World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(CASE REPORT)

Check for updates

Extraocular sebaceous carcinoma of the lateral neck: Molecular exclusion of Muir-Torre syndrome and management of sporadic Stage III Disease

Alireza Izadian Bidgoli [1], Jennifer Flores [1], Elise Collins [1], Jennifer Ejeh [2], Mareena Ayad [3], Jessica Jahoda [4, 5] and Mohamed Aziz [5, *]

[1] *American University of the Caribbean, AUC, St. Maarten.*
[2] *Ross University School of Medicine, Barbados.*
[3] *Medical University of the Americas, Nevis, St. Kitts and Nevis.*
[4] *Memorial Healthcare System, Pembroke Pines, FL, USA.*
[5] *Research Writing & Publication (RWP), LLC, NY, USA.*

World Journal of Biology Pharmacy and Health Sciences, 2026, 26(03), 048-054

Publication history: Received on 25 April 2026; revised on 02 June 2026; accepted on 04 June 2026

Article DOI: https://doi.org/10.30574/wjbphs.2026.26.3.0337

Abstract

Extraocular sebaceous carcinoma (SC) is a rare and aggressive adnexal malignancy that may mimic other cutaneous cancers and can be associated with Muir-Torre syndrome, creating diagnostic and management challenges. A 72-year-old man presented with an 18-month history of a slowly-growing, intermittently ulcerated, non-tender left lateral neck nodule associated with occasional bleeding. Imaging demonstrated a vascularized neck lesion with suspicious left cervical lymphadenopathy, while dermoscopy suggested an adnexal tumor.

Punch biopsy showed an infiltrative dermal neoplasm with sebaceous differentiation, pagetoid spread, and perineural invasion. Immunohistochemistry (IHC) demonstrated diffuse positivity for androgen receptor, EMA, p63, and adipophilin, confirming the diagnosis of sebaceous carcinoma, whereas S100 and HMB-45 were negative. The tumor was staged as pT2N1M0 (stage III). Molecular testing showed microsatellite stability, excluding Lynch/Muir-Torre syndrome and supporting a sporadic etiology related to chronic ultraviolet (UV) exposure.

The patient underwent Mohs micrographic surgery with sentinel lymph node biopsy and selective neck dissection, followed by adjuvant external beam radiotherapy because of nodal involvement and perineural invasion. At 18 months of follow-up, he remained disease-free, with no evidence of local recurrence or distant metastasis. This case highlights the importance of histopathologic, IHC, and molecular evaluation in distinguishing sporadic extraocular sebaceous carcinoma from hereditary syndromic disease and guiding multidisciplinary management.

Keywords: Extraocular sebaceous carcinoma; Muir-Torre syndrome; Germline mutations in mismatch repair; Microsatellite instability; Mohs micrographic surgery; External beam radiation therapy; Ultraviolet

1. Introduction

Sebaceous carcinoma (SC) is a rare and aggressive malignancy of the sebaceous gland epithelium. [1] The extraocular variant of SC presents a distinct and often underappreciated diagnostic challenge. [2] What makes extraocular SC particularly consequential from a clinical standpoint is its common association with Muir-Torre syndrome (MTS), a phenotypic variant of Lynch syndrome caused by germline mutations in mismatch repair (MMR) genes. This association is stronger for extraocular than for periocular disease, and its recognition carries life-altering implications: patients with MTS face substantially elevated risks of visceral malignancies, particularly colorectal and endometrial cancers, and

* Corresponding author: Mohamed Aziz.

Copyright © 2026 Author(s) retain the copyright of this article. This article is published under the terms of the Creative Commons Attribution License 4.0.

their 5-year cause-specific survival is significantly lower than that of patients with sporadic SC (52.5% versus 78.2%). [3] The obligation to exclude MTS before attributing any extraocular SC to sporadic origins is therefore not a formality; it is a clinical imperative.

We report a case of sporadic extraocular SC of the left lateral neck in a 72-year-old male with a prior history of sebaceous adenoma and basal cell carcinoma, presenting at pT2 N1 M0 (Stage III). Comprehensive molecular profiling confirmed MMR proficiency and microsatellite stability, formally excluding MTS and classifying the tumor as sporadic, attributable to decades of UV exposure and field cancerization. This case illustrates the diagnostic complexity, the critical role of molecular workup, and the multidisciplinary management required for extraocular SC outside the eyelid.

2. Case Presentation

2.1. Clinical Presentation and Initial Workup

A 72-year-old male presented to his dermatologist with an 18-month history of a slowly enlarging, non-tender left lateral neck nodule. Progressive enlargement, intermittent ulceration, and bleeding on minor contact were the primary drivers of the current presentation. He had a prior history of a sebaceous adenoma excised from the scalp 12 years earlier and basal cell carcinoma of the right cheek treated with Mohs surgery 8 years prior.

Past medical history included controlled type 2 diabetes mellitus and hypertension. He reported decades of cumulative, unprotected UV exposure and was a former smoker with a 30-pack -year smoking history. Family history was notable for colorectal carcinoma in his father and endometrial carcinoma in a maternal aunt. These details were recorded but, in this scenario, did not trigger a pre-diagnosis molecular workup at the initial visit.

Dermatologic examination revealed a 2.4 × 1.9 cm firm, yellowish-pink, partially ulcerated nodule with irregular borders on the left lateral neck. Left level II cervical lymph nodes were palpable, mildly enlarged, and non-tender. Baseline labs, including CBC, CMP, and LFTs, were within normal limits, except for mildly elevated fasting glucose. Chest X-ray showed no significant findings.

2.2. Radiological Findings and Differential Diagnosis

Ultrasound of the left neck demonstrated a hypoechoic, vascularized soft-tissue nodule (2.4 × 1.9 × 1.3 cm) with two enlarged left level II cervical lymph nodes showing loss of fatty hila. CT neck with contrast confirmed the primary lesion and regional lymphadenopathy. CT chest, abdomen, and pelvis showed no pulmonary nodules, hepatic lesions, or distant lymphadenopathy.

Dermoscopy revealed yellowish globules, irregular vessels, and white structureless areas consistent with an adnexal neoplasm. Differential diagnosis included sebaceous carcinoma, basal cell carcinoma (metatypical variant), poorly differentiated squamous cell carcinoma, Merkel cell carcinoma, and metastatic adenocarcinoma with sebaceous differentiation.

The multidisciplinary tumor board reviewed clinical and radiological findings. High clinical suspicion for sebaceous carcinoma was noted based on lesion morphology, location, and adnexal history. The panel recommended a punch biopsy as the immediate next step. Although the family history was noted, molecular screening was not initiated at this juncture. Consultations with urology and gastroenterology were deferred pending pathologic confirmation, with plans to revisit systemic screening following diagnosis based on the histopathologic findings.

2.3. Pathology, IHC, and Final Diagnosis

Punch biopsy demonstrated a poorly circumscribed, infiltrating dermal tumor in irregular lobules and nests with focal comedonecrosis. Centrally located cells exhibited multivacuolated, foamy cytoplasm characteristic of mature sebaceous differentiation, surrounded by peripheral basaloid cells with vesicular nuclei and prominent nucleoli. High mitotic activity (>10 mitoses/10 HPF), nuclear pleomorphism, perineural invasion, and, critically, pagetoid spread into the overlying epidermis were identified. (Figure 1 A, B, C) Pathology differential diagnosis included clear cell squamous cell carcinoma, clear cell basal cell carcinoma, balloon cell melanoma, metastatic renal cell carcinoma (clear cell type), and xanthogranuloma.

IHC panel confirmed sebaceous differentiation and guided the final diagnosis. The androgen receptor (AR) was diffusely positive, strongly supporting the sebaceous lineage. EMA (epithelial membrane antigen) positive in sebaceous cells, p63

Positive in peripheral basaloid cells, and adipophilin positive (lipid droplet marker confirming sebaceous differentiation). Negative reaction was noted with S100 and HMB-45 (excludes melanoma).

The final diagnosis was well-differentiated SC of the left lateral neck, with pagetoid spread and perineural invasion. Diagnosed by histomorphology and IHC. pT2 N1 M0 (Stage III). Molecular testing was deferred at the time of diagnosis.

As SC outside the eyelid carries a particularly heightened association with MTS, screening for MMR gene mutations was recommended. The molecular profile was entirely negative, demonstrating retained MMR protein expression, microsatellite stability, a low tumor mutational burden (TMB), and absence of a germline mutation, collectively excluding Lynch syndrome and Muir-Torre syndrome in this patient. The SC was therefore classified as sporadic, arising in the context of cumulative ultraviolet exposure and field cancerization rather than a hereditary MMR-deficiency syndrome.

2.4. Multidisciplinary Tumor Board Presentation and Definitive Management

The tumor board reconvened with dermatology, head and neck surgery, medical oncology, radiation oncology, pathology, and genetic counseling (the latter to formally close the Lynch syndrome question following the negative germline result). The negative molecular profile directly shaped several management decisions.

Wide local excision via Mohs micrographic surgery (MMS) was performed, with final clear margins confirmed on the third stage. Concurrent sentinel lymph node biopsy (SLNB) was performed, given the radiologically suspicious regional lymphadenopathy. One of the two sampled left level II nodes was positive for metastatic sebaceous carcinoma, prompting completion of a selective left neck dissection. Two additional nodes in the neck dissection specimen were examined and found to be negative.

Given the adverse pathologic features, perineural invasion, nodal involvement, and the requirement for multi-stage Mohs resection, adjuvant external beam radiation therapy (EBRT) was recommended to the primary surgical bed and the left regional nodal basin. A dose of 60 Gy in 30 fractions was delivered using intensity-modulated radiation therapy (IMRT). The patient tolerated radiotherapy with grade 1–2 dermatitis and grade 1 mucositis, both managed conservatively.

The MSS / low-TMB / low PD-L1 profile did not meet criteria for immune checkpoint inhibitor therapy based on current evidence. Platinum-based chemotherapy (cisplatin or carboplatin) was discussed as a potential systemic option for this stage III presentation. However, it was ultimately deferred given the patient's complete surgical resection, clear final margins, and comorbidities (type 2 diabetes, borderline renal function for cisplatin). Watchful waiting with close surveillance following adjuvant RT was the consensus decision. The patient was counseled on sun-protective behaviors, regular dermatologic surveillance, and the importance of promptly reporting new lesions.

2.5. Outcome and Follow-Up

The patient completed Mohs surgery and adjuvant radiotherapy without major complications. Grade 1 dermatitis resolved with topical management within three weeks of completing RT. No systemic therapy was administered. He was maintained on his baseline medications for diabetes and hypertension throughout the treatment course without significant interaction.

Given the sporadic, MMR-proficient nature of the tumor, follow-up was structured according to standard guidelines for locally advanced cutaneous carcinoma: clinical skin examination with dermoscopy and regional lymph node assessment every three months for the first two years, transitioning to six-month intervals thereafter. Imaging, including neck ultrasound, was performed at 6 and 12 months post-treatment.

At the 12-month follow-up, clinical examination, neck ultrasound, and chest/abdominal/pelvic CT were all negative for local recurrence or distant metastasis. A standard age-appropriate colonoscopy was performed and showed two small tubular adenomas, resected endoscopically, with no features of Lynch-associated pathology. Pathology of the polyps showed no MMR deficiency. The patient remained disease-free at eighteen months and transitioned to annual dermatologic surveillance with continued oncologic follow-up.

The patient was extensively counseled on the sporadic nature of his malignancy and the absence of hereditary risk, and the importance of lifelong sun protection. He expressed relief at the negative genetic result and remained engaged and compliant with the surveillance program. There was no evidence of disease at 18 months.

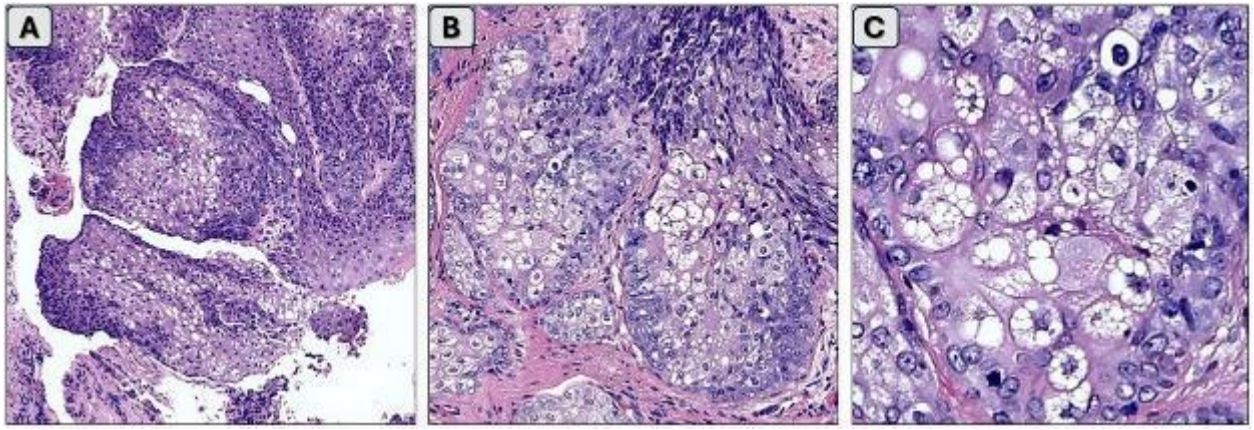

Figure 1 Microscopic findings of sebaceous carcinoma

1A**:** Low-power view showing a poorly circumscribed, infiltrating dermal tumor in irregular lobules and nests (H&E stain X20).; 1B**:** Intermediate power view showing two lobules with central and peripheral cells (H&E stain X40).; 1C**:** High-power view showing centrally located cells with multivacuolated, foamy cytoplasm, characteristic of mature sebaceous differentiation. The central cells are surrounded by peripheral basaloid cells with vesicular nuclei and prominent nucleoli (H&E stain X60).

3. Discussion

3.1. Background (History, epidemiology, risk factors, WHO classification, and Pathogenesis):

SC is classified by the World Health Organization (WHO) into two broad categories: periocular and extraocular. [4] Periocular SC, arising from the Meibomian glands or the glands of Zeis, is the more common and better-characterized form. Extraocular SC, by contrast, is poorly understood in terms of its histogenesis; no definitive evidence of carcinoma arising from pre-existing sebaceous glands at extraocular sites has been established, and current evidence points to p63+/keratin 5+ progenitor cells within the sebaceous duct or interfollicular epidermis as the probable cell of origin. [5]

Epidemiologically, SC predominantly affects older adults, with a peak incidence in the seventh and eighth decades of life, and a male-to-female ratio of approximately 1.4:1 in recent population data. [4] More than 98% of cases occur in patients aged 40 or older. [1] Recognized risk factors include male sex, white and Asian ethnicity, cumulative ultraviolet radiation (UVR) exposure, prior radiation therapy, immunosuppression, and pre-existing nevus sebaceous. [2,6] Muir-Torre syndrome, present in approximately 23% of SC cases, carries the most serious prognostic implications. [3] Whole-exome sequencing has identified three distinct molecular subtypes of SC: a UV-damage signature subtype, characterized by a high somatic mutation burden and poorly differentiated infiltrative histopathology; a subtype associated with MMR gene deficiency and typically better differentiated; and a paucimutational subtype, predominantly represented by ocular SC. [7] UV-damage SC, the subtype most relevant to extraocular disease arising on chronically sun-exposed skin, carries transcriptomic and mutational profiles closely resembling those of cutaneous squamous cell carcinoma, supporting a keratinocytic cell of origin in a subset of cases. [7]

Histologically, SC demonstrates irregular sebaceous lobules within the dermis, with multivacuolated foamy cytoplasm in mature sebaceous cells, peripheral basaloid cells, comedonecrosis, and variable pagetoid spread. The WHO recognizes three histological grades, with high-grade status serving as an independent predictor of advanced disease and poor outcomes. [4] Immunohistochemically, adipophilin and androgen receptor are the most sensitive and specific markers of sebaceous differentiation, while EMA positivity and S100/HMB-45 negativity help exclude melanocytic lesions. [1,4]

3.2. Comparative Analysis of Our Case with Existing Literature.

The present case shares several clinicopathological features with previously reported extraocular SC cases while differing in important ways that merit discussion.

In terms of demographic and clinical profile, our patient, a 72-year-old Caucasian male with a history of prior sebaceous adenoma and basal cell carcinoma, decades of occupational UV exposure, and a presenting neck nodule, aligns well with

the established epidemiological profile of sporadic extraocular SC. Giridhar et al. (2020), in a systematic review and individual patient data analysis of 206 extraocular SC cases, reported a median age at presentation of 65 years (range 11–96 years), with the head and neck as the dominant site of involvement. [8] The SEER-based analysis by Hou et al. (2014) of 52 SC patients at the Mayo Clinic similarly identified a mean age of 72.7 years, a strong male predominance (75%), and the back, cheek, and nose as the most common extraocular locations. [9] Our patient's tumor size (2.4 × 1.9 cm) and regional nodal involvement (pN1) are consistent with the more aggressive presentations described in both series.

The histopathological constellation in our case, multivacuolated foamy cytoplasm, comedonecrosis, pagetoid epidermal spread, perineural invasion, and high mitotic activity exceeding 10 mitoses per 10 high-power fields, reflects the UV-damage molecular subtype described by North et al. (2018), which characteristically exhibits poorly differentiated, infiltrative histopathology and arises on chronically sun-exposed skin. [7] This stands in contrast to the MSI-associated subtype, which tends toward better differentiation and well-circumscribed borders, as seen in MTS-associated cases reported by Pallikkalakathu et al. (2024) and Bui et al. (2022). [10,11]

The most distinctive feature of our case lies in its confirmed sporadic etiology. Many published extraocular SC cases are reported in the context of Lynch syndrome or MTS, such as the case by Pallikkalakathu et al. (2025) of a 70-year-old male with Lynch syndrome-associated extraocular SC of the forehead managed with MMS. [10] Our patient's family history, colorectal carcinoma in the father and endometrial carcinoma in a maternal aunt, created a clinically plausible concern for MTS, yet comprehensive molecular profiling demonstrated retained MMR protein expression, microsatellite stability, low tumor mutational burden, and absence of a germline mutation, conclusively excluding the hereditary diagnosis. The management pathway that followed, MMS with sentinel lymph node biopsy, selective neck dissection, and adjuvant IMRT to 60 Gy in 30 fractions, parallels the approach advocated by Giridhar et al. for cases with adverse pathological features, where complete surgery with regional lymph node dissection is standard and adjuvant radiotherapy is considered appropriate for patients with perineural invasion, nodal involvement, or incomplete resection. [8]

4. What Have We Learned from This Case?

This case highlights several learning experiences that extend beyond the management of a single patient.

The first is diagnostic. Extraocular SC on the neck of an elderly male with a prior sebaceous adenoma and a history of occupational sun exposure should prompt immediate consideration of SC in the differential diagnosis, even before histopathologic evaluation is available. The dermoscopic finding of yellowish globules and irregular vessels, the firm yellowish-pink ulcerated nodule, and the adnexal tumor history collectively constitute a recognizable clinical signature that, when present together, should raise the index of suspicion and expedite biopsy. It is recommended to avoid the reflexive diagnosis of such lesions as basal cell carcinoma on clinical grounds alone, a pitfall well documented in the literature. [2]

The second learning experience concerns the mandatory molecular workup for MTS in any extraocular SC, regardless of age or apparent risk profile. Our patient's family history, colorectal carcinoma in the father and endometrial carcinoma in a maternal aunt, satisfied the threshold for germline testing. That testing returned entirely negative, reclassifying the tumor as sporadic and directly shaping management decisions: the absence of MTS eliminated the need for enhanced visceral surveillance. It altered the intensity of genetic counseling for family members. This sequence, histopathologic diagnosis first, molecular workup second, management stratification third, is suggested to be the standard workflow for every extraocular SC.

The third learning experience is therapeutic. In the absence of MSI or elevated PD-L1 expression, there was no evidence base for immune checkpoint inhibitor therapy in this patient. The decision to defer cisplatin-based chemotherapy in favor of watchful waiting following complete surgical resection with adjuvant IMRT was clinically sound and reflects the current evidence that systemic therapy adds little to complete resection in MMR-proficient, low-TMB disease. [1,4]

Abbreviations

- Sebaceous carcinoma (SC);
- Immunohistochemistry (IHC);
- Muir-Torre syndrome (MTS);
- Germline mutations in mismatch repair (MMR);
- Microsatellite instability (MSI); Tumor mutational burden (TMB);

- Mohs micrographic surgery (MMS);
- External beam radiation therapy (EBRT);
- Ultraviolet (UV).

5. Conclusion

Extraocular SC of the lateral neck is an uncommon malignancy that demands a structured, multidisciplinary approach and a mandatory evaluation for Muir-Torre syndrome before any management decisions are finalized. This case contributes to the limited literature on sporadic extraocular SC arising in the context of confirmed MMR proficiency, where the tumor's aggressive behavior, pagetoid spread, perineural invasion, and regional nodal metastasis at Stage III were attributable to decades of cumulative UV exposure and field cancerization rather than hereditary MMR deficiency. The negative germline result was not merely a reassuring finding; it was a decision-driving one, directing the patient away from enhanced visceral surveillance and toward a management strategy anchored in surgical precision, adjuvant radiotherapy, and structured dermatologic follow-up. At 18 months, the patient remains disease-free.

We present this case to reinforce the diagnostic algorithm for extraocular SC, to document a well-characterized sporadic example with complete molecular profiling, and to highlight the clinical value of distinguishing sporadic from hereditary disease in shaping both treatment and surveillance.

Compliance with ethical standards

Acknowledgments

Special thanks to Grace Durham, Imran Shahid, and Kush Kanjia for their assistance in reviewing the final manuscript. Additionally, we appreciate the assistance of Grammarly's language editor and the Manus 1.6 program, which provided valuable writing support by identifying and correcting errors in grammar, spelling, punctuation, and writing style, ultimately enhancing the manuscript.

Disclosure of conflict of interest

All authors make the following declarations:

- Payment/services information: All authors have declared that they received no financial support from any organization for the submitted work.
- Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might be interested in the submitted work.

Statement of ethical approval

The present research work does not include any studies on animal or human subjects conducted by any of the authors. This study was conducted as a retrospective review of archival pathology material collected during routine clinical care. All data were fully de-identified prior to analysis.

Statement of informed consent

Informed consent for the publication of this case was obtained from the patient.

References

[1] **Neelakantan** IV, Di Palma S, Smith CE, McCoombe A. Sebaceous Gland Carcinoma. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Aug 14. Available from: https://ncbi.nlm.nih.gov/books/NBK562223/

[2] Swali R, Nwannunu C, Tiring S. Sebaceous Carcinoma: A Rare Extraocular Presentation of the Cheek. EMJ Dermatology. 2020.

[3] Shanks A, Laun J, Holstein A, Varshney S, Messina J, Cruse CW. A rare concurrence of Muir-Torre-associated sebaceous carcinoma in the setting of a lipedematous scalp. Case Reports in Plastic Surgery and Hand Surgery. 2020 Jan 1;7(1):124-9.

[4] Dhamale SS, Baghel A, Kanak K, Sardesai V. Sebaceous Carcinoma. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Nov 24. Available from: https://www.ncbi.nlm.nih.gov/books/NBK610689/

[5] Takeuchi D, Ishida M, Yasuda E, Ueda K, Hirose Y. Ocular and extraocular sebaceous carcinomas: A retrospective study with emphasis on the presence of in situ lesion and discussion and review of the histogenesis of extraocular sebaceous carcinoma. Oncology Letters. 2023 Jun 21;26(2):337.

[6] 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. Clinical Cancer Research. 2021 Jan 15;27(2):389-93.

[7] North JP, Golovato J, Vaske CJ, Sanborn JZ, Nguyen A, Wu W, Goode B, Stevers M, McMullen K, Perez White BE, Collisson EA. Cell of origin and mutation pattern define three clinically distinct classes of sebaceous carcinoma. Nature Communications. 2018 May 14;9(1):1894.

[8] Giridhar P, Kashyap L, Mallick S, Dutt Upadhyay A, Rath GK. Impact of surgery and adjuvant treatment on the outcome of extraocular sebaceous carcinoma: a systematic review and individual patient data analysis of 206 cases. International journal of dermatology. 2020 Apr;59(4):494-505.

[9] Hou JL, Killian JM, Baum CL, Otley CC, Roenigk RK, Arpey CJ, Weaver AL, Brewer JD. Characteristics of sebaceous carcinoma and early outcomes of treatment using Mohs micrographic surgery versus wide local excision: an update of the Mayo Clinic experience over the past 2 decades. Dermatologic Surgery. 2014 Mar 1;40(3):241-6.

[10] Dhamale SS, Baghel A, Kanak K, Sardesai V. Extraocular Sebaceous Carcinoma in Lynch Syndrome: A Sentinel Cutaneous Clue to Muir-Torre Syndrome. Cureus. 2025 Jul 18;17(7).

[11] Bui A, Shah S, Winston N, Mahmoud A. Muir-Torre syndrome: abdominal sebaceous carcinoma. Cureus. 2022 Dec 29;14(12).

[12] Na HY, Park JH, Shin SA, Lee S, Lee H, Chae H, Choung H, Kim N, Chung JH, Kim JE. Targeted sequencing revealed distinct mutational profiles of ocular and extraocular sebaceous carcinomas. Cancers. 2021 Sep 26;13(19):4810.

[13] Chen X, Hao Y, Chou M, Yang J. Epidemiology of the non-head and neck sebaceous carcinoma and implications for distant metastasis screening. Frontiers in Oncology. 2024 May 10;14:1395273.