Treatment of Metastatic Eyelid Carcinoma

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Purpose: The aim of this study was to report management and outcomes in patients affected by eyelids carcinomas involving regional lymph nodes.

Methods: We have retrospectively analyzed the data of patients affected by eyelids carcinoma with nodal involvement. The clinical records of 10 patients with malignant eyelid carcinoma and regional nodal metastasis treated between September 2011 and March 2015 have been analyzed.

Results: The study included 5 women and 5 men (median age 54,5 years; range 37–80 years). The most common tumor was the squamous cell carcinoma (4 cases) followed by sebaceous carcinoma (2 cases): 1 case of epidermoid carcinoma, 1 case of malignant melanoma, 1 case of Merkel carcinoma, and 1 case of basal cell carcinoma. All patients were treated by surgical resection; in 2 cases, orbital exenteration was required. The treatment of regional nodal metastasis consisted of parotidectomy and radical neck dissection followed by radiation therapy. None of the patients developed local recurrence. Three patients died: one, affected by Merkel cell carcinoma, died after 2 months because of metastatic dissemination to the lung; another one, affected by epidermoid carcinoma involving the orbit, died because of liver metastasis; the third one, affected by malignant melanoma, died because of other causes. The follow-up time ranged from 9 to 36 months (median 19.3 months).

Conclusions: Patients affected by advanced malignant eyelid carcinoma need to be strictly controlled because metastasis can develop at least 5 years after surgical treatment. Therapy may include a combination of local surgery, neck dissection, and radiation.

Key Words: Eyelids carcinoma, lymph nodes, neck dissection

The incidence of eyelid carcinomas is estimated to be in the literature 5% to 10% of all cutaneous tumors.[1] The most frequent are the epithelial tumors, represented by the basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and sebaceous carcinoma (SebCa). The most frequent non-epithelial tumors are melanoma of the eyelid, and Merkel cell carcinoma (MCC).

The BCC accounts for 86% to 96% of all eyelid tumors, SCC accounts for 3.4% to 12.6%, SebCa accounts for 0.6% to 10.2%, and melanoma and MCC account for <1% of all eyelid tumors.[1–3]

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The criterion standard treatment is represented by the surgical removal of the primary lesion with negative margins eventually followed by local flaps for reconstruction.

Unfortunately, some cases require the orbital exenteration. In case of aggressive lesion that metastasizes to the regional lymph nodes, the therapy consists in total parotidectomy and neck dissection. Herein we report our experience in the management of metastatic eyelid carcinoma.

MATERIALS AND METHODS

The clinical records of these patients with advanced malignant eyelid carcinoma and nodal metastasis, treated between September 2011 and March 2015 at University of Naples Federico II, Head and Neck Department, have been evaluated.

The study included 5 women and 5 men (median age 54.5 years; range 37–80 years). The most common tumor was the SCC (4 cases; 40%) followed by SebCa in 2 cases (20%), 1 case of epidermoid carcinoma (10%), 1 case of malignant melanoma (10%), 1 case of MCC (10%), and 1 case of BCC (10%). The clinical examination included a complete adnexal and ocular examination, and the palpation of the lymph nodes of parotid and cervical region. Patients and tumors characteristic are shown in Table 1. In all patients, Doppler-ultrasonography of parotid, submandibular, and cervical nodes was performed. All patients presented parotid metastasis at the time of diagnosis confirmed with a fine-needle aspiration biopsy (FNAB) (Fig. 1).

All patients underwent a computed tomography (CT) scan or magnetic resonance imaging (MRI) examination of the orbit, maxilla, salivary glands, and neck, to evaluate the ocular infiltration and the regional nodal metastasis. Positron emission tomography (PET)-CT scan of total body was performed to exclude distant metastasis. The clinical tumor mode metastasis (TNM) is reported in Table 2.

All patients were treated with radical surgery of the primary tumor and frozen section to control the margins. The treatment of regional nodal metastasis consisted of total parotidectomy with nerve sparing, if there were not clinical signs of nerve involvement, and radical neck dissection followed by radiation therapy. Our research was approved by local institutional review board.

RESULTS

All 10 patients were treated by surgical resection of the tumor with frozen section control of margins; in 2 cases, orbital exenteration was required because of the orbital infiltration (1 case of MCC and 1 case of epidermoid carcinoma). Symptoms of orbital involvement were: exophthalmos, ocular motility deficit, and loss of vision.

TABLE 1. Patient and Tumor Characteristics

Median age (range), y	54.5 (37–80)
Location	
Upper eyelid	6 (60%)
Lower eyelid	1 (10%)
Internal cantus	1 (10%)
External cantus	2 (20%)
Median tumor size (range), cm	1.8 (0.9–4)
Histological type	
Squamous cell carcinoma	4 (40%)
Sebaceous carcinoma	2 (20%)
Epidermoid carcinoma	1 (10%)
Malignant melanoma	1 (10%)
Merkel carcinoma	1 (10%)
Basal cell carcinoma	1 (10%)

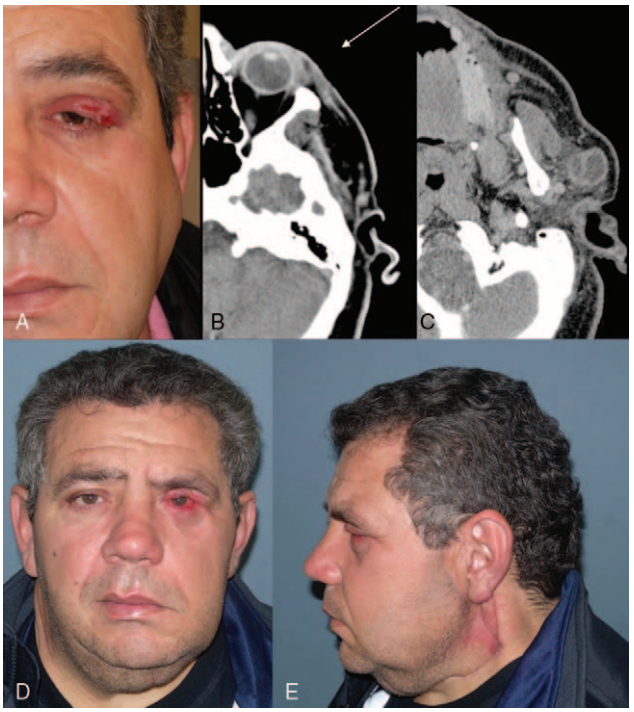

FIGURE 1. Patient affected by squamous cell carcinoma of the upper left eyelid (A). Computed tomogrpahy scans examination of the same patient showing the left eyelid lesion (B) and the nodal metastasis in his left parotid gland (C). Postoperative photo of the patient after eyelid surgery, parotidectomy and radical neck dissection followed by radiotherapy; frontal view (D). Lateral view (E).

According with literature, for cutaneous malignancies arising on the anterior and lateral part of the face, the treatment of regional nodal metastasis consisted of total parotidectomy and radical neck dissection (levels I–V).[4,5]

The pathological TNM and the staging are reported in Table 3. Histopathological examination showed 30% of occult metastasis. Radiation therapy was required in all cases, because of the extra capsular involvement, nodal metastases, and perineural invasion. One of these patients developed chronic dry eye and cataract, as side effect of radiation.

The patients affected by MCC and epidermoid carcinoma received also systemic chemotherapy because of distant metastasis detected during follow-up PET-CT total body examination.

The disease-specific and overall survival rates for all patients were 80% and 70%, respectively. None of the patients developed local recurrence, but unfortunately the patients with MCC died after 2 months from diagnosis because of metastatic dissemination to the lung, and the patients affected by epidermoid carcinoma died after 9 months from diagnosis because of liver metastases. Also the patient affected by malignant melanoma died because of a stroke.

TABLE 2. Clinical TNM

Merkel cell carcinoma	T3bN1Mo
Epidermoid carcinoma	T3bN1Mo
Basal cell carcinoma	T2bN1Mo
Malignant melanoma	T2aN1Mo
Squamous cell carcinoma	T2aN1Mo
Squamous cell carcinoma	T2bN1Mo
Squmous cell carcinoma	T1N1Mo
Squamous carcinoma	T2bN1Mo
Sebaceus cell carcinoma	T1N1Mo
Sebaceus cell carcinoma	T1N1Mo

TNM, tumor mode metastasis.

TABLE 3. Pathological TNM and Staging

Carcinoma	pTNM	Stage	Parotid Metastasis	Neck Occult Metastasis
Merkel c.	T3bN1M0	IIIb	+	II-III Levels
Epidermoid c.	T3bN1M0	IIIb	+	–
Basal cell c.	T1N1M0	IIIb	+	–
Malignant Melanoma	T2aN1M0	IIIb	+	–
Squamous cell c.	T2aN1M0	IIIb	+	–
Squamous cell c.	T2bN1M0	IIIb	+	–
Squamous cell c.	T1N1M0	IIIb	+	–
Squamous cell c.	T2bN1M0	IIIb	+	–
Sebaceous c.	T1N1M0	IIIb	+	I Level

c, carcinoma; TNM, tumor mode metastasis.

DISCUSSION

Malignant eyelid tumors seem to be easy to diagnose on the basis of history and clinical signs and symptoms during the clinical examination, but sometimes malignant periocular skin lesions can mimic benign pathology. For instance, a cystic BCC can resemble a hidrocystoma; furthermore, sebaceous gland carcinoma classically mimics a chalazion.

When the diagnosis and the treatment are delayed, orbital invasion by periocular tumors can occur and should be suspected in case of recurrent lesions with an orbital mass, globe displacement, limitation of eye movement, numbness, and loss of vision. Therefore, a biopsy, in case of suspicious lesions, is always recommended.

Perineural invasion worsens the prognosis, and sometimes is followed by nodal involvement.[6] The management of these lesions is related to the histopathology and clinical stage, according to the 7th Edition for Eyelid Carcinoma Classification System from the American Joint Committee on Cancer.[4] In this retrospective study, we report our experience on 10 patients affected by metastatic carcinoma of the eyelid. The first site of metastasis was the parotid gland in all 10 cases, followed by regional lymph nodes, levels I to V detected only during the hystopathological examination (30% micrometastasis). In one case we report distant metastasis to the lung, and in another case to liver.

The management of eyelid carcinoma consists of complete surgical excision of the primary lesion with margin control. In case of aggressive lesion that metastasizes to the regional lymph nodes, the therapy consists in total parotidectomy with nerve sparing, if there is no sign of nerve involvement, and radical neck dissection given that micro metastasis can occur.

We generally recommend adjuvant radiotherapy to regional lymph nodes in presence of nodal involvement, extra capsular infiltration, perineural invasion, or recurrent tumors.

The role of sentinel node biopsy has been recommended for early detection of metastasis in regional lymph nodes but is outside the aim of this study, and is widely described in the literature[5,7,8,9]

In the management of eyelid tumors, radiation has been used for adjuvant treatment of high-risk carcinoma with perineural invasion, or as primary treatment of advanced disease, or as palliative treatment. Systemic chemotherapy (cyclophosphamide, methotrexate, 5-fluorouracil, cisplatin, and etoposide) has been used in patients with extensive nodal disease in patients affected by Merkel carcinoma.[10] Topical chemotherapy (including Imiquimod 5%

cream, 5-fluorouracil eye drops, and Mitomycin C eye drops, and interferon alpha-2 b eye drops) has been used as both primary and adjuvant therapy for SebCa or SCC with a tumor control of 100% in all the 4 cases treated.[11]

In case of metastatic or advanced carcinoma not eligible to surgical excision or radiotherapy, targeted therapy against the hedgehog pathway for BCC or epidermal growth factor receptor for SCC seems to be a valid therapy to avoid the tumor progression.[12]

After the treatment of the eyelid carcinoma, it is important to continue a strictly surveillance of the patient to exclude local recurrence, or local and distant metastases. During each visit, the surgical site and the neck should be carefully examined. In case of cervical adenopathy, a Doppler sonography is recommended, and in case a suspicious node is noted, an FNAB has to be performed. Ophthalmological examination is recommended with the same frequency, to detect recurrence on the conjunctival surface or in the tarsal plate.

A CT scan or MRI of the head and neck region may be appropriate, in addition to the careful clinical examination of the patient during the follow-up period in case of relapse. A PET-CT scan of total body for lung and liver metastases is appropriate for advanced carcinoma. Most cases of nodal metastasis occur within the first 2 to 3 years after treatment of carcinoma, and in some cases, late metastasis can occur.[13–14]

CONCLUSIONS

In our experience, a radical surgery of the primary eyelid lesion, associated with total parotidectomy with nerve sparing, if there is no sign of nerve involvement, and radical neck dissection followed by radiotherapy, in selected cases, is an effective treatment for nodal invasion of the parotid glands and cervical lymph nodes.

Longer follow-up is necessary to assess the duration of tumor control.

Patients with eyelid carcinoma need to be strictly controlled; the frequency and the duration of the clinic controls are related on the histology and on the stage of tumor. For BCC, SebCa, SCC, melanoma, and MCC, at least a five year follow-up is required: every 3 months during the first year, then every 6 months for the other years. From the third year, the follow-up control is recommended once per year.

The eyelid tumors need a careful management since a misdiagnosis, a nonradical surgery or an inappropriate follow-up, it causes a high risk of metastases and the death of the patients.

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