Extraocular sebaceous carcinoma as a rapidly growing back mass: a case report

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Abstract

Sebaceous carcinoma is a rare cutaneous malignancy that frequently mimics other dermatologic conditions. Extraocular subtypes are uncommon, but when present are frequently located in the head and neck region. Herein, we present a patient with a rapidly growing upper back mass eventually diagnosed as sebaceous carcinoma and managed with wide surgical excision. Currently, sparse literature exists to guide management of such patients. This case highlights not only the diagnostic challenges of sebaceous carcinoma, but also the need for further studies to investigate therapeutic interventions and long-term outcomes.

Keywords: extraocular sebaceous carcinoma, sebaceous carcinoma, back mass

Introduction

Sebaceous carcinoma is a rare cutaneous tumor that is frequently located in the periorbital region and aggressive in nature [1,2]. Despite the tendency of sebaceous carcinoma to arise in the meibomian and Zeis glands of the eyelid, extraorbital sites reported in the literature range from the parotid gland to the great toe [2,3]. Approximately 25% of cases of sebaceous carcinoma are extraocular with a focus in the head and neck region, an area with an abundance of sebaceous glands [4].

Commonly mimicking benign dermatologic conditions, definitive diagnosis of sebaceous carcinomas is often delayed, increasing morbidity and mortality for patients [5]. The incidence of extraocular sebaceous carcinoma has been estimated to be 0.06 per 100,000 person-years with an increased incidence in elderly patients and men [1,6]. The typical presentation involves a slowly growing painless nodule with associated bleeding in a third of cases [5,7]. Because of the paucity of cases, little literature exists to guide treatment or quantify prognostic factors. Herein, we present a case of an older man with an exophytic, nodule of the upper back eventually diagnosed as sebaceous cell carcinoma, exemplifying several challenges of diagnosis and management related to this pathology.

Case Synopsis

A 72-year-old man presented to our institution for evaluation of a progressively enlarging upper back mass (**Figure 1**). He had a past medical history of squamous cell carcinoma of the shoulder and basal cell carcinoma of the ear excised several years prior. The patient was in his usual state of health until eight months before presentation when he noticed a "pea sized" nodule on his back suspected at the time to be a sebaceous cyst. However, the mass gradually increased in size and started to bleed. As a result, he re-presented to the dermatology clinic 6 months later for assessment. There had only been a slight

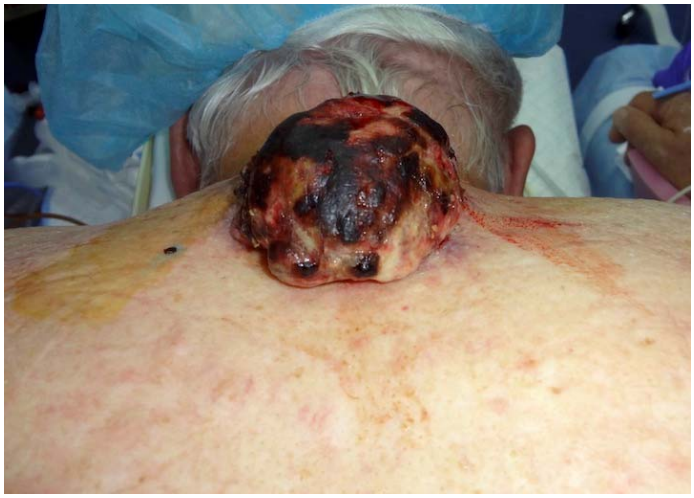

Figure 1. *Fungating, friable nodule located on the upper middle back of the patient. The mass had grown rapidly over a period of months, eventually becoming sensitive to touch and interfering with quality of life.*

increase in size, so he was scheduled for excision the following month. Increased bleeding and subsequent rapid growth in the interval month prompted an emergency department visit for expedited imaging.

Magnetic resonance imaging (MRI) revealed a 6.3×3.0×5.6cm soft tissue mass in the midline of his lower neck and upper back, approximately at the level of C7 through T1 (**Figure 2**). The mass was composed of heterogeneous soft tissue with an internal area of necrosis and was noted to invade subcutaneous fat planes. No extension into adjacent musculature or the paraspinous region was noted. A 1.3×0.7cm enhancing lymph node was observed lateral to the mass, raising suspicion for regional nodal metastasis. On arrival for subsequent biopsy, the patient's mass was fungating with bleeding at the surface and sensitivity to touch. He reported increased difficulty sleeping on his back and increased fatigue, but denied other constitutional symptoms.

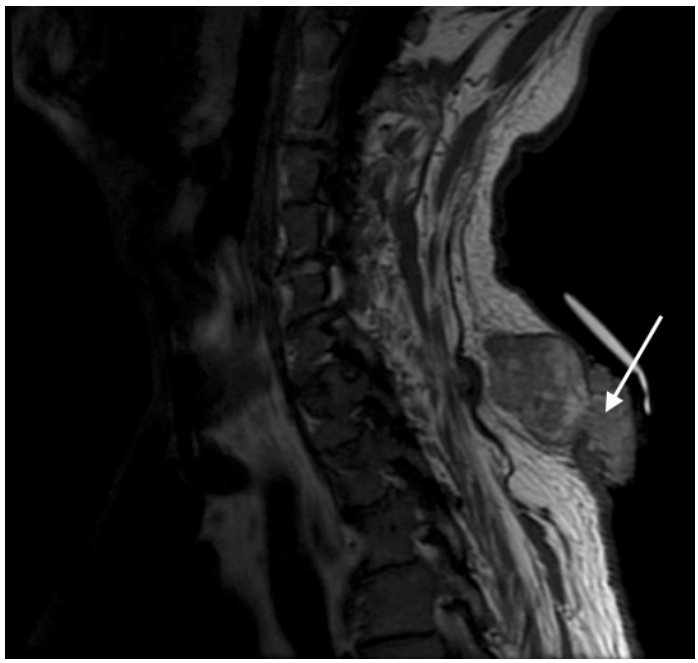

Figure 2. *T2 MRI sequence with a sagittal view of a 6.3×3.0×5.6cm soft tissue mass located approximately at the level of C7 through T1 demonstrating heterogenous composition and an internal area of necrosis. White arrow indicates location of mass.*

A biopsy of the mass was performed and showed a tumor with sebaceous features with vacuolated cytoplasm, confirmed by positive adipophilin immunostaining (**Figure 3**). Frequent mitosis and moderate pleomorphism were observed. Additional immunohistochemistry stains supporting a diagnosis of sebaceous carcinoma include positive stains for GATA binding protein 3 and androgen receptor. Further evaluation of tumor phenotype demonstrated preserved nuclear expression of all mismatch repair proteins (MutL homolog 1, PMS1 protein homolog 2, MutS homolog 2, and MutS homolog 6). The tumor proportion score (TPS = percentage of programmed death-ligand one positive tumor cells with complete or partial membranous staining) was 4% and the combined positive score (CPS = programmed death-ligand one positive tumor cells and immune cells / total number of viable tumor cells x 100) was 5.6%.

The patient underwent staging computed tomography (CT) of the chest, abdomen, and pelvis which did not suggest any evidence of metastatic disease. After discussion with the oncology consultant, the patient underwent lymphoscintigraphy, subsequent sentinel lymph node biopsy (SLNB), and wide excision of the mass. The strongest signal was located in a right posterior shoulder node with an additional, weaker signal at the base of the left posterior neck (**Figure 4**). The navigator sentinel node machine was used to identify these two nodes and their positions were marked before 1.8mL of isosulfan blue dye was

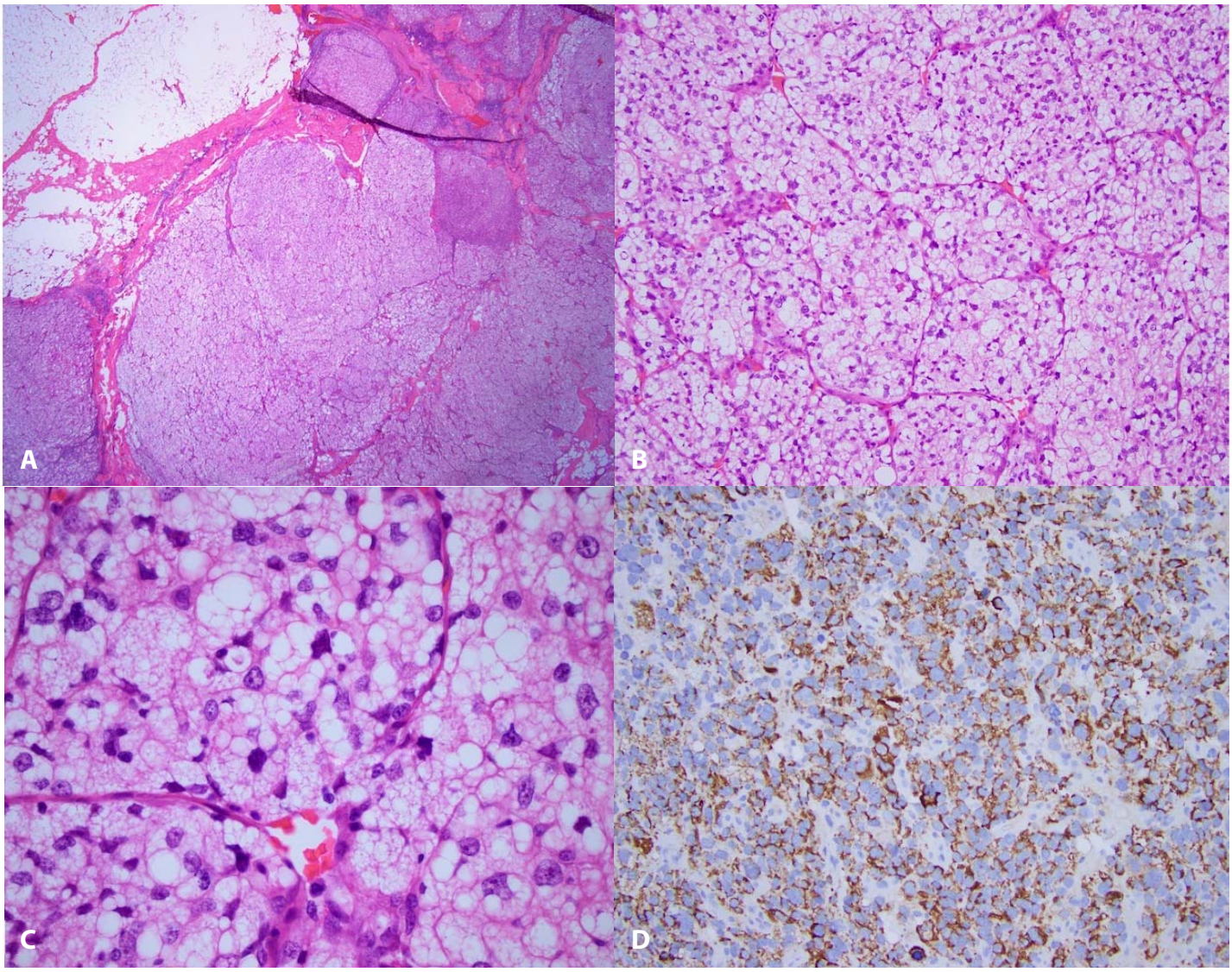

Figure 3. *Histologic evaluation consistent with sebaceous carcinoma. H&E,* ***A)*** *tumor is seen in subcutaneous adipose tissue, 20×;* ***B)*** *demonstrating tumor cells arranged in small nests separated by thin fibrovascular septa consistent with sebaceous differentiation, 200×;* ***C)*** *demonstrating sebaceous differentiation in the form of vacuolated cytoplasm with multiple vacuoles pushing against central round nuclei, 600×.* ***D)*** *Adipophilin immunostaining that confirms vacuolated cytoplasm and sebaceous differentiation, 200×.*

injected around the upper half of the tumor at the time of surgery. Forty minutes after the blue dye was injected, a 10×8cm oval area of tissue that included the tumor mass was incised through skin and subcutaneous tissue. As there did not appear to be invasion of muscle or spinous processes on pre-operative imaging, the deep margin of the excised specimen included muscle fascia but did not go deeper.

All remaining margins appeared grossly normal (**Figure 5**). The aforementioned lymph nodes were then removed, with the left neck node requiring careful dissection to separate it from the immediately adjacent spinal accessory nerve. All specimens were sent to pathology for evaluation. Consistent with the previous biopsy, the mass was identified as sebaceous carcinoma, 6cm in its greatest dimension, with all margins negative. Neither lymphovascular nor perineural invasions were identified. Both the right shoulder and left neck lymph nodes were benign.

Postoperatively the patient recovered well, but noted intermittent spasms of the left shoulder, possibly related to the proximity of his sentinel node to cranial nerve 11. However, he was able to shrug his shoulders symmetrically on exam and the spasms

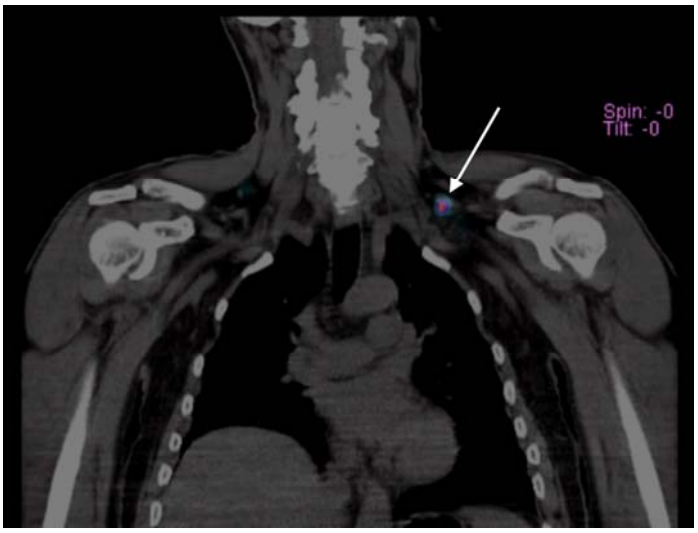

Figure 4. *Nuclear medicine lymphoscintigraphy with a coronal view of the left posterior neck node highlighting the proximity to the course of the spinal accessory nerve. White arrow indicates location of node.*

gradually resolved. Given the patient's absence of metastatic disease on imaging, negative pathology from sentinel lymph node biopsies, and negative surgical margins, our multidisciplinary team decided that any adjuvant treatment would be minimally efficacious and thus was not recommended. Instead, the patient will undergo regular monitoring with serial imaging and periodic follow up. At his most recent visit, now four months postoperatively, his examination and imaging showed no evidence of tumor recurrence.

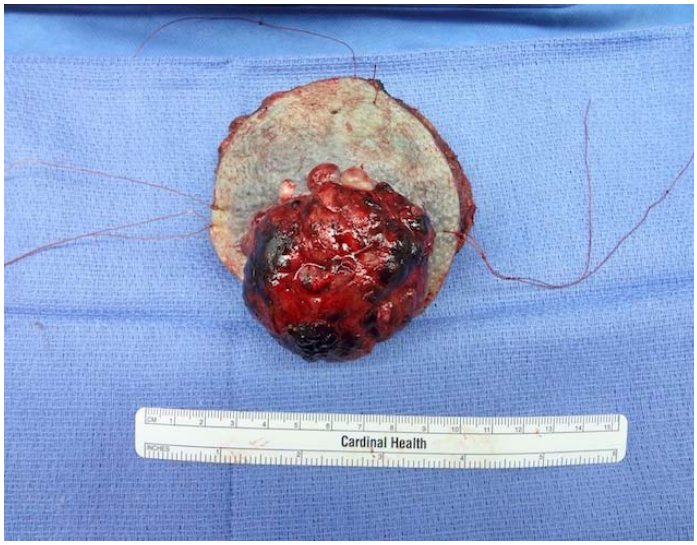

Figure 5. *Intraoperative image of the specimen after surgical excision.*

Case Discussion

Sebaceous carcinomas frequently resemble molluscum contagiosum, pyogenic granuloma, keratoacanthoma, and squamous cell carcinoma [7,8]. Given the varied clinical presentation and asymptomatic growth period, diagnosis and treatment of extraocular sebaceous carcinoma is often delayed [7]. Diagnosis requires pathologic confirmation of neoplastic cells with sebaceous differentiation, which can frequently be done by conventional microscopic methods. These common features include vacuolated cytoplasm, high mitotic activity, and nuclear pleomorphism [9]. However, immunohistochemistry often aids in cases with poor differentiation or less obvious findings to avoid confusion with other dermatologic malignancies such as basal cell and squamous cell carcinoma [9,10]. In a study by Plaza et al. investigating the role of immunohistochemistry in identifying sebaceous carcinoma, the sensitivity and specificity of adipophilin immunoreactivity to separate sebaceous carcinoma from basal cell carcinoma and squamous cell carcinoma were 100% [9]. Although this study only showed a 33.3% expression of androgen receptor in sebaceous carcinomas, others have shown 100% expression and promote androgen receptor as a sensitive marker of sebaceous differentiation [11].

Though extraocular sebaceous carcinoma is typically regarded as less aggressive than its ocular counterpart, extraocular tumors have also been reported in the literature to metastasize regionally and even distantly in rare cases [12,13]. Older case series have reported rates of nodal disease as high as 21% [14]. However, in a retrospective review from 2009 of 1,349 cases of sebaceous carcinoma, both ocular and extraocular, 1.7% of patients had clinical or pathologic evidence of lymph node involvement and 5.3% of patients received radiation therapy [1]. In a population-based analysis of prognostic indicators in sebaceous carcinoma of the head and neck, it was found that 1.14% of patients were node-positive. The rate of metastasis was closely related to the degree of tumor differentiation, but nodal metastasis was not ultimately an independent prognostic factor in the analysis [15]. Despite these

low rates of nodal involvement, the determination of which patients warrant sentinel lymph node biopsy (SLNB) lacks guidelines and remains a critical discussion. Tryggvason et al. noted a higher incidence of regional metastases in ocular cases compared to extraocular (4.4% versus. 0.9%), suggesting that SLNB should be considered only for eyelid tumors, but not for non-eyelid head and neck tumors [16]. By contrast, other authors advocate for routine SLNB for both extraocular and ocular cases despite the decreased risk [17]. Given the lack of consensus on the subject, radiographical evidence of lymph node enlargement on MRI, and rapid growth of our patient's lesion, we decided to pursue SLNB at the time of surgical excision in this case.

Surgical excision is accepted as the mainstay of treatment for both ocular and extraocular sebaceous carcinoma. However, recommendations on surgical margins as well as data on local recurrence and metastasis remains heavily based on ocular cases. A 5-6mm margin of normal appearing tissue surrounding ocular lesions is typically accepted. However, local recurrence has been approximated as 36% within 5 years with a 5-year mortality up to 30% [18]. Mohs micrographic surgery has also been used as an alternative, with local recurrence rates of 11-12% for ocular lesions [18,19]. Extending this technique to extraocular cases, Mohs surgery has also been used in a few cases of sebaceous carcinoma in cosmetically-sensitive areas such as the cheek [7,20]. Despite these favorable studies, both Mohs techniques and wide excision may be problematic in multifocal cases with "skip areas" [19]. In our case, with limited data on Mohs in the extraocular population, the location of the lesion, and the ability to close primarily with wide margins, we did not pursue Mohs surgery.

Similar to the divergent beliefs about the role for SLNB in extraocular cases, much debate exists over the role of radiation therapy. Adjuvant radiation after surgical excision in cases with lymph node involvement has been successful in several studies [21,22]. In addition, adjuvant therapy has been used for cases of extensive local invasion and recurrent disease [22,23]. For aggressive tumors that metastasize or recur despite several wide excisions and radiotherapy, several combinations of chemotherapeutic agents have been tried with variable success [24,25]. Based on treatment regimens for other head and neck malignancies, chemotherapy regimens for sebaceous carcinoma are typically cisplatin-based and frequently combined with 5-fluorouracil (5FU) and paclitaxel [24-26]. Responses in several case reports range from shrinkage of metastatic lesions to complete response with several years follow up. In a report by Murthy et al. a combination of carboplatin and 5FU followed by radiation allowed for an eyelid-sparing exenteration in a locally advanced case [26]. Orcuto et al. reported complete resolution of an aggressive scalp sebaceous carcinoma following 5FU, cisplatin, docetaxel, and capecitabine maintenance therapy [24]. Current research is focused toward targeted therapies including regulation of the retinoic acid receptor beta, androgen receptor, and epidermal growth factor receptor. Combinations of androgen receptor antagonists, retinoic acid receptor agonists, and/or immunotherapy with anti-PD1 antibodies may prove beneficial as more prospective evidence emerges [27].

An additional diagnostic challenge of extraocular sebaceous carcinoma is its strong association with Muir-Torre Syndrome (MTS), a variant of Lynch syndrome that is similarly caused by mutations in DNA mismatch repair (MMR) genes [28]. Muir-Torre Syndrome is characterized by the presence of at least one sebaceous gland neoplasm (sebaceous adenomas, sebaceous carcinomas, and keratoacanthomas) and at least one visceral malignancy [28]. Because the sebaceous neoplasm is often the first malignancy identified, screening for MTS becomes crucial to identify patients who require additional cancer surveillance and genetic testing [27]. Some experts urge for tumor testing of all sebaceous carcinomas for MMR defects and microsatellite instability to assess for risk of MTS, whereas others argue that the clinical utility of these tests remains unclear [29,30]. To identify patients at highest risk for MTS, Roberts et al. developed the Mayo MTS risk score algorithm. This algorithm includes a total score ranging from 0 to 5 based on four variables: age at diagnosis of sebaceous neoplasm, total number of sebaceous neoplasms,

personal history of Lynch-related cancer, and a family history of any Lynch-related cancer [29]. Based on their data, the authors recommend that all patients with Mayo MTS risk score of two or higher undergo germline MMR genetic testing [29].

Given the importance of screening all patients with sebaceous neoplasms for MTS, we applied the Mayo MTS risk algorithm to our patient. Because he was 72 at the time of sebaceous neoplasm diagnosis, he receives a 0 for the age variable (patients younger than 60 at time of diagnosis receive one point). Although he had a history of squamous cell carcinoma and basal cell carcinoma, the patient did not have any history of prior sebaceous neoplasms, personal history of Lynch-related cancer, or family history of Lynch-related cancer. Consequently, he received 0 points for all variables and a total Mayo MTS risk score of 0. Given that his Mayo MTS risk score was 0 and the nuclear expression of all MMR genes was preserved on immunohistochemistry, his risk of MTS was extremely low. As a result, he did not require additional genetic testing or screening for Lynch syndrome-associated cancers.

Conclusion

This case highlights the diagnostic challenges of sebaceous carcinoma that particularly impact those with extraocular disease. It also emphasizes the need for additional studies to determine ideal guidelines for MTS screening as well as the role of SLNB and radiation for management. Further investigation is needed to conclude the appropriate long-term monitoring regimen for these patients.

Potential conflicts of interest

The authors declare no conflicts of interests.

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