salivary gland are briefly discussed.

Keywords: *Carcinosarcoma, rhabdomyosarcoma, salivary gland, submandibular gland, true malignant mixed tumor*

Introduction

Carcinosarcoma of the salivary gland is a rare and aggressive malignancy with a poor prognosis. Around 70 cases have been described in the literature. These neoplasms are composed of malignant epithelial and mesenchymal elements. This report describes a new case of carcinosarcoma arising in the submandibular gland with a rhabdomyosarcoma component, without clinical or histological evidence of a preexisting pleomorphic adenoma. Till date, only two case reports have described carcinosarcoma with a rhabdomyosarcoma component in the salivary glands.[1,2] Both were in the parotid gland.

Case Report

A 50-year-old male presented with a left-sided submandibular swelling for 6 months, with a rapid increase in size for 2 months. He also had complaints of difficulty in breathing. Examination revealed a large, firm, mobile mass. Ultrasound of the neck demonstrated a 7-cm homogenous mass with well-defined margins and posterior acoustic enhancement. Computed tomography (CT) revealed a homogenous mass in the left submandibular gland extending into the adjacent muscle. Following contrast, there was marked homogeneous enhancement greater than that of the normal submandibular gland parenchyma and muscle. The margins were well defined. CT chest revealed bilateral lung metastases. Fine-needle aspiration of the mass showed clusters of spindle-shaped cells with moderate to marked atypia and few epithelial cells showing increased nuclear-to-cytoplasmic ratio with coarse chromatin, in a background of necrosis. Extensive workup did not reveal any other malignancy.

The patient underwent total excision of the left submandibular gland mass and left modified radical neck dissection. The resected specimen was sent for histopathological examination.

Formalin-fixed, paraffin-embedded sections were examined with routine hematoxylin and eosin stain. Immunohistochemistry (IHC) was performed on 3 μ sections cut from paraffin blocks according to the manufacturer's instructions. The antibodies used are given in Table 1.

Grossly, the excised submandibular gland mass measured 16 cm × 7 cm × 6 cm. The mass was encapsulated and the external

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Address for correspondence:
Dr. Suma M. Narayana, Department of Pathology, Kidwai Memorial Institute of Oncology, Dr. M. H. Marigowda Road, Bengaluru, Karnataka, India.
E-mail: mnsuma19@gmail.com

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surface was nodular. Cut surface revealed a gray-white tumor measuring 6 cm × 6 cm × 5 cm with areas of hemorrhage and necrosis [Figure 1a].

Microscopically, the tumor was composed of two components – carcinoma and sarcoma. The former was that of adenocarcinoma with neoplastic cells arranged in a glandular pattern [Figure 1b]. The latter was mainly composed of malignant spindle to ovoid cells in sheets and fascicles resembling fibrosarcoma [Figure 1c]. Frequent mitoses (>20/10 hpf) with areas of necrosis were present. Foci of rhabdomyosarcoma, containing sheets and clusters of cells with abundant eosinophilic cytoplasm and eccentric round nuclei, were observed [Figure 1d]. Fourteen regional lymph nodes were negative for tumor. No coexisting pleomorphic adenoma component was identified.

Both the carcinoma and sarcoma cells were positive for cytokeratin (CK) and negative for CD10 [Figure 2a]. The carcinoma cells were strongly positive for CK 5/6 [Figure 2b] and weakly positive for epithelial membrane antigen (EMA) [Figure 2c]. P63 was positive in scattered spindle cells [Figure 2d]. The spindle cells were strongly positive for vimentin [Figure 3a] and desmin [Figure 3b] but were negative for CD34, CD31, S100, and H-caldesmon. The rhabdomyosarcoma cells were positive for myogenin [Figure 3c]. Ki67 proliferation index was more than 80% [Figure 3d].

The patient developed respiratory complications due to lower respiratory tract infection, 6 weeks after the surgery and passed away.

Discussion

Carcinosarcoma is a malignant tumor composed of a mixture of both carcinomatous and sarcomatous elements. It is also known as true malignant mixed tumor. Carcinosarcoma of the salivary glands is a rare tumor with about 70 cases reported in the literature.[1-4] Carcinosarcoma of the salivary glands was first described by Kirklin *et al.* in 1951.[3] Carcinosarcoma is an extremely rare and aggressive tumor.[4] It accounts for only 0.04%–0.16% of all salivary gland tumors.[2] The patients' age range from 14 to 87 years.[4] There is no gender predilection. Many patients had a history of recurrent pleomorphic adenoma, and several cases have developed in a preexisting pleomorphic adenoma (carcinosarcoma ex pleomorphic adenoma).[5-8] Some cases, however, arose *de novo*, in the absence of a previous pleomorphic adenoma.[4,9] The etiology is unknown. Accumulation of genetic mutations such as loss of heterozygosity (LOH) at 17p13.1, 17q21.3, and 18q21.3 could be a factor. Allelic losses in three genetic loci were seen to occur at high rates: 17p13, which is the location of the p53 gene (73% of targets), 17q in the location of the nm-23 gene (55% of targets), and 18q in the

Table 1: Details of the antibodies used

Antibody	Dilution	Manufacturer	Antibody clone
CK	1:80	Biogenex	C11
CD10	1:40	Biogenex	56C6
CK5/6	Ready to use	Biogenex	D5/16B4
EMA	1:100	Biogenex	E29
P63	1:40	Biogenex	4A4
CD34	1:40	Biogenex	QBEND/10
CD31	1:40	Biogenex	9G11
S100	1:200	Biogenex	EP32
H-caldesmon	Ready to use	Biogenex	H-CD
Vimentin	1:200	Biogenex	V-9
Desmin	Ready to use	Biogenex	D33
Myogenin	1:100	Dako	F5D
Ki67	1:60	Biogenex	BGX-297

CK: Cytokeratin, EMA: Epithelial membrane antigen

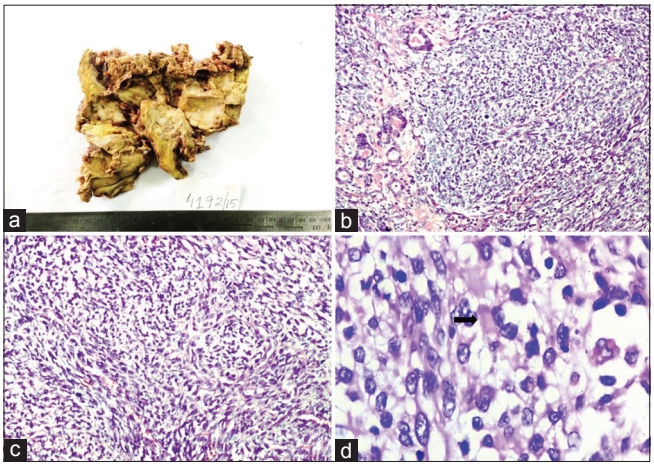

Figure 1: (a) Cut surface of the tumor showing gray-white areas; (b) section shows tumor cells forming glandular structures with an adjacent spindle cell component (H and E, ×10); (c) spindle cells arranged in intersecting fascicles (H and E, ×10); (d) tumor cells with large vesicular nuclei, prominent nucleoli with a rhabdomyoblast in the center (arrow) (H and E, ×40)

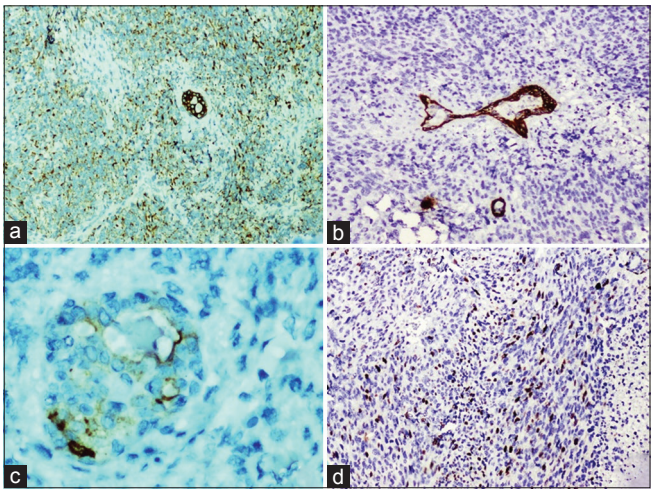

Figure 2: (a) Tumor cells positive for cytokeratin in both the carcinoma and sarcoma components (×10); (b) tumor cells of the adenocarcinoma component strongly positive for cytokeratin 5/6 (×10); (c) tumor cells weakly positive for epithelial membrane antigen (×40); (d) tumor cells showing scattered positivity for p63 (×10)

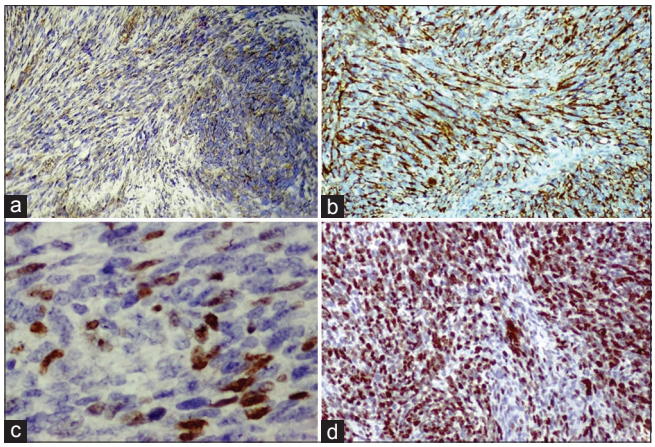

Figure 3: (a) Tumor cells weakly positive for vimentin (×10); (b) tumor cells strongly positive for desmin (×10); (c) tumor cells showing nuclear positivity for myogenin (×40); (d) tumor cells showing nuclear positivity in >80% of the cells for Ki67 (×10)

location of the DCC gene (50% of targets).[10,11] Irradiation of pleomorphic adenoma has also been implicated as an etiologic factor.[8] Two schools of thought exist as to the origin of carcinosarcomas. The convergence hypothesis states that polyclonal stem cells of the epithelial and mesenchymal components play a causative role. The divergence hypothesis postulates a monoclonal origin from a single totipotent stem cell with divergent differentiation.[12] Götte *et al.* hypothesized that the tumor originated from a myoepithelial cell precursor.[13] Other authors have postulated that the tumor originates from inner ductal cells or a pluripotent primitive cell.[6] In the cases reported, majority (66%) occurred in the parotid gland, followed by the submandibular gland (19%), and the minor salivary glands in the palate (14%).[3-5] Other sites include the cheek, tongue, and the supraglottis.[3-5]

The tumor often presents as a rapidly enlarging mass that may or may not be associated with pain. If the parotid gland is involved, signs of facial nerve palsy are commonly seen.

Macroscopically, the neoplasm is either well delineated or poorly circumscribed with infiltrative borders. Focal areas of hemorrhage and necrosis may be present. Microscopically, it is characterized by the presence of two malignant components – an epithelial (carcinomatous) and a mesenchymal (sarcomatous) component. The carcinomatous component is usually a poorly differentiated adenocarcinoma, an undifferentiated carcinoma, or a squamous cell carcinoma, and the sarcomatous component is usually a chondrosarcoma.[4] However, the sarcomatous component in the reported cases is varied and includes spindle cell sarcoma not otherwise specified, fibrosarcoma, osteosarcoma, and rhabdomyosarcoma.[2,4,5,9] Perineural invasion, angioinvasion, and tissue destruction are common. Lymphatic spread is less common.[3]

The immunohistochemical profile varies depending on the observed components of the tumor. Usually, the carcinomatous component is positive for CK and EMA, and the sarcomatous component is vimentin positive. However, in very poorly differentiated tumors, the carcinomatous component may show only focal or weak-positive staining for cytokeratins or EMA.

The prognosis of these tumors remains unfavorable, with rates of mortality at 5 years varying between 48% and 100%. This is clearly worse in comparison with that of carcinoma ex pleomorphic adenoma, probably because of the absence of the sarcomatous component.[14]

In a review by Gnepp, 58% of patients died as a result of the tumor.[4] Staffieri *et al.*, in a review of 19 cases of *de novo* carcinosarcomas, found that 31.6% of patients died of the tumor.[9] The median period of survival after the diagnosis was 10 months.[9] In 63% of cases, there was no evidence of recurrence after a median period of 22.4 months.[9]

Although ultrasonography and CT scan are essential, the histologic examination is crucial to establish a definitive diagnosis.

Regarding therapy, the data in the available literature suggest that surgical resection (histologically negative margins) should always be associated with neck dissection including levels I, II, III and IV, and adjuvant radiotherapy. Some authors have suggested the combination of adjuvant chemotherapy with adjuvant radiotherapy.[3] However, the role of chemotherapy has not been well established.

Conclusion

It can be seen from the review of literature that carcinosarcoma of the salivary gland is a rare neoplasm with rapid disease progression and an unfavorable prognosis. Even rarer is carcinosarcoma with a rhabdomyosarcoma component in the salivary gland, with only two case reports in the English literature. To establish a definite diagnosis and provide suitable therapy, histological examination and IHC are essential and help to rule out benign neoplasms, the exclusively epithelial malignant tumors of the salivary glands and submandibular and/or parotid lymph node metastases.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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