Sebaceous Carcinomas of the Skin: 24 Cases and a Literature Review

Roger HABER[1], Maxime BATTISTELLA[2], Cecile PAGES[1], Martine BAGOT[1,3], Celeste LEBBE[1,3] and Nicole BASSET-SEGUIN[1,3]
[1]Department of Dermatology and Venereology, [2]Department of Pathology, Université Paris 7, Saint Louis Hospital, 1 Avenue Claude Vellefaux, FR-75010 Paris, France. E-mail: nicole.basset-seguin@aphp.fr
Accepted Apr 27, 2017; Epub ahead of print Apr 27, 2017

Sebaceous carcinoma (SC) is a highly aggressive tumour arising from the sebaceous glands (1). SC is a rare neoplasm that represents 1% of all eyelid tumours and 4.7% of malignant epithelial eyelid tumours. The majority of SC are located in the head and neck region, primarily in the periocular area (75%), i.e. eyelid, orbit and conjunctiva, where sebaceous glands of Meibomius and Zeis are the most common (1–3). SC may occur sporadically or be part of Muir-Torre syndrome (MTS), a rare autosomal-dominant genodermatosis characterized by sebaceous neoplasms and one or more visceral malignancies (4). SC most commonly presents as a gradually enlarging, firm nodule or as an ulcerated papule or plaque in elderly individuals (1), and can mimic basal cell carcinoma, squamous cell carcinoma, pyogenic granuloma, metastatic tumour or benign adnexal tumours (1, 2). Diagnosis of SC is therefore often delayed (5, 6) and confirmed only by histology (1, 3, 5). The disease is classified as either ocular (OSC) or extraocular (EOSC) depending on the location of the primary lesion (1–3, 6). Heterogeneity in incidence patterns, associated cancer risks (3, 6, 7) and mortality (6, 7) have been reported between OSC and EOSC, but are still controversial. Standard surgical resection with wide margins and Mohs micrographic surgery are common treatments for SC (3, 8, 9). However, to date, there are no tumour-specific staging system or management guidelines for EOSC (5). The aim of this study was to determine the demographic, clinical and histopathological characteristics, treatment strategy and prognosis of SC in a series of patients and to compare these results with published data.

METHODS

All patients presenting to Saint Louis Hospital, Paris, a major skin cancer referral centre in France, from 1995 to 2015, with a confirmed histology of SC of the skin, were included in this retrospective study. Sex, age, race, immune status (immunodepression in HIV and transplantation), family history, tumour location, tumour size, stage and extent of disease, pathology report, imaging techniques, time to diagnosis, lymph node involvement, metastasis, radiation use, surgery type and extent, chemotherapy and survival data were collected through patients charts. SC were classified as OSC when occurring in orbital sites (eyelid, orbit, and conjunctiva) or EOSC if elsewhere (lip, external ear, scalp or neck, trunk and upper and lower limb). Diagnosis was confirmed histologically in all cases (3).

RESULTS

Twenty-four patients with SC were identified between 1995 and 2015. Ten had MTS, 21 had EOSC (4 of whom had 2 primary SC) and 3 had OSC (Table SI[1]). Median age at diagnosis was 68 years overall (range 44–94 years) and 64.5 years in cases of MTS. There was a slight predominance of men (62.5%). Seventy-five percent of cases occurred in Caucasians. Risk factors of SC were present in 58% of cases and included MTS (41.6%, 10 cases) and immunosuppression (16.6%, 4 cases, of which one with MTS). No case of previous irradiation on the site of SC was noted. Family history of SC was found in 10 patients, 9 of whom had MTS. Most frequently involved skin sites were the nose (10 lesions, 35.7%) and the scalp/neck (5 lesions, 17.8%). Time to diagnosis ranged from 1 to 5 years in 39.2% of cases and less than 1 year in the 4 cases of recurrent SC. SC presented mostly as a painless, pink or yellow, round nodule, or as a diffuse thickening or a pedunculated lesion (Fig. S1[1]). Frequently associated malignancies included colorectal carcinoma (33%) and urogenital carcinoma (16.6%), all occurring in patients with MTS.

Colonoscopy was performed in all cases of MTS. Lymph node sampling was performed in 2 cases because of aggressive clinical and histological features; pathology results were negative in all cases. There was only one case of lung metastasis that occurred in an immunocompromised patient with MTS.

Wide surgical excision was the major treatment in all cases. Margins of 5–6 mm were used only for small lesions (diameter <6 mm), mostly located on the face, with no aggressive clinical or histological pattern. Margins of 2 cm and more were used for recurrent lesions and those with aggressive clinical/histological features. There was no case of amputation or use of adjuvant radiotherapy or of chemotherapy. In the patient with lung metastasis, treatment included wide surgical excision of the primary SC and pulmonary lobectomy. Median follow-up duration was 3 years (range 3 months to 11 years). Overall, physical examination with or without regional lymph node ultrasonography was performed every 6 months for the first year then yearly. Lesions did not recur in 85.7% of cases; all recurrences (16.6%) occurred less than 5 years after initial diagnosis. There was no statistically significant relationship between initial tumour size and time to recurrence (Pearson correlation coefficient $=0.25$). During the follow-up period, cause of death was attributable to colon cancer in one case; none was attributable to the SC.

[1]https://doi.org/10.2340/00015555-2685

doi: 10.2340/00015555-2685
Acta Derm Venereol 2017; 97: 959–961

DISCUSSION

The median age at diagnosis in this study corroborated previous reports of higher incidence in patients with advanced age (6). A slight predominance of incidence among men was also reported previously (6); whereas others demonstrated a female predominance (7). In accordance with Dasgupta et al. (6), the majority of patients in the current study were Caucasians (75%). Previously accepted features of SC as a cutaneous neoplasm with female and Asian predominance should therefore be reconsidered (3, 10).

In our series, we observed 3 OSC (10.7%) and 25 EOSC (89.2%); the prevalence of EOSC is obviously related to the fact that the cases were recruited in a dermatological centre.

Patients with MTS develop SC in 30% of cases (11–13) and diagnosis of a single sebaceous neoplasm should prompt consideration of a diagnosis of MTS, irrespective of family history (3). MTS was observed in 41.6% of SC in this study. Diagnosis relied on immunohistochemistry of 4 DNA mismatch repair proteins (MLH1, MSH2, MSH6, and PMS2) as a screening test and on molecular analysis in cases of strong family history of malignancy regardless of the results of immunohistochemistry. As reported in the literature (12), the most common locations of visceral malignancy in our study are colorectal (57%) and genitourinary tract (28%).

The main histological appearance of SC in this study consisted of an unencapsulated, lobular, dermally based proliferation of sebaceous and undifferentiated cells (3). Because of the variety of tumour growth and clinical presentations, diagnosis of SC can be late, as was seen in some cases in this study, with almost 15% of primary SC being diagnosed after 5 years (3).

In this study, and in accordance with previous reports, our cases of SC presented before or concurrently with internal malignancy in approximately 42% of patients with MTS (12). This underlines the importance of malignancy screening in MTS and follow-up with colonoscopy every 3–5 years, starting at 25–30 years of age, yearly mammography and endometrial biopsy every 3–5 years in women over 50 years of age (14).

In accordance with the literature (8), advanced imaging studies were conducted before radical lymph node dissection, when lymphadenopathy was palpable on physical examination, and when the primary lesion exhibited aggressive features, such as perineural invasion, poor differentiation, orbital invasion, or size >20 mm. MRI was done for preoperative evaluation of large and locally aggressive tumours to rule out deep tissue involvement.

Wide local excision has been the standard treatment of SC in this study and was performed for all cases. Mohs micrographic surgery (MMS) could also be considered, particularly in cosmetically sensitive areas, such as the eyelids and face, but is not performed in our centre (3, 6, 9). Previously reported local recurrence rates ranged from 4% to 28% for both OSC and EOSC (3, 6, 8). MMS has been associated with lower local recurrence rates than wide local excision for periorbital sebaceous carcinoma, but fewer studies detailing outcomes of MMS for extraorbital sebaceous carcinoma have been published. In this study, local recurrences occurred in 16.6% of cases, always less than 5 years after initial diagnosis, and were not related to initial tumour size. Recurrent disease was treated with surgical re-excision in all cases.

Kyllo et al. (3) suggested that sentinel lymph node biopsy should be reserved for OSC >10 mm in diameter. Previous reports showed that the cause of death was attributable to SC in 31% of patients (14); orbital involvement had a worse survival compared with non-orbital involvement in some reports (15), and had a similar survival in others (14). Other recent studies have demonstrated lower rate of cancer-specific mortality (between 3% and 6.7%) (15). In this study, no death was attributable to SC. These may be due to a greater awareness of SC, to the larger proportion of EOSC in our series, and to more adequate surgical management that improved treatment outcomes.

To our knowledge, this is the largest European study on SC. The most frequently involved site was the nose. All patients with a single sebaceous neoplasm should have mismatch repair mutation analysis to search for MTS, irrespective of family history. Regular follow-up to monitor for visceral malignancy is needed in all cases of MTS. Larger prospective and molecular studies are needed to learn more about this rare cutaneous neoplasm.

REFERENCES

1. Nelson BR, Hamlet KR, Gillard M, Railan D, Johnson TM Sebaceous carcinoma. J Am Acad Dermatol 1995; 33: 1–15.
2. Buitrago W, Joseph AK. Sebaceous carcinoma: the great masquerader: emerging concepts in diagnosis and treatment. Dermatol Ther 2008; 21: 459–466.
3. Kyllo RL, Brady KL, Hurst EA. Sebaceous carcinoma: review of the literature. Dermatol Surg 2015; 41: 1–15.
4. Ponti G, Losi L, Di Gregorio C, Roncucci L, Pedroni M, Scarselli A, et al. Identification of Muir-Torre syndrome among patients with sebaceous tumors and keratoacanthomas: role of clinical features, microsatellite instability, and immunohistochemistry. Cancer 2005; 103: 1018–1025.
5. Chang AY, Miller CJ, Elenitsas R, Newman JG, Sobanko JF. Management considerations in extraocular sebaceous carcinoma. Dermatol Surg 2016; 42: 57–65.
6. Dasgupta T, Wilson LD, Yu JB. A retrospective review of 1349 cases of sebaceous carcinoma. Cancer 2009; 115: 158–165.
7. Rao NA, Hidayet AA, McLean IW, Zimmerman LE. Sebaceous carcinomas of the ocular adnexa: a clinicopathologic study of 104 cases, with 5-year follow-up data. Hum Pathol 1982; 13: 113–122.
8. Panda BB, Parija S, Pujahari S, Mallick J. Sebaceous gland carcinoma of eyelid – a tarnished masquerade. J Clin Diagn Res 2016; 10: 3–5.
9. Berlin AL, Amin SP, Goldberg DJ. Extraocular sebaceous carcinoma treated with Mohs micrographic surgery: report of a case and review of literature. Dermatol Surg 2008; 34: 254–257.
10. Singh RS, Grayson W, Redston M, Diwan AH, Warneke CL, McKee PH, et al. Site and tumor type predicts DNA mismatch repair status in cutaneous sebaceous neoplasia. Am J Surg Pathol 2008; 32: 936–942.
11. Hussain RM, Matthews JL, Dubovy SR, Thompson JM, Wang

G. UV-independent p53 mutations in sebaceous carcinoma of the eyelid. Ophthal Plast Reconstr Surg 2014; 30: 392–395.
12. John AM, Schwartz RA. Muir-Torre syndrome (MTS): an update and approach to diagnosis and management. J Am Acad Dermatol 2016; 74: 558–566.
13. Danialan R, Mutyambizi K, Aung P, Prieto VG, Ivan D. Challenges in the diagnosis of cutaneous adnexal tumours. J Clin Pathol 2015; 68: 992–1002.
14. Vasen HF, Blanco I, Aktan-Collan K, Gopie JP, Alonso A, Aretz S, et al. Revised guidelines for the clinical management of Lynch syndrome (HNPCC): recommendations by a group of European experts. Gut 2013; 62: 812–823.
15. Erovic BM, Goldstein DP, Kim D, Al Habeeb A, Waldron J, Ghazarian D, et al. Sebaceous gland carcinoma of the head and neck: the Princess Margaret Hospital experience. Head Neck 2013; 35: 316–320.