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Case Report

Skin Metastasis from a Parotid Neoplasm

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Abstract

Salivary duct carcinomas are rare tumors known for their predominant location in the parotid gland, its aggressive behavior and high rate of recurrence. It resembles pathologically and immunophenotypically to high-grade ductal breast adenocarcinoma. This report presents an additional case of cutaneous metastasis from a salivary duct carcinoma of parotid gland. We have found thirteen more cases in the literature and we have noticed that every case follow a different treatment scheme. The limited number of cases reported in the literature make difficult to design a treatment protocol. However, new emerging clinical studies are comparing gene and protein expression levels between salivary duct carcinoma and breast carcinoma to identify future targeted therapy.

Keywords: Adenocarcinoma; Parotid Neoplasms; Neoplasm Metastasis; Skin Neoplasms

Introduction

Salivary duct carcinoma, described by Kleinsasser., *et al*. in 1968 for its similarity to ductal breast carcinoma [1], is a rare tumor of the salivary gland with an incidence of 1 - 3% among all salivary tumors [2]. It usually appears in the sixth decade of life, being more prevalent in men than women (3:1.8). The parotid is the salivary gland most commonly affected (80%) and occasionally it can arise in the submandibular gland (8%) [3]. Pain, swelling and facial palsy are some of the symptoms the patient may complain. It is well known for its aggressive behavior and its high local (48%) and distance (48%) recurrence. Two thirds of the patients are diagnosed in an advanced stage of the disease, being 42, 40, 30 and 23% the global survival in five years for stages I, II, III and IV respectively [4].

From the pathological and immunophenotypical point of view, salivary duct carcinoma resembles high- grade ductal breast adenocarcinoma. Both of them share immunoreactivity for androgen receptor, carcinoembryonic antigen, gross cystic disease fluid protein and occasionally human epidermal growth factor receptor 2 (HER2/neu) over expression. The main differences between both tumors are estrogen and progesterone-receptors positive, practically never present in parotid ductal carcinoma [5]. So, despite the fact that both have similar behaviors, it should be highlighted the rarity of cutaneous metastases in salivary duct carcinoma.

Cutaneous metastases are unusual and they appear in 0.7-9% among all oncologic patients [6]. The frequency of this cutaneous metastatic disease tends to be linked with the primary tumor in

each sex. In case of salivary duct carcinoma, it has been recorded 2% in men and 1% in women [7].

Case Report

A 67 years old woman was referred to our hospital due to a progressive erythematous plaque on her right neck that looked like an erythema annulare centrifugum. Physical exploration also revealed a 3 cm lesion in her right parotid gland without signs of facial nerve palsy. Thorough surveys which included skin biopsy, fine-needle aspiration cytology (FNAC) of the parotid lesion and a neck magnetic resonance imaging (MRI) (Figure 1) were performed. The MRI showed lesions within the parotid gland (the biggest one 1.8 × 1.6 cm) with aggressive signs suggesting a neoplastic tumor. Also, cervical nodes were evident in I, II, III and IV levels in the right side. The parotid FNAC was positive for neoplastic cells and the pathology result from the skin biopsy was lymphangitic carcinomatosis. With these results, a positron emission tomography- compute tomography (PET-CT) scan was requested, which was negative for distant metastases.

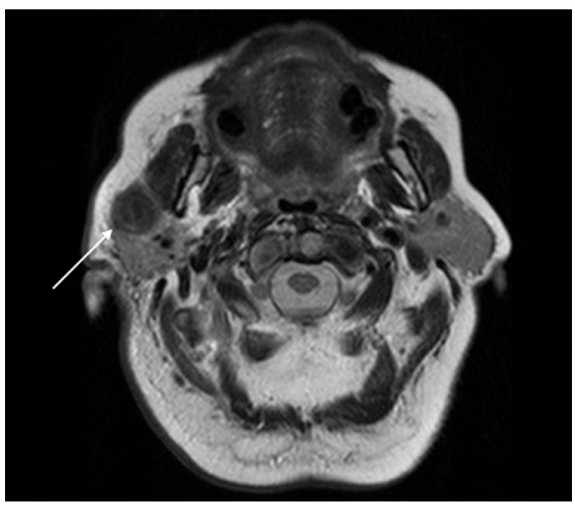

Figure 1: T2 hypointense lesion of 1.8 x 1.6 cm that does not enhance with intravenous contrast.

After classifying the lesion as a stage IV (T3N2bM0) in the TNM staging system and discussing the case in the Head and Neck Committee, surgery was decided (radical parotidectomy with modified radical neck dissection).

The pathology of the surgical specimen revealed (Figure 2) a high-grade salivary duct carcinoma with cystic degeneration and comedonecrosis as well as extensive lymphovascular and perineural invasion. The tumor cells were positive to cytokeratin 7, p63 (focal) and carcinoembryonic antigen, versus negativity to cytokeratin 20, Bcl-2, smooth muscle actin, estrogen receptors and progesterone receptors. The Ki67 cell proliferation index was 20 - 40%. Her-2/neu by fluorescence in situ hybridization (FISH) was negative. It had 100% positive androgenic receptors. Regarding neck dissection specimen, carcinoma metastases were evidenced in the 43 isolated lymph nodes with extensive lymphovascular invasion.

Figure 2: Histological examination. A Infiltration of parotid gland by salivary ductal carcinoma with areas of comedonecrosis. Hematoxylin and eosin (H and E) 10x. B Staining with p63 showing the component of intraductal carcinoma in the glandular tissue. 20x.

Subsequently, she received adjuvant chemoradiation (biweekly Epirubicin and Cyclophosphamide for 4 cycles followed by weekly Paclitaxel for 6 cycles; 42.40Gy in 16 fractions) with complete clinical response and disappearance of dermal infiltrated lesions. However, two months after finishing the adjuvant treatment, the erythematous skin plaque reappeared (Figure 3) and its malignancy was confirmed by biopsy. So then, she began with a new chemotherapy treatment with carboplatin-vinorelbine (Carbo-VNR) for 4 cycles, improvingthe skin lesion, and later anti-androgen therapy (Bicalutamide) was introduced. Two years after surgery, the skin metastasis persisted and, due to patient deterioration, different therapeutic attitudes were established (a third line of chemotherapy with Capecitabine for 6 cycles, a fourth line with Eribulin for 6 cycles and a fifth line with Caelyx for 5 cycles). The disease pro-

gressed regardless of the different treatments. In the last PET-CT scan, carcinomatous lymphangitis was found in the left upper lobe of the lung, a metastatic lesion in the left iliac bone and another in the left ethmoides. The patient died 5 years after her initial clinical presentation.

Figure 3: Reappearance of the erythematous and pruritic annular plaque with central regression of skin color on her right neck and chest after surgery.

Results and Discussion

Malignancies of the parotid gland are uncommon, as are the cutaneous metastases from them. Cutaneous metastases or inflammatory metastatic carcinoma, classically associated with breast cancer since 1886 [8], are characterized by tumor cells predominantly in dermal lymphatics (carcinoma erysipelatoides) or blood vessels (carcinoma telangiectodes). These lesions are often associated with poor prognosis [9] and its appearance after treatment of the primary tumor can be an indication of recurrence.

The clinical appearance is usually an erythematous patch or plaque, although other morphologies have been described such as angiokeratoma-like lesions, bullae, nodules, purpuric violaceous plaques and pseudovesicles. The lack of fever or leukocytosis may suggest the correct diagnosis. However, cutaneous metastases can be unnoticed sometimes by mimicking bacterial infections (like acute paronychia), viral infections (like zoster herpes) or cutaneous tumors (like epidermoid cysts or pyogenic granulomas). They can even appear in hidden tumors yet to be diagnosed, as in our case. Generally, tumors that tend to invade veins often present themselves as cutaneous metastasis in skin sites at a distance from the primary tumor. Cancers that tend to invade lymphatic channels tend to appear in the skin in the later course of the disease overlying the area of the primary tumor [7].

This article reports a rare case of cutaneous metastasis from a salivary duct carcinoma of parotid gland. Thirteen more cases have been published in the literature (Table 1) and, after analyzing them, we have noticed that the most common sites of cutaneous metastases were neck and chest, although it has also been reported in other places like face or scalp. We have also observed that there isn't any protocol of treatment for these cases, probably due to its low incidence. The standard treatment for salivary duct carcinoma is removal of the affected gland (total parotidectomy in this case) and ipsilateral neck dissection, followed by postoperative radiotherapy with or without concurrent chemotherapy. However, none of the cases reported in the literature has undergone the same treatment scheme.

Source	Age/Gender	Primarytumor	Treatment	Skin Metastasis
Allyson Black., *et al*. [12]	60/F	Left parotid gland	Surgery + radiotherapy; Posterior palliative chemotherapy.	Left pruritic erythematous rash involving the left pinna and neck.
Juber Hauiji., *et al*. [13]	83/F	Right parotid gland	Palliative radiotherapy	Indurated eruption with infiltrating nodules and ulceration on her right neck and chest.

Jeffrey L. Pollock., *et al*. [14]	38/M	Right parotid gland	Surgery; chemoradiation for recurrent tumor mass (6600rads; methotrexate, fluorouracil, cyclophosphamide). Doxorubicin and dacarbazine for the cutaneous metastasis.	Nodules from the midline to the right anterior axillary line in a zosteriform distribution
Julide Tok., *et al*. [15]	62/M	Left parotid gland	Chemotherapy (doxorubicin HCL, cisplatin and cyclophosphamide). After skin metastases appearance, palliative treatment.	Round firm papules and nodules on the scalp
Andrea Zanca., *et al*. [16]	76/F	Right parotid gland	Surgery	Erysipelas-like inflammation on the right cheek and periauricular area
Philip R. Cohen., *et al*. [5]	71/M	Left parotid gland	Surgery + chemoradiation (60Gy; cisplatin)	Erythematous dermal plaque from his neck to his upper abdomen.
Philip R. Cohen., *et al*. [5]	69/M	Left parotid gland	Docetaxel subsequently concurrent chemoradiation (45Gy and cetuximab)	Large hemorrhagic- appearing purpuric dermal plaque from his right face and neck to his mid- abdomen
Piha-Paul SA., *et al*. [17]	73/M	Unknown	Surgery, chemoradiation and systemic chemotherapy with carboplatin and paclitaxel.	Large ecchymotic area with partial central clearing from the neck to the xiphoid process.
Piha-Paul SA., *et al*. [17]	70/M	Unknown	Docetaxel and radiation with concomitant cetuximab.	Large ecchymotic and violaceous area from the neck to the midxiphoid process
F.G. Aloi., *et al*. [18]	42/M	Right parotid gland	Surgery + radiotherapy (6000rads); Skin metastasis treated with vincristine, cyclophosphamide, Adriamycin	Erythematous plaque on the right neck
P.Plantin., *et al*. [19]	63/F	Left parotid gland	Surgery + Chemoradiation (carboplatin, epirubicin and 5- fluorouracil)	Right facial erythema
Robert A. Schwartz., *et al*. [8]	60/M	Left parotid gland	Surgery; Recurrent tumor removed; Skin metastases treated with palliative radiotherapy (4140rads)	Redness and orange skin changes
Ahmet Eroglu., *et al*. [20]	58/F	Left parotid gland	Surgery at least three times for recurrence. Skin metastases treated by removal biopsy.	Round and hard mass upper left parietal region
F = Female, M = Male, Surgery = Parotidectomy and ipsilateral neck dissection				

Table 1: Characteristics of salivary duct carcinoma patients with cutaneous metastases.

Several factors are associated with poor prognosis (male, positive margins, high-grade tumor, perineural invasion, nodal disease, strong HER2 protein expression…). However, new emerging clinical studies are comparing gene and protein expression levels between salivary duct carcinoma and breast carcinoma to identify future targeted therapies for these cases. Some authors like Dalin., *et al* [10] or Al-Qahtani., *et al.* [11] suggest that androgen-deprivation therapy could be investigated in the majority of salivary duct carcinomas as well as HER2 inhibition for Trastuzumab therapy due to their improvement of disease-free survival and overall survival.

Conclusion

Salivary duct carcinoma is one of the most aggressive head and neck tumors, which means it needs an aggressive therapy. Local and distant recurrences have been described, although few cases have been reported with cutaneous metastases affectation. It is important that in any patient with a metastatic skin lesion resembling breast carcinoma, carcinoma of the parotid gland should be considered in the absence of a definite primary tumor.

Conflict of Interest

The authors have no other funding, financial relationships, or conflicts of interest to disclose.

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