Intracranial Metastasis of Carcinoma ex Pleomorphic Adenoma by Contiguity Through the Facial Nerve. Case report and literature review

Metástase Intracraniana de Carcinoma ex Adenoma Pleomórfico por Contiguidade Através do Nervo Facial. Relato de caso e revisão de literatura

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ABSTRACT
The central nervous system (CNS) is a common site of metastasis for a number of malignant tumors. Lung, breast, skin (melanoma), kidney and colorectal neoplasms form the most common group of primary sites that send distant metastases to the CNS, always via the hematogenous route. Delayed diagnosis, tumor aggressiveness, and failed primary treatment contribute to this evolution of secondary brain involvement. CNS metastases of salivary gland neoplasms are rare, with few cases reported in the literature. In the case here presented, a young male patient presents a peculiar situation of a carcinoma ex pleomorphic adenoma that developed metastasis to the brain by contiguity through the facial nerve. The outcome, as expected, was poor and the patient died.

Keywords: Carcinoma ex pleomorphic adenoma; Metastasis; Facial nerve

RESUMO
O sistema nervoso central (SNC) é sítio comum de metástases para uma série de tumores malignos. Neoplasias de pulmão, mama, pele (melanoma), rins e colorretais formam o grupo mais comum de sítios primários que enviam metástases ao SNC à distância, sempre pela via hematogênica. Diagnóstico tardio, agressividade do tumor e tratamento primário falho são situações que contribuem para essa evolução do acometimento secundário do encéfalo. Metástases para o SNC de neoplasias de glândulas salivares são raras, com poucos casos relatados na literatura. O caso aqui apresentado de um paciente jovem masculino configura uma situação peculiar de carcinoma ex adenoma pleomórfico que evoluiu com metástase para o encéfalo por contiguidade através do nervo facial. O desfecho, como esperado, foi ruim com o paciente indo a óbito ao final.

Palavras-chave: Carcinoma ex-adenoma pleomórfico; Metástase; Nervo facial
INTRODUCTION

Salivary gland tumors are relatively uncommon, representing 2 to 6.5% of all head and neck neoplasms\(^1\). Due to their morphological diversity and broad clinical presentation, they represent a diagnostic challenge for surgeons and pathologists. The parotid gland is the most affected site by salivary gland tumors, accounting for 80 to 85% of the cases. Among these, the pleomorphic adenoma is the most common benign neoplasm, and may manifest in all age groups, but there is prevalence in the 5th decade of life. It occurs in both sexes, with a ratio of 1 man to 3 women.

They are usually unilateral, indolent, slow-growing tumors that appear as a single, painless mass with well-defined boundaries in the parotid gland region. If malignant, the tumor is called carcinoma ex pleomorphic adenoma. It originates from a primary or recurrent adenoma, and often there is a long time lag between the primary tumor and metastasis\(^7\). The risk of recurrence ranges from 0.4 to 45%, depending on the surgical technique\(^5\): 20 to 45% after enucleation, 2 to 5% after parotid lobectomy and up to 0.4% after radical parotidectomy\(^6\).

This study is a case report of a young male patient who presented after 22 years of parotid lobectomy, recurrence of the lesion as carcinoma ex pleomorphic adenoma with development of contiguous metastasis in the CNS through the facial nerve.

CASE PRESENTATION

Male, white, 36-year-old patient, with a history of surgical resection of left parotid pleomorphic adenoma in 1994, who sought for medical care in May 2016 due to hoarseness, dysphagia and left facial paralysis. Cranio cervical magnetic resonance imaging showed an expansive lesion in the left parotid gland and facial nerve thickening with impregnation by gadolinium (Figure 1).

**Figure 1.** Postcontrast T1-WI axial (A) and sagittal (B) planes. C. T2-WI shows mass in the posterior fossa, compressing pons and the left hemisphere of the cerebellum.
The nerve was infiltrated throughout its extra- and intracranial course until its emergence in the brainstem, forming an extra-axial mass that compressed it, spreading through the lower cranial pairs to the left jugular foramen. The findings were consistent with malignant degeneration of the now ex pleomorphic adenoma associated with perineural dissemination along the facial nerve. The patient underwent extended total parotidectomy with extracranial facial nerve resection and cervical lymphadenectomy by oncologic surgery, followed by intracranial resection of the lesion by neurosurgery. Only partial resection was performed due to the absence of a cleavage plane with the brainstem and the affected low cranial pairs. It evolved satisfactorily in the postoperative period, maintaining Grade VI House-Brackmann facial paresis and dysphonia as definitive sequela. There was still dysphagia after the procedure, but with full recovery within a few weeks.

He underwent adjuvant treatment with chemotherapy and local irradiation, reaching a considerable reduction of the tumor mass, with delimitation of the cleavage plane with the brainstem, along 9 months after the intervention. The patient then underwent a new neurosurgical approach for total resection of the extra-axial lesion in the posterior fossa (Figure 2).

Three months after the procedure, the patient evolved with a significant neurological decline. Magnetic resonance imaging (MRI) showed non-communicating hydrocephalus and the patient underwent an endoscopic third ventriculostomy. There was no significant clinical improvement and he remained hospitalized for treatment of other systemic complications (meningoencephalitis, pneumonia). He evolved with a further decline in neurological status about two weeks after the last procedure, and a new gadolinium contrast-enhanced MRI showed numerous nodules by affecting the cerebral hemispheres, pineal gland, cerebellum, pons, and bulb (Figure 3), following the evolutionary pattern of secondary CNS involvement by carcinoma ex pleomorphic adenoma. There was a rapidly progressive worsening of the patient’s general condition, and the patient passed away during the same hospitalization within a few days.

![Figure 2](image2.png)

**Figure 2.** Postcontrast T1-WI axial (A) and sagittal (B) planes demonstrate tumor reduction after radiation and chemotherapy.

![Figure 3](image3.png)

**Figure 3.** Postcontrast T1-WI axial (A) and sagittal (B) planes show absence of tumor in the postoperative (day 2)

**DISCUSSION**

Pleomorphic adenoma represents 70% of the salivary gland tumors, presenting high recurrence rates and malignant transformation, resulting in a carcinoma ex pleomorphic adenoma, it is directly related to the disease duration, the patient age and the size of the tumor, and also it can occur in about 3 to 4% of cases.

The term pleomorphic is related to the variety of connective components, which are due to the multipotential properties of myoepithelial cells. It is a well-circumscribed, encapsulated tumor with incomplete capsule or infiltration by tumor cells.
It may have epithelial, myoepithelial, ductal cells and stroma, areas with keratinizing squamous cells, myxoid, fibrous, cartilaginous and bony areas interspersed in a background similar to mesenchyme.

Carcinoma ex pleomorphic adenoma has high malignancy, which histopathological diagnosis depends on macroscopic elements of malignant transformation, such as poor definition and/or infiltrative tumor margins, hemorrhage, necrosis and presence of mixed elements. The biopsy of a pleomorphic adenoma prior to the carcinoma ex pleomorphic adenoma at the same site, following transformation, may be considered as a diagnostic criterion.

Malignancy is more frequent when only partial excision of the pleomorphic adenoma is performed. Such situation is common, since its exeresis aims the conservation of the facial nerve, even at the expense of leaving part of the tumor.

The evolution to ex pleomorphic carcinoma is usually slow, 15 years on average. Nevertheless, there are reports in the literature of an interval of up to 51 years between the removal of the pleomorphic adenoma and the subsequent development of carcinoma ex-pleomorphic adenoma. Similar to that described in the available literature, the case in question has evolved within 22 years.

The main metastatic sites of ex pleomorphic adenocarcinoma are the bones, lungs, and cervical lymph nodes, usually across the hematogenous route for spread. The CNS is described as a site of metastasis as well, but at a much lower incidence. The remarkable difference in the CNS involvement by contiguity through the facial nerve, which was not reported in the literature so far. Moreover, the metastasis present in the patient has not been described in medical reports. Confirmation of neurogenic dissemination was possible due to gadolinium enhancement from the facial nerve in the parotid region to the posterior floor of the brain.

Malignant transformation of the pleomorphic adenoma is not considered uncommon. However, metastatic dissemination to the CNS is rare, and the limited literature shows the hematogenous route as the only one of involvement. Until this report, we had not found any mention of contiguous metastatic spread of carcinoma ex pleomorphic adenoma in the national or international literature. The perineural invasion of the tumor to the facial nerve nucleus in the brainstem makes this case report unique, serving to address all the specialties involved regarding this possibility of metastatic presentation of the disease.

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