CASE AND RESEARCH LETTER

[Translated article] Sebaceous Carcinoma: A Case Series of 7 Patients

Carcinoma sebáceo. Estudio descriptivo de 7 casos

To the Editor,

Sebaceous carcinoma (SC) is a rare but potentially aggressive malignant skin neoplasm, often categorized-based on its anatomical location-into ocular, or extraocular neoplasm. Both tumors behave differently, show as primary or secondary neoplasms, and be associated with the Muir–Torre syndrome (MTS).[1]

Patients diagnosed with SC registered in the pathology lab database of Hospital Universitario Fundación Alcorcón, Madrid, Spain from January 1998 through December 2022 were studied. Data were obtained after reviewing all health records, biopsies, and the patients' demographic, clinical, histopathological characteristics, treatment, and evolution.

A total of 7 cases of SC diagnosed over the past 24 years were identified. The most relevant characteristics are seen in Table 1. The patients' median age was 85 years (range from 55 to 94), 4 patients were men and 3 were women. In 6 of the cases, the tumor was found on the head and neck, while 2 were periocular tumors. Clinically, they showed as erythematous-orange papules or nodules, with a median size of 2 cm (range from 0.4 cm to 5 cm) (Fig. 1A–C). The median time to diagnosis was 5 months (range from 3 to 36 months). Histopathological confirmation of neoplastic cells with sebaceous differentiation, with various degrees of differentiation and atypia, supported by immunohisto-chemical stains such as adipophilin, androgen receptors, or cytokeratin 5/6, was required for diagnosis (Fig. 1D–F).

Two patients had a past medical history of cancer, without family history, 1 nephrectomized renal carcinoma, and 1 simultaneous diagnosis of melanoma, squamous cell carcinoma, and SC.

A thoraco-abdominopelvic CT scan was performed as an additional study in 5 out of the 7 patients, without any pathological findings being reported. Except for 1 patient who died before surgery due to sepsis, treatment was surgical, with wide excision until the fascial plane with clinical margins of 1 cm. The patients' median follow-up was 2 years (range from 6 months to 14 years), and no recurrences or metastases have been identified to this date in any of the patients. Two patients died within the first year after diagnosis due to infections (acquired pneumonia). None of the patients met the criteria for MTS according to the Mayo principles (Table 2).[2] The microsatellite instability testing came out negative in all 3 patients.

Table 1 Most relevant demographic characteristics.

No.	Sex	Age, years	Location	Muir–Torre[a]	TAP	Treatment[c]	Metastasis/relapse	Year
1	Man	88	Inner canthus	No	Normal	No	No	2005
2	Woman	94	Cheek	No	No	Yes	No	2005
3	Woman	86	Neck	No	Normal	Yes	No	2008
4	Man	61	Upper eyelid	No[b]	No	Yes	No	2015
5	Man	55	Scalp	No	Normal	Yes	No	2016
6	Man	85	Scalp	No[b]	Normal	Yes	No	2020
7	Woman	85	Abdomen	No[b]	Normal	Yes	No	2021

TAP, thoraco-abdominopelvic.
[a] Defined as a patient who meets > 2 criteria of the Mayo MTS risk score.
[b] Negative microsatellite instability screening.
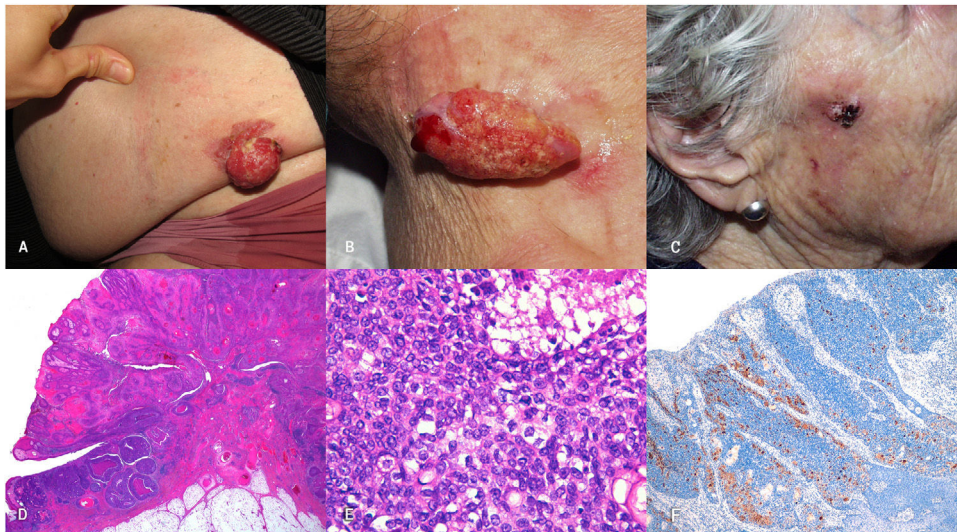[c] Wide excision with clinical margins.

Figure 1 (A–C) Clinical images of 3 patients. (A) 5 cm proliferative, exophytic, erythematous, friable, and ulcerated lesion in left hemiabdomen. (B) 4 cm × 2 cm exophytic, pedunculated, erythematous, friable, and eroded lesion in right lateral cervical area. (C) 2 cm erythematous, ulcerated, friable tumor on the right cheek. (D–F) Histopathological image. Hematoxylin and eosin stain. Panoramic view. Exophytic neoplastic proliferation with in situ component in left margin (D). Hematoxylin and eosin ×400. Areas of in situ sebaceous carcinoma built with mature and immature sebocytes (E). Immunohistochemical staining with adipophilin ×40. Immunoreactivity for adipophilin in mature sebocytes (F).

SC has an estimated incidence rate of 2.4 cases per million individuals per year,[3] and is often found in the periocular region in up to 75% of the cases reported.[4] It is slightly more common in men (58%), with a mean age of 67.9 years.[1]

SC often starts as a painless, ulcerated nodule or papule of a red-orange color, and can disguise as various entities, such as blepharitis, chalazon, etc., which is why the definitive diagnosis is often delayed, thus increasing morbidity and mortality.[1,4–6]

Diagnosis requires histopathological confirmation of sebaceous differentiation. Well-demarcated tumors show microvacuolated clear cells with large, vesicular, or hyperchromatic nuclei with prominent nucleoli, which happen to be scarce or rare in the moderate or poorly differentiated ones. Due to the similarities to other skin neoplasms, immunohistochemistry can be very helpful (EMA [well-demarcated tumors], androgen receptors [nuclear staining], adipophilin [cytoplasmic vacuoles], and high molecular weight cytokeratins [CK 5/6]).[1,4–6]

Surgical excision is accepted as the gold standard for the management of SC, both ocular and extraocular, being Mohs micrographic surgery the first-line therapy.[1,3–6] The 5-year overall survival rate of SC is 78% for localized and regional disease and 50% for metastatic disease, which is why close follow-up of patients is advised, with recommendations for check-ups every 6 months for 3 years and then on a yearly basis.[1,3]

MTS is a phenotypic variant of hereditary non-polyposis colorectal cancer (Lynch syndrome) due to dominantly inherited mutations in DNA repair genes and defined by an increased predisposition to sebaceous neoplasms.[7–9] Although MSI (microsatellite instability) screening (MSH1, MSH2, MLH1, PMS2) was the previously advised screening method in all patients with SC,[3] in the latest guidelines, SMT screening in periocular SC is ill-advised. Instead, individualized recommendations for extraocular SC are advised.

Table 2 Mayo Muir–Torre syndrome risk score.

Variable	Score
Age at diagnosis (years)[a]	
≥60 years 0	0
<60 years 1	1
Total no. of sebaceous neoplasms	
1	0
≥2	2
Personal history of a Lynch syndrome[b]-related cancer	
No	0
Yes	1
Family history of a Lynch syndrome-related cancer	
No	0
Yes	1

Mayo Muir–Torre syndrome risk score. Scores of the 4 variables are added to create an overall score, with a possible range from 0 to 5. Scores ≥ 2 have a sensitivity rate of 100% and a specificity rate of 81% to predict germline mutations in the Muir–Torre Syndrome.

[a] The Mayo MTS risk score is applicable to patients with sebaceous adenomas, sebaceous epitheliomas/sebaceomas, and sebaceous carcinomas.

[b] Lynch syndrome-related cancers include colorectal, endometrial, ovarian, small bowel, urinary tract (renal pelvis and ureter), and biliary tract carcinomas.

Recent publications recommend initial screening with clinical criteria using the Mayo MTS risk score.[2,10]

In conclusion, the low incidence of SC and its nonspecific clinical presentation should tip us off on the need

for establishing high clinical suspicion to avoid diagnostic and therapeutic delays, being histopathological examination being of paramount importance. We should mention that while routine screening for SMT is ill-advised, immuno-histochemistry is a cost-effective additional test available in most laboratories in Spain and should be considered in all patients with sebaceous carcinomas. In full compliance with the latest clinical practice guidelines, we recommend initial screening using the Mayo MTS risk score, followed by immunohistochemistry, and genetic testing if criteria are met.

Conflicts of interest

None declared.

References

1. Owen JL, Kibbi N, Worley B, Kelm RC, Wang JV, Barker CA, et al. Sebaceous carcinoma: evidence- based clinical practice guidelines. Lancet Oncol. 2019:699–714, http://dx.doi.org/10.1016/S1470-2045(19)30673-4.
2. Kibbi N, Worley B, Owen JL, Kelm RC, Bichakjian CK, Chandra S, et al. Sebaceous carcinoma: controversies and their evidence for clinical practice. Arch Dermatol Res. 2020;312:25–31, http://dx.doi.org/10.1007/s00403-019-01971-4.
3. Sargen MR, Starrett GJ, Engels EA, Cahoon EK, Tucker MA, Goldstein AM. Sebaceous carcinoma epidemiology and genetics: emerging concepts and clinical implications for screening, prevention, and treatment. Clin Cancer Res. 2021;27:389–93, http://dx.doi.org/10.1158/1078-0432.CCR-20-2473.
4. Knackstedt T, Samie FH. Sebaceous carcinoma: a review of the scientific literature. Curr Treat Options Oncol. 2017;18:47, http://dx.doi.org/10.1007/s11864-017-0490-0.
5. Wu A, Rajak SN, Huilgol SC, James C, Selva D. Cutaneous sebaceous carcinoma. Aust J Dermatol. 2020;61:e283–92, http://dx.doi.org/10.1111/ajd.13234.
6. Orr CK, Yazdanie F, Shinder R. Current review of sebaceous cell carcinoma. Curr Opin Ophthalmol. 2018;29:445–50, http://dx.doi.org/10.1097/ICU.0000000000000505.
7. Flux K. Sebaceous neoplasms. Surg Pathol Clin. 2017;10:367–82, http://dx.doi.org/10.1016/j.path.2017.01.009.
8. John AM, Schwartz RA. Muir–Torre syndrome (MTS): an update and approach to diagnosis and management. J Am Acad Dermatol. 2016;74:558–66, http://dx.doi.org/10.1016/j.jaad.2015.09.074.
9. Bhaijee F, Brown AS. Muir–Torre syndrome. Arch Pathol Lab Med. 2014;138:1685–9, http://dx.doi.org/10.5858/arpa.2013-0301-RS.
10. Roberts ME, Riegert-Johnson DL, Thomas BC, Rumilla KM, Thomas CS, Heckman MG, et al. A clinical scoring system to identify patients with sebaceous neoplasms at risk for the Muir–Torre variant of Lynch syndrome. Genet Med. 2014;16:711–6, http://dx.doi.org/10.1038/gim.2014.19.

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