Carcinosarcoma (True Malignant Mixed Tumor) of the Submandibular Salivary Gland

SUBMANDİBULAR TÜKRÜK BEZİNİN KARSİNOSARKOMU (GERÇEK MALİGN MİKS TÜMÖRÜ)

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Summary

Introduction: Carcinosarcoma (true malignant mixed tumor) of salivary gland origin are a very rare and extremely aggressive neoplasm. By definition, it is composed of both malignant epithelial and malignant mesenchymal elements.

Case report: We report a rare case of submandibular salivary gland carcinosarcoma (true malignant mixed tumor) which occured in a 72-year-old women. At histologic examination, the tumor showed biphasic differentiation with an epithelial component made up of well-differentiated squamous carcinoma, and a mesenchymal component, revealing fibrosarcoma. Immunohistochemical studies confirmed two separete populations of tumor cells, corresponding to the histologic growth pattern.

Conclusion: Carcinosarcomas are aggressive neoplasms which in general rapidly develop metastasis or recur after resection and have a poor prognosis despite therapy

Key Words: Carcinosarcoma, Malignant mixed tumor, Submandibular salivary gland

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Özet

Giriş: Tükrük bezinin karsinosarkomu (gerçek malign mikst tümörü), çok nadir ve oldukça agresif bir neoplazmdır. Hem malign epitelyal hem de malign mezenkimal elemanları içermesiyle tanımlanabilir.

Olgu sunumu: Submandibular bezde 72 yaşındaki kadın hastada saptadığımız nadir bir karsinosarkom (gerçek malign mikst tümör) olgusunu sunduk. Histolojik değerlendirmede tümör epitelyal komponenti iyi diferansiye skuamöz karsinom, mezenkimal komponenti fibrosarkom olan bifazik diferansiyasyon göstermekteydi. İmmünohistokimyasal çalışmalar, histolojik büyüme paternleriyle uyumlu olarak iki ayrı tümör hücre popülasyonunu konfirme etti.

Sonuç: Karsinosarkomlar hızla gelişen metastazları yada rezeksiyondan sonra görülen rekürrensleriyle agressif neoplazmlardır ve tedaviye rağmen kötü prognoza sahiptir.

Anahtar Kelimeler: Karsinosarkom, Malign mikst tümör, Submandibular tükrük bezi

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Carcinosarcoma (true malignant mixed tumor) is composed of both malignant epithelial and malignant mesenchymal components. Carcinosarcoma is a very rare neoplasm, accounting for 0.05% of salivary gland tumors and 0.16% of malignant salivary gland tumors (1). Even rarer is a carcinosarcoma (true malignant mixed tumor) arising in the pleomorphic adenoma of the salivary gland (2). Since it was first described in 1951 by Kirklin et al. (3), there have only been approximately 60 cases reported in the English-language literature (1-14).

The most common malignant epithelial component is squamous cell carcinoma or adenocarcinoma, whereas the most common malignant mesenchymal component is chondrosarcoma, followed by fibrosarcoma, leiomyosarcoma, osteosarcoma, and liposarcoma (4).

In the salivary gland-revised WHO (5) and AFIP classification (6), carcinosarcoma belongs to the category of malignant mixed tumors, together with carcinomas arising in a benign mixed tumor (carcinomas ex-pleomorphic adenoma) and metastasizing mixed tumors (a controversial entity in which both the primary salivary gland tumor and its metastatic lesions are composed of typical benign-appearing mixed tumors). Malignant mixed tumors manifest an origin from a pre-existing pleomorphic adenoma (7,8). Moreover, there is a rare subset of salivary gland carsinosarcoma that arises "de novo", that is, they are not derived from pre-existing or co-existing benign mixed tumor (1).

We report another case of the rare carcinosarcoma (true malignant mixed tumor) of the submandibular salivary gland and present the results of immunohistochemical studies. In addition, the literature is reviewed, and the possible histogenesis and pathogenesis of carcinosarcoma of the salivary gland are briefly discussed.

Clinical Summary

A 72-year-old women presented with a 4-year history of a hard asymptomatic lump of the right submandibular area which, for 6 months prior to admission, had

undergone rapid growth. A large, hard mass under the mandible (on the right side) was found on clinical examination. The laboratory data were unremarkable. The overlying skin was normal. There were no enlarged lymph nodes or distant metastases. Computed tomography imaging revealed a 7-cm unhomogenous submandibular tumor. On MRI examination, the mass also showed central areas of necrosis and calcification. The excision of the right submandibular salivary gland was performed. Before operation, the mandible was clinically and radiographically free of tumor; this was confirmed at surgery. With a course of chemotherapy after the surgery, the patient is currently free of disease 1 year after the initial diagnosis.

Pathological Findings

Macroscopically, the specimen weighed 40 g and measured 7x 6x5 cm. The cut surface revealed a relatively well-defined, gray-white, heterogenous tumor that measured 4x3.5x3 cm. Focal necrotic and cystic changes were evident. Microscopically, the tumor was mainly composed of two components, carcinoma and sarcoma. The former was that of well-differentiated keratinizing squamous cell carcinoma (Figure 1). The latter was composed of fibrosarcoma (Figure 2). Mitotic figures were readily identified and necrosis was also present. In addition, in the periphery of the tumor, a focus of coexisting pleomorphic adenoma was present characterized by clusters of benign epithelial and myoepithelial cells entrapped in abundant hyalinized and cartilaginous matrix (Figure 3).

The immunohistochemical results are summarized in the Table 1. Stains were performed on formalin-fixed, paraffin-embedded tissue sections using a panel of monoclonal antibodies as follows: Cytokeratin, S100 protein, actin, smooth muscle actin, vimentin, desmin, glial fibrillary acidic protein (GFAP), chromogranin, epithelial membrane antigen (EMA) (Figure 4).

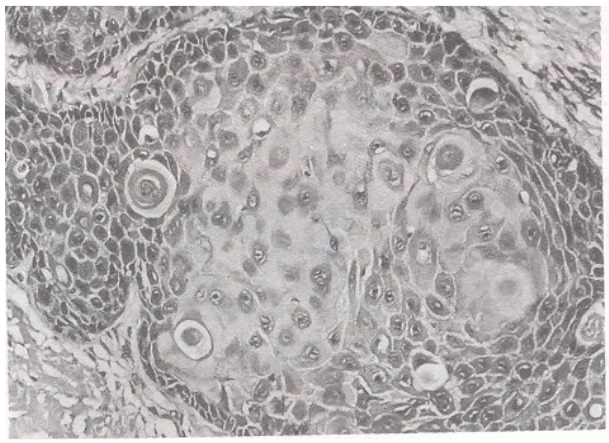

Figure 1. Histology of the carcinomatous component of the tumor-squamous cell carcinoma (hematoxylin-eosin, original magnifitionx200)

Discussion

Carcinosarcoma (true malignant mixed tumor) of the salivary gland is a biphasic neoplasm in which both the epithelial and stromal components fulfill histologic and cytologic criteria for malignancy. Two subtypes can be defined: one is carcinosarcoma ex pleomorphic adenoma, as reported exemplarily by Garner et al. (9), and comprises the majority of carcinosarcomas. The second group is defined by de novo carcinosarcomas without evidence of pre-existing pleomorphic adenomas, as reported by Latkovich and Johnson (10) and Bleiweiss et al. (7).

Clinically, carcinosarcomas present as large masses developing from a rapidly enlarged pre-existing salivary gland tumor (4,11). In our patient the tumor showed this

Figure 2. Fibrosarcomatous component (hematoxylin-eosin, original magnifition x 100).

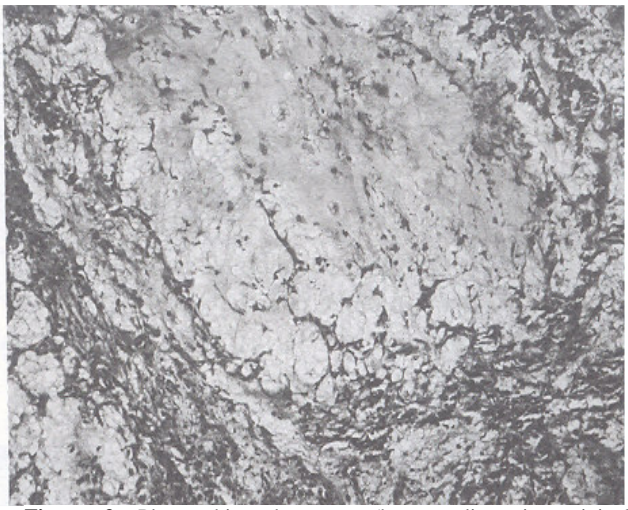

Figure 3. Pleomophic adenoma (hematoxylin-eosin, original magnifition x 100).

Table 1. Immunohistochemical findings in submandibular gland carcinosarcoma

Antibody (Clone)	Source	Epithelial areas	Sarcomatous areas
Cytokeratin (AE1-AE3)	DAKO	+	_
EMA (E29)*	Neo Markers	+	_
Actin (HHF35)*	Neo Markers	_	_
Vimentin (V9)*	Neo Markers	_	+
S100 (S1/61/69)*	Neo Markers	_	_
Smooth muscle actin (1A4)*	Neo Markers	_	_
GFAP (GA-5)*	Neo Markers	_	_
Chromogranin (LK2H10+PHE5)*	Neo Markers	_	_
Desmin (D33)*	Neo Markers	_	_

*monoclonal

characteristic clinical development. Local recurrence, hematogenous and lymphatic spread are frequent (4,12).

Gnepp summarized 43 cases of carcinosarcoma of the salivary glands published in the literature. The mean age was 58 years (range, 14-87 years). There was no sex predominance. Among 37 patients with available data, 21 tumors were from parotid glands, 8 from submandibular glands, 5 from the palate, 2 from unspecified major salivary glands, and 1 from the tongue (1).

Histologically, carcinosarcomas are biphasic neoplasms consisting of both malignant epithelial and stromal components. The epithelial components exhibit malignant glandular, squamous and undifferentiated carcinoma. The most common mesenchymal components are chondrosarcoma and fibrosarcoma. Undifferentiated sarcoma, osteosarcoma, liposarcoma and rhabdomyosarcoma are seen very rarely (1,4,13,14). Our patient showed a combination of fibrosarcoma and squamous carcinoma. Our case report shows some of the histologic features already reported by others, such as coexistence of squamous cell carcinoma and fibrosarcoma.

Immunohistochemically, our case is unusual, because two completely different staining patterns were seen. The epithelial component stained for keratin and EMA, sarcomatous component for vimentin.

The origin of the malignant mixed tumors has been subject of intensive debate for years. An association with clinical history of pleomorphic adenoma has been documented in one third of cases (1,4). Histologic evidence of coexisting or preexisting pleomorphic adenoma in true malignant mixed tumors of the salivary gland is therefore a quite common observation (13,14). The clinical and histologic relationship of true malignant mixed tumors and pleomorphic adenomas, as well as results of immunohistochemical studies, have led some investigators to postulate that the origin of salivary gland carcinosarcomas and pleomorphic adenomas could be from a common precursor cell (13,14).

Figure 4. Immunohistochemical stain for vimentin in fibrosarcomatous component (Vimentin staining, original magnification x 100).

Treatment should be complete surgical removal of the tumor and followed by radiation, chemotherapy or both.

Carcinosarcomas are aggressive neoplasms which in general rapidly develop metastasis or recur after resection and have a poor prognosis despite therapy (1,4,13,14).

In summary, this case represents a rare, carcinosarcoma (true malignant mixed tumor) arising in the pleomorphic adenoma of carcinosarcoma of the submandibular gland. Diagnosis of malignant mixed tumor of the salivary gland may be possible from the recognition of definitive malignant epithelial and sarcomatous components.

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