Biological Behavior of the Sebaceous Carcinoma of the Head

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BACKGROUND. **The reports in the literature indicate that extraocular sebaceous carcinoma (SC), in contrast to orbital SC, is less aggressive and rarely metastasizes.**

METHODS. **Of 2422 epithelioma cases observed over 10 years, 8 (0.33%) resulted as histologically proven SCs, all of which were located in the head.**

RESULTS. **The clinical behavior of these tumors was observed by following patients for an average period of 50 months. Three of the tumors originated from the orbital region and five from other areas of the head (extraocular). In one case, the SC was associated with renal carcinoma (Muir-Torre syndrome). None of the orbital tumors metastasized, whereas two of the five cases of extraocular carcinoma metastasized to the locoregional lymph nodes.**

CONCLUSION. **It should be stressed that in this case study aggressive biologic behavior was observed in carcinoma arising from extraorbital areas.**

F. BASSETTO, MD, R. BARAZIOL, MD, M. V. SOTTOSANTI, MD, C. SCARPA, MD, AND M. MONTESCO, MD HAVE INDICATED NO SIGNIFICANT INTEREST WITH COMMERCIAL SUPPORTERS.

"TRUE" SEBACEOUS carcinoma (SC) is still the subject of discussion from a histopathologic and clinical point of view. Macroscopically, it presents as a hard nodule that tends to enlarge rapidly,[1,2] and if it is of orbital origin, it can be confused with a calathion or nonspecific inflammatory processes (unilateral conjunctivitis, blepharitis, tarsitis, blepharoconjunctivitis, or keratocongiuntivitis with pagetoid invasion of the epidermis).[3]

Histologically, it is classified in the group of sebaceous neoplasias that is divided in three categories: sebaceous adenoma, basal cell carcinoma with sebaceous differentiation, and SC.[4] Three other entities cause confusion in the diagnosis of sebaceous neoplasias: nevus sebaceous of Jadassohn, adenoma sebaceous of Pringle, and adenomatoid sebaceous hyperplasia.[5]

The nomenclature and the criteria for the classification of sebaceous tumors are still subjects of discussion.[6–9]

SC histologically consists of well-circumscribed lobules of neoplastic cells, with eosinophil cytoplasm and severe atypia, some of which have foamy or glassy lobules; cytologic atypia, including nuclear pleomorphism and frequent mitosis, is always present (Figure 1).[10]

The average age of onset is approximately 70 years old. It can affect men and women in varying degrees, and there is little agreement in the literature on the incidence in the two genders.[5,7,8,11,12] The general frequency of this tumor varies from 0.2% to 4.6% of all malignant cutaneous neoplasias.[7,13]

This neoplasia occurs more commonly on the head (75%), with selective affinity for the eyelid or, less frequently, on the scalp or other areas of the face. It can, however, arise anywhere: the skin of the trunk (15%) or of the limbs (10%).[14,15]

The ocular adnexa contain various sebaceous glands from which carcinomas may arise, including the Meibomian glands, the glands of Zeis, those contained in the caruncle and in the hair follicles of the eyebrow. Some are multicentric in origin, whereas in a small number of cases, the precise site of origin cannot be determined.[16–19]

SC constitutes 0.2% to 0.8% of palpebral tumors, 1.0% to 3.2% of all malignant lesions of the eyelids, and 2.8% of invasive neoplasias of the orbit.[20] Occasionally, this tumor develops after irradiation therapy to the area.[7,21–24]

Ocular SC is described as more aggressive[18,25,26] with locoregional and/or distant metastasis and/or intracranial extension.[26–28] Fifteen percent to 30% of patients affected by ocular SC develop metastasis to the lymph nodes, with a 5-year death rate of 20% after the occurrence of metastasis. Pagetoid growth increases the possibility of metastasis to 41% from 11% in absence of this growth pattern.[29] SC of extraorbital origin in the head is considered less locally aggressive and rarely has the tendency to develop metastasis.

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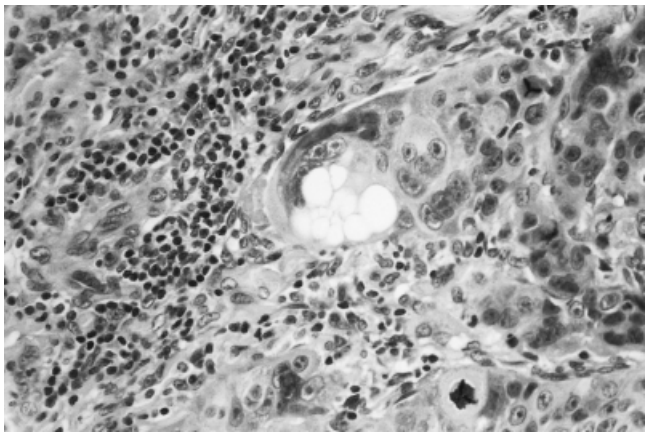

Figure 1. Histologic pattern of SC.

From a therapeutic point of view, a safe excision margin has been shown to be 5 to 6 mm from the edges that are macroscopically visible.[30]

SC can be found in relationship to visceral neoplasias. In such instances of Muir-Torre syndrome, 66% of the associated neoplasias are intestinal, 38% urogenital, and 9% hematologic.[31–37]

Methods

From a retrospective study of 2422 epitheliomas histologically diagnosed over a period of 10 years, 8 (0.33%) "true" SCs were identified in seven patients. The SCs were separated by site or origin: orbital (three cases) and extraorbital (five cases). The clinical behavior of these neoplasias was followed for a minimum period of 7 months (because of patient demise) and a maximum of 108 months (average follow-up of 50 months).

Case Reports

A 68-year-old man presented with a clinical history of recurrent Bowen's disease to the inferior left eyelid initiating 10 years before. The last excision performed on a suspicious recurrence histologically revealed a SC. A widened excision was performed, and in the follow-up of 108 months, he has had no recurrence or metastasis.

A 72-year-old man presented with SC of the right inferior eyelid in partnership with renal carcinoma. The case was classified as Muir-Torre syndrome associated with visceral neoplasias (bowel 66%, urogenital 38%, hematologic 9%) and sebaceous neoplasias (SC 49%, keratocanthoma 26%, and others 25%). The patient died 7 months later because of metastasis of renal carcinoma.

A man, 61 years old, was subjected to ablation of SC of the internal canthus of the left eye; 2 years later, a second SC was found on the left ear and was immediately ablated. After 3 months, the homolateral laterocervical lymph nodes and parotid gland were clinical sites of metastases. He underwent parotid gland excision and laterocervical dissection; in the following 84 months, he was disease free.

An 83-year-old man underwent excision of SC in the right temporal area. The patient died after 24 months from other causes without developing recurrence or metastasis of the sebaceous neoplasia.

A woman, 83 years old, underwent excision of SC in the left preauricolar area. The patient died after 8 months from other causes.

A 54-year-old woman underwent a first excision of SC of the left parietal lobe of the scalp, which recurred after 6 months. A second excision was performed to 1 cm from the borders with prophylactic homolateral laterocervical lymph node dissection and chemotherapy treatment. After 1 year, the neoplasia metastasized to the homolateral undermandible lymph nodes, and thus, gland ablation was carried out. After another year, during which the patient was submitted to radiotherapy, a contralateral lymph node metastasis was diagnosed. The patient underwent therapeutic dissection. After 9 months, the patient presented with a subcutaneous nodule in the right preauricolar area, which the fine-needle aspiration biopsy confirmed as metastasis. The patient refused further treatment, and the nodule maintained the same dimension at follow-up. Since the first appearance of disease 48 months before, the patient has been followed by clinical controls every 4 months (Figure 2).

An 81-year-old man underwent excision of epithelioma in the left parietal area, which turned out to be SC at the histologic examination. After a year, the patient remains free of disease (Table 1).

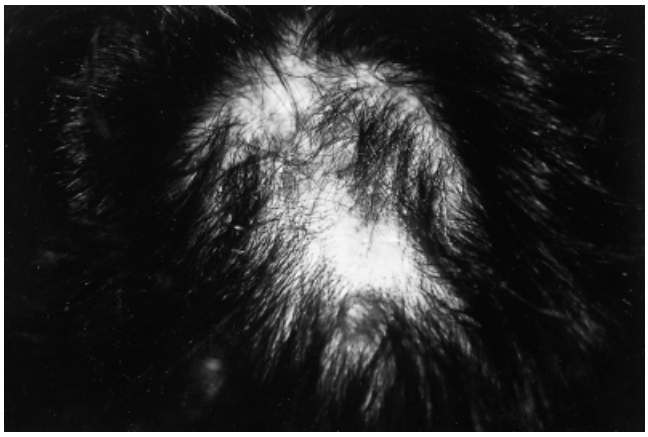

Figure 2. Clinical aspect of extraocular SC.

Table 1. Classification of SC Used in This Study

Patient	*Age (Years)*	*Gender*	*History*	*Site*	*Clinical Diagnosis*	*Follow-up*
O.G.	68	M		Lower lid	Bowen D. recidivist	Surgical excision no evidence of disease after 9 years
M.G.	72	M	Kidney Ca	Lower lid	Squamous cell carcinoma	Died for metastasis of kidney Ca
B.L.	61	M		Internal canthus	Squamous cell carcinoma	Surgical excision at internal canthus
				Left ear	Squamous cell carcinoma	After 2 years of surgical excision at left ear, after 3 months metastasis ⇒ radical neck dissection no evidence of disease after 7 years
C.E.	83	M		Temporal area	Aspecific Epith.	Died for other causes at 2 years
P.E.	83	F		Preauricolar area	Aspecific Epith.	Died for other causes at 8 months
M.V.	54	F		Scalp	Aspecific Epith.	Surgical excision after 6 months recurrence ⇒ surgical excision +radical neck dissection+chemotherapy after 1 year metastasis undermandible ⇒ gland excision + radiotherapy for 1 year, but metastasis at contralateral lymph nodes ⇒ radical neck dissection, after 9 months metastasis at preauricolar area ⇒ no surgical excision, after 2 years of follow-up every 4 months
M.G.	81	M		Parietal region	Aspecific Epith.	Surgical excision, no evidence of disease after 1 year

Results

The three patients who presented with lesions to the orbital area were males (between 61 and 72 years old). The lesions revealed various clinical characteristics.

Objectively, at the moment of the surgery, some characteristics were common: the rapid growth in the previous 2 months, ulcerations, bleeding, and pruritus. The macroscopic characteristics were different: The dimensions of the neoplasia at the time of the excision varied from 0.8 to 1.5 cm.

The clinical diagnosis was recurrence of Bowen's disease in the first case and squamous cell carcinoma in the other two.

The five patients that presented with extraorbital lesions were two females and three males, aged between 54 and 83 years. One male was classified in two groups having presented with a lesion in the internal cantho and another in the right ear. The dimension of the lesions, which grew rapidly from the time of diagnosis, went from 1.5 to 3 cm. The clinical appearance was not uniform (described as pea-like, disepithelized, crater-like, and sessile shank). All of the patients reported bleeding and secretions, whereas pruritus was a varying symptom.

Discussion

The objective characteristics and the clinical behavior of true SC are still the subject of discussion in the literature. Particularly debated is whether there is a different local aggressiveness and biologic behavior between periorbital and extraorbital SC. Most of the literature reports conclude that carcinoma in the orbital area is more aggressive.[18,26]

Rao[18] reported 104 cases of ocular SC with 23 deaths caused by metastases (22%). Wolfe[20] described 43 patients with ocular SC with 14 metastases.

Table 2. Behavior of Extraocular Cutaneous SC Reported as SC

References	Number of Extraocular SC	Number of Metastasis	Number of Deaths
5	6	–	–
38	5	3	1
39	1	1	–
14	2	2	–
Present work	5	2	–

Rulon and Helwig[5] analyzed five cases of carcinoma in extraorbital areas without stressing metastasis. Wick[38] stressed that three of five extraorbital carcinoma cases developed metastases, resulting in death of the patients.

The site of the metastasis is often the lymph nodes; King et al.[39] identified a case of extraocular SC with abdominal metastasis.

Other authors have reported metastases extending to the liver, the small bowel, the urinary tract, the lung, and the brain.[40]

The discussion on the biologic behavior of the neoplasia is still open.[41] Mellette et al.[42] believed that the biologic behavior of extraorbital tumors is not significantly different from tumors arising from the eyelids.

Hernandez and Banos[14] reported that in two patients lymph node metastases of extraocular SC were observed, concluding that these metastases have a "relatively" low aggressiveness and that they do not spread beyond the barrier of the regional nodes (Table 2).

In our patients, we found locoregional lymph node metastasis in only the cases of extraorbital origin of the SC. In both cases, the follow-up has been sufficiently long (48 to 84 months) to affirm that the neoplasia has presented only locoregional aggressiveness (lymph nodes, parotid gland, subcutaneous tissue) without invasion of distant organs. The lack of therapeutic standardized protocols led to the use of chemotherapy and radiotherapy in one case where the local aggressiveness was particularly invasive (local recurrence after 6 months).

The exact incidence of metastasis to locoregional lymph nodes or to distant sites of extraocular SC is still controversial because of the relatively low number of cases with sufficient follow-up.

Hasebe,[43] Metze et al.,[44] and Sinard[45] suggested to consider the presence of histologic and immunohistochemistry indices and prognostically unfavorable ones, which include small differentiation, the presence of lymphocytic or vascular invasion, and the presence of a pattern of pagetoid cells. In our patients, the correlation between these prognostic indices, methasthasis, and survival was not considered in this study.

In conclusion, SC is an unusual cutaneous tumor that is poorly understood because of its rarity. Undisputed is the biologic aggressiveness of the carcinoma that arises at the orbital level. It is important, however, not to underestimate carcinoma of extraorbital origin, which can metastasize to the locoregional lymph nodes or in rare cases distant organs.[46]

In this retrospective study, the locoregional aggressive behavior shown in two cases of extraorbital carcinoma has been reported. Looking at the aggressiveness of this type of carcinoma, which is commonly localized, the authors emphasize the need for an early clinical diagnosis and surgery with a safe margin of excision. With respect to the treatment of draining of the lymph node stations, a strict follow-up with therapeutic dissection is necessary followed by radiotherapy and/or chemotherapy when metastasis occurs. In the two cases observed from 4 to 7 years, metastasis has not appeared at distant sites.

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