TRUE MALIGNANT MIXED TUMOR (CARCINOSARCOMA) OF THE PAROTID GLAND – CASE REPORT

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REZUMAT

Obiectiv: Tumora malignă mixtă adevărată (carcinosarcomul) este o tumoră extrem de rară în patologia glandelor salivare, fiind formată atât din elemente carcinomatoase, cât și sarcomatoase. Majoritatea acestor tumori sunt localizate la nivelul glandei parotide.

Material și metodică: Autorii prezintă cazul unei paciente în vârstă de 53 de ani din mediul urban, nefumătoare, ce a fost internată în Clinica ORL Timișoara în 2006, prezintând o formațiune în regiunea parotidiană stângă, aparută afirmativ cu 5 luni înaintea internării, crescând progresiv în dimensiuni. Sunt discutate diagnosticul și modalitățile de tratament ale acestei entități patologice.

Rezultate: Rezultatele histopatologice au evidențiat un carcinosarcom de glandă parotidă cu arii de degenerare adenocarcinomatoasă (componenta epitelială) combinate cu arii fibrosarcomatoase. Pacienta a beneficiat de parotidectomie totală cu conservarea nervului facial și a efectuat tratament radioterapic postoperator. Concluzii: Cazul prezintă interes datorită frecvenței foarte scăzute a acestui tip de tumoră în patologia tumorală malignă a glandelor salivare. Datorită agresivității acestui tip de neoplasm este necesar un tratament radical ce combină excizia chirurgicală și radioterapie. După o urmărire clinică de 13 luni, pacienta a decedat datorită metastazelor pulmonare.

Cuvinte cheie: carcinosarcom, tumoră malignă mixtă adevărată, tumoră glandă parotidă

ABSTRACT

Objective: True malignant mixed tumor (carcinosarcoma) is an extremely rare tumor in salivary glands pathology, consisting of both carcinomatous and sarcomatous components. The majority are seen in the parotid gland. Material and method: We report here a case of a 53 year old female patient from urban area, nonsmoker, who was admitted in ENT Department Timișoara in 2006, for a mass in the left parotid region, which appeared five months before, gradually increasing in size. We discuss diagnostic and treatment of this pathologic entity. Results: Histopathological results revealed a parotid gland carcinosarcoma, exhibiting features of adenocarcinoma (epithelial element) and fibrosarcomatous areas. Our patient underwent total parotidectomy with facial nerve preservation and radiotherapy. Conclusions: The case is of interest because of its rarity. Because carcinosarcomas are aggressive neoplasms a radical treatment is necessary, which combines surgical excision and radiotherapy. After a clinical follow-up of 13-months, the patient died due to lung metastases.

Key Words: carcinosarcom, true malignant mixed tumor, parotid gland tumor

INTRODUCTION

Malignant mixed tumors are less than 2% of all mixed tumors of salivary glands.¹ Malignant mixed tumors are classified as 3 distinct histological types: carcinoma ex pleomorphic adenoma, benign metastasizing pleomorphic adenoma and carcinosarcoma.² Carcinoma ex pleomorphic adenoma refers to a carcinoma arising in a benign mixed tumor, representing approximately 99% of cases.¹ Occasionally, metastatic lesions are identified in patients with a history of pleomorphic salivary adenoma, which, on detailed pathological evaluation,
are found to exhibit all the histological hallmarks of the preceding benign lesions. Carcinosarcoma or true malignant mixed tumor is a biphasic malignant tumor in which both the stromal and epithelial components suffer malignant degeneration. Carcinosarcoma remains an extremely rare and aggressive entity. It accounts for only 0.04-0.16% of all salivary gland tumors. The first case of salivary gland carcinosarcoma was described by Kirklin et al. in 1951. Since then until 2006, there have been reported 71 cases of salivary gland carcinosarcoma in the English-language literature. Salivary gland carcinosarcoma could arise in a preexisting pleomorphic adenoma (so-called carcinosarcoma ex pleomorphic adenoma) or could not present any remnants of a benign mixed tumor (so-called carcinosarcoma de novo).

CASE PRESENTATION

Patient G.A., female, aged 53 years, from urban area, was admitted in the ENT Department Timisoara in May 2006 for a mass in the parotid region, which appeared five months ago, gradually increasing in size. The patient was treated during this period with anti-inflammatory drugs, without any clinical improvement. At admission facial motor problems or ear sensory disturbances were not present.

Clinical Exam:

**Inspection:** deformation of the left parotid gland region by a 4/3 cm size tumor.

**Palpation:** reveals 4/3 cm size tumor, well circumscribed, with hard consistency, fixed to deep planes, sensitive to touch. The superjacent skin aspect was normal.

General examination, buccopharyngoscopy, anterior and posterior rhinoscopy, indirect laryngoscopy, nasal endoscopy, hypopharango-laryngo-endoscopy with 70° endoscope revealed no pathological evidence.

Laboratory examination revealed only a minor anemia. Chest X-ray shows no active or disabling pleuropulmonary lesions. The preoperative CT scan of the neck showed an irregular margined soft tissue mass in the left superficial lobe of the parotid gland, 4/3 cm in size, without any neck lymph node.

With these clinical and laboratory data has been established a presumptive diagnosis of left parotid tumor, possibly malignant.

Regarding differential diagnosis, other diseases that might enter into discussion are: secondary lymph node from septic processes of the mouth, chronic parotiditis, syphilis, tuberculosis and actinomycosis, Hodgkin’s disease, neurofibroma, lymphosarcoma, metastatic tumors, primary or metastatic melanoma.

Regarding histology, a particular attention should be given to biphasic synovial sarcoma, carcinoma ex pleomorphic adenoma, collision tumors, giant cell carcinoma, salivary duct carcinoma with an infiltrating desmoplastic component, sarcomatoid variant of salivary duct carcinoma, spindle cell carcinoma and others sarcomas.

Based on these data, after patient consent, has been performed total parotidectomy with preservation of facial nerve. (Figs. 1, 2)

![Figure 1. Intraoperative aspect.](image1)

![Figure 2. Intraoperative aspect.](image2)

The histopathological examination revealed a solid mass poorly circumscribed that measured 4/3/3 cm, apparently partially encapsulated, with increased consistency. The specimen was fixed in 10% buffered formalin, embedded in paraffin and the routine hematoxylin-eosin sections were obtained. For pointing mucoproteins, the diagnosis was complete with a PAS (periodic acid-Schiff) staining. Final histopathologic examination of the specimen revealed a biphasic pattern composed of both carcinomatous and sarcomatous elements. The malignant epithelial cells presented pleomorphic, egg-shaped, vesicular nuclei exhibiting high mitotic activity, giving the appearance of adenocarcinoma. The sarcomatous part was composed by spindle cell tumor with
elongated hyperchromatic nuclei, bounded on the periphery of strips of connective tissue infiltrated by inflammatory cells. (Figs. 3,4) Histochemical isolated were noted PAS+ areas in the mesenchymal component. Immunohistochemical reactions for Cytokeratin, Vimentin and S-100 protein supplements the diagnosis, without being critical.

DISCUSSION

Carcinosarcoma is a rare salivary gland neoplasm, comprising 0.04-0.16% of all salivary gland tumors. Carcinosarcoma is a biphasic neoplasm in which both the epithelial and mesenchymal component reveal features of malignancy. Kirklin et al. from Mayo Clinic first described mixed carcinoma and sarcoma of the parotid gland in 1951. King et al. in 1967 first used the term true malignant mixed tumor (carcinosarcoma). The number of reported carcinosarcomas of the salivary glands in the literature is limited. Gnepp et al. summarized 43 cases of carcinosarcoma of the salivary glands published in the literature. The majority of these tumors are from the parotid glands, followed by submandibular glands and palate. There is no gender predominance. The mean age at presentation was 58 years with a range of 14-87 years. Many cases are seen to arise in a pre-existing benign mixed tumor.

Carcinosarcomas of the salivary glands most often arise in the parotid gland. (65% of cases). 19% of cases have been reported in the submandibular gland. Any minor salivary gland can be involved, although the palate is the most common. Carcinomas have been described in several organs, including uterus, bladder, lung and others.

Because of its rareness, the molecular changes, clonality and the origin of this tumor are still controversial. The tumorigenesis of carcinosarcomas has been debated and the arguments can be divided into two antithetical hypothesis. One hypothesis is called the “convergence hypothesis” and states that multiclonal stem cells of the epithelial and mesenchymal components play a causative role. The other, called the “divergence hypothesis” postulates a monoclonal origin from a single totipotent stem cell with divergent differentiation. The latter hypothesis is more favored. Gotte et al. hypothesized that the tumor originates from a myoepithelial cell precursor. Other investigators have postulated that the tumor originates from inner cells or a pluripotent primitive cell.

The tumor presents as a mass that may be rapidly enlarging. In some cases, the mass is painful; the pain may be localized, referred, or both. If the parotid gland is involved, signs of facial nerve weakness/paralysis are commonly encountered. Our patient had no sudden painful increase in neck mass size or any signs of facial weakness.

Cytological examination (aspiration cytology) represent an uncertain diagnostic method. Fine needle aspiration (FNA) studies can be used for preoperative evaluation, but the rare incidence, the great diversity of tumor cell types, the heterogenic cytological details
can limit an accurate assessment.

Correct diagnosis is confirmed only by histopathology in paraffin, sometimes needing additional immunohistochemical investigation for a final diagnosis of certainty. Carcinosarcoma is a biphasic tumor in which the carcinomatous component is usually a poorly differentiated adenocarcinoma, an undifferentiated carcinoma, or a squamous cell carcinoma. It may also include adenoid cystic carcinoma, epithelial myoepithelial carcinoma and salivary duct carcinoma. The sarcomatous component is usually a chondrosarcoma. Other reported sarcomatous elements include spindle cell sarcoma NOS, fibrosarcoma, osteosarcoma, leymyosarcoma, undifferentiated sarcoma, mixoid sarcoma and rarely liposarcoma, rhabdomyosarcoma or the combination of these sarcomas and also myoepithelial malignant proliferation.

In our case, histological aspects revealed combination between the characteristics of adenocarcinoma representing epithelial components and sarcomatous elements. The immunohistochemical panel varies, depending on the observed biphasic components of the tumor. Generally, the carcinomatous component is usually cytokeratin and EMA positive. However, it should be noted that in very poorly differentiated tumors, the carcinomatous component may show only focal or weak positive staining for cytokeratins or EMA, a feature that is sometimes encountered in very poorly differentiated cancers of the head and neck. In such cases, electron microscopy may be helpful. The sarcomatous component is vimentin positive. S-100 Protein is utilized for pointing chondromatous component and actin is useful to highlight possible muscular component.

Histological criteria for diagnosis of malignancy are: cell dysplasia, vascular, lymphatic and perineural invasion, infiltrative tumoral growth, necrosis, calcifications. One or two of those listed are sufficient criteria for the diagnosis of malignancy. It is important to take note of significance of dysplastic aspect for diagnosis of malignancy.

Few genetic studies have been performed on these tumors, owing to their rarity. However, abnormalities in chromosomes 7, 8, 9, 10, 12, 13, 17 and 18 have been described. A recent study performed by Vekony et al., published in 2009, showed specific amplifications of MUC 20 (Mucin-20) in mesenchymal elements and BMI-1 (a proto-oncogene found to be deregulated in several neoplasms, including salivary gland tumors) observed in both element loci.

Carcinosarcoma is an aggressive, high-grade malignancy, and aggressive therapy employing radical surgery with and without adjunctive radiotherapy and chemotherapy is used. Radical neck dissection is appropriately reserved for patients with neck lymph nodes.

Carcinosarcoma shows tendency to recurrence and distant metastasis. Recurrent disease develops in approximately two thirds of patients and metastases in about half. In a review by Gnepp et al. published in 1993, 58% of patients died. In a review of 19 cases of the novo carcinosarcomas by Staffieri et al., 31.6% of patients died. The median period of survival after diagnosis was 10 months; in 63% of cases, there was no evidence of recurrence after a median period of 22.4 months. Tumor spread may occur by direct extension, or by hematogenous, lymphatic or perineural invasion. The lungs are the most common site of metastasis.

In our study the patient died due to distant metastases developed in the lungs after a period of 13 months following diagnosis.

The prognosis is unfavorable, studies reporting 56% overall 5-year survival and 31% 10-year survival. There is a good correlation between stage and local extension of the tumor and prognosis. Facial nerve palsy and grade of malignancy are important prognostic factors.

CONCLUSIONS

The case reported in this article is a carcinosarcoma, which combines both features of adenocarcinoma and fibrosarcomatous elements. It is reported because of the rarity of carcinosarcoma in malignant tumoral pathology of salivary gland.

Diagnosis may be difficult with conventional histology. It therefore has to be adequately supported by immunohistochemical investigations. In controversial cases, carcinosarcoma diagnosis should be diagnosed by electron microscopy.

Although the number of reported cases is limited, the combination of radical surgical excision and radiotherapy seems currently to be the treatment of choice for salivary carcinosarcoma.

REFERENCES