Nasal Sebaceous Carcinoma: A Case Report and Review of the Literature

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Sebaceous carcinoma arising from the nasal vestibule is exceedingly rare, with 3 cases previously reported. We have described the case of a 69-year-old man with an indolent exophytic growth on the medial aspect of his right nasal vestibule. Incisional biopsy demonstrated sebaceous carcinoma. The clinical and pathologic features, in addition to the surgical course and the postoperative outcome, are discussed. We also report our findings from a review of the reported data, focusing on the diagnosis and treatment of this rare skin malignancy.

J Oral Maxillofac Surg 78:82-86, 2020

An estimated 1 in 5 Americans will have developed skin cancer by the age of 70 years.[1,2] Skin cancers can be classified as nonmelanoma skin cancer (NMSC) and melanoma, with NMSC cases accounting for one third of all US cancer cases and more than 95% of all skin cancer cases.[2-4] Of the NMSC cases, 75% will be basal cell carcinoma,[3] 20% squamous cell carcinoma,[5,6] and 5% will include rare entities such as adnexal carcinoma, Merkel cell carcinoma, dermatofibrosarcoma protuberans, and sebaceous carcinoma. Although rare, this subset of NMSC should be considered in every differential diagnosis, given the significant differences in the prognosis, treatment, and follow-up protocols.

In the present case report and review of the reported data, an exceedingly rare NMSC arising from the cutaneous sebaceous glands, a sebaceous carcinoma (SC), is discussed. Oral and maxillofacial surgeons (OMSs), with frequent examination of the head and neck region in their daily practice, are likely to encounter NMSC. Despite the familiar clinical appearance, this rare subset of NMSC can have a more aggressive potential, and OMSs should familiarize themselves with these less common lesions.

Case Report

A 69-year-old man with a medical history significant for diabetes mellitus, hypertension, and gastroesophageal reflux disease had been referred by his primary physician to the maxillofacial oncology and reconstructive surgery clinic. He presented with a 4-year history of a slowly enlarging mass of the right nasal vestibule. His chief complaint was the presence of the mass and intermittent symptoms of pain when the lesion was irritated by nose blowing. No previous biopsy or treatment had been rendered. He denied any significant increase in size in the previous few months, unintentional weight loss, fevers, chills, or night sweats. His social history was unremarkable, because he was a nonsmoker and nondrinker. On physical examination, a fleshy 4 × 6-mm exophytic mass with associated telangiectasia was appreciated on the medial aspect of the right nasal vestibule along the membranous columella (Fig 1). The anterior nasal speculum examination showed that the lesion was limited to this area, with no other lesions within the nasal cavity. No palpable lymphadenopathy was present.

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Conflict of Interest Disclosures: None of the authors have any relevant financial relationship(s) with a commercial interest.

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Received July 2 2019

Accepted August 13 2019

0278-2391/19/31034-1

https://doi.org/10.1016/j.joms.2019.08.011

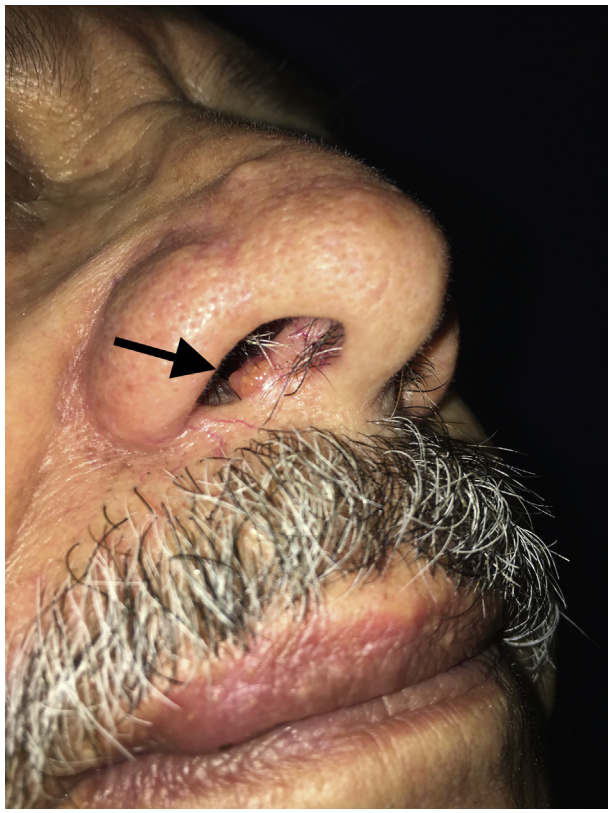

FIGURE 1. Photograph showing 4-mm × 6-mm exophytic mass of the right nasal vestibule.

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To confirm the diagnosis, an incisional biopsy of the specimen was performed with the patient under local anesthesia. Hematoxylin and eosin-stained sections showed nests of mildly atypical cells with foamy, finely vacuolated cytoplasm and distinct cell borders. Minimal mitotic activity was present, with no evidence of necrosis. The initial pathology analysis revealed a well-differentiated sebaceous carcinoma (Fig 2). Given the rarity of this diagnosis, a dermatologic–pathologic review was conducted, which confirmed the original diagnosis.

The patient was then taken to the operating room for wide local excision (WLE) and immediate reconstruction with a full-thickness skin graft from the supraclavicular region. Intraoperative frozen section analysis revealed clear margins, and the patient underwent an uneventful postoperative course. The final pathologic review confirmed the presence of clear margins. The patient underwent surveillance for longer than 12 months without evidence of recurrence (Fig 3).

Discussion

NMSC is a frequently diagnosed entity that is especially common in the head and neck region.[7] Sebaceous carcinoma, as the name suggests, is a cancer of the sebaceous glands. First described in 1891 by Allaire, cases of sebaceous carcinoma can be grouped as originating from the periorbital Meibomian and Zeis glands and those arising in extraocular sites.[8] Therefore, periorbital sebaceous carcinoma has been among the most common (38.7%), comprising 1.0 to 5.5% of all malignant eyelid neoplasms.[7,9] Extraocular sebaceous carcinoma of the head and neck can involve the face (26.8%), scalp and neck (8.7%), external ear (3.2%), and lip (0.8%).[10] In addition, 8 cases of intraoral sebaceous carcinoma have been described in the reported data.[11] Extraocular sebaceous carcinoma has been associated with a 29% recurrence rate and 21% metastatic rate.[12] The 5-year overall survival for those with sebaceous carcinoma

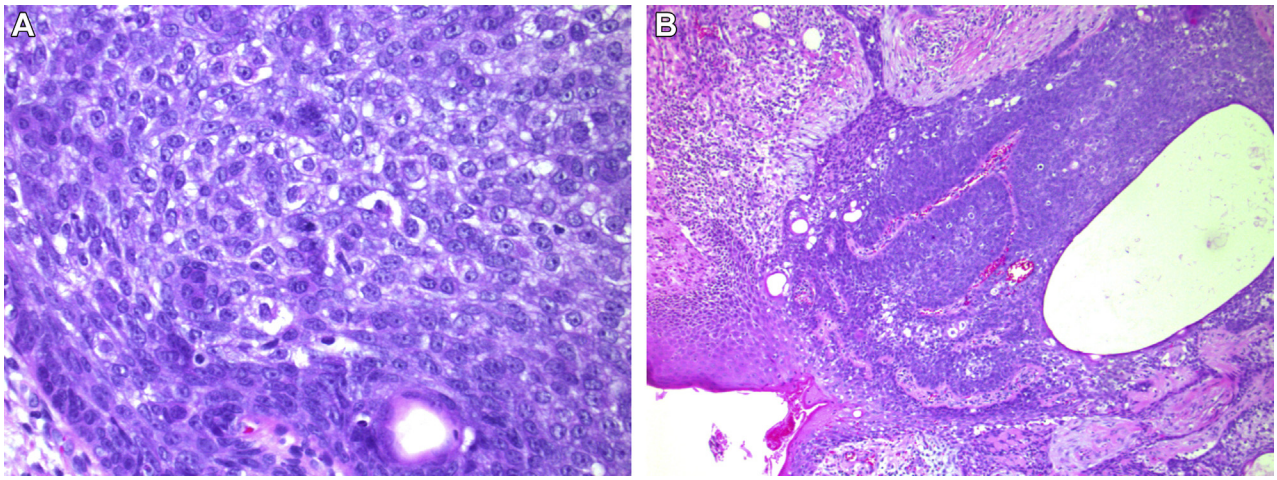

FIGURE 2. *A,* Hematoxylin and eosin-stained section showing well-differentiated sebaceous carcinoma with nests of mildly atypical cells and foamy, finely vacuolated cytoplasm and distinct cell borders (original magnification ×40). *B,* Hematoxylin and eosin-stained section showing minimal mitotic activity and no evidence of necrosis (original magnification ×10).

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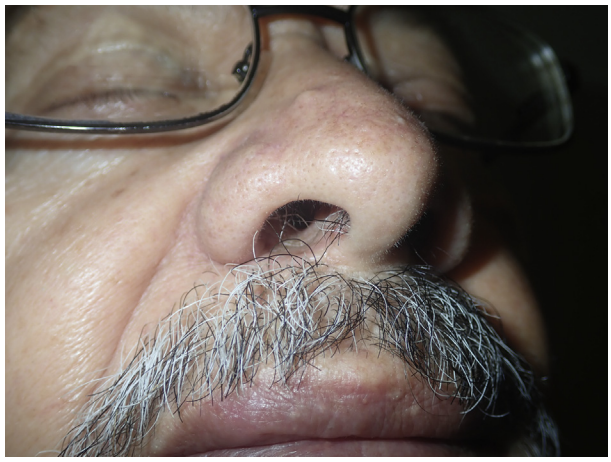

FIGURE 3. Follow-up photograph at 6 months postoperatively.

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has been reported to be 68 to 71.1%, with a 10-year overall survival of 45.9% and mortality ranging from 6 to 50%, with no difference in survival patterns between those with ocular and extraocular disease.[7,12-14] The exact cause of sebaceous carcinoma is unknown, although a number of pathways and genes have been implicated, including Wnt/β-catenin, p53/KRAS, PTEN, and LEF-1 gene.[15] The risk factors for sebaceous carcinoma include advanced age, a history of irradiation, immunosuppression, Muir-Torré syndrome (MTS), and familial retinoblastoma.[10,16] Sebaceous carcinoma arising from the nasal vestibule was found in 3 case reports of this rare entity. Dasgupta et al[17] reported a case of a sebaceous carcinoma of the nasal vestibule that had been treated with WLE and local flap reconstruction without recurrence during the 24-month follow-up period. Bir et al[18] reported on a mass arising from the right nasal vestibule that had been treated with simple excision but had recurred 12 months after the initial treatment. Murphy et al[19] treated a sebaceous carcinoma of the right nasal vestibule with WLE that subsequently required repeat excision to achieve tumor-free margins. However, 2 months later, the patient had presented with a sebaceous carcinoma of the contralateral side that was treated with simple excision.[19] At the 18-month follow-up examination, neither lesion had recurred.[19]

DIAGNOSIS

Clinically, sebaceous carcinoma will present as a painless heterogeneous lesion and range from flesh-colored, umbilicated papules to subcutaneous nodules or tumors with exophytic growth. However, the presentation can vary substantially and should not be considered reliable for diagnosis.[9,14] In addition, 25 to 30% of patients will present with bleeding as their primary concern.[9,20] In the 3 previously reported cases of sebaceous carcinoma in the nasal vestibule, epistaxis, crusting, and a nonhealing ulcerated mass were the presenting symptoms.[17-19]

The diagnosis of the sebaceous carcinoma can be complicated by the ambiguous clinical presentation in that they resemble the more common skin malignancies such as basal cell carcinoma (BCC). Sebaceous carcinoma can present as a recurrent lesion previously misdiagnosed as BCC.[21] Therefore, the diagnosis should be determined histologically, rather than clinically. Immunohistochemical staining, specifically MLH1 and MSH2, to assess for MTS, can help to differentiate sebaceous carcinoma from other clinically similar lesions.[10,13] The myriad of clinical presentations can lead to a delay in the diagnosis by 1 to 2.9 years on average and can potentially contribute to increase the morbidity and mortality.[7,13]

MUIR-TORRÉ SYNDROME

MTS, a variant of hereditary nonpolyposis colon cancer (Lynch syndrome), is an autosomal dominant condition caused by mutation in the MSH2 or MSH1 genes, accounting for nearly 90% and 10% of cases, respectively. MTS is characterized by the presence of at least 1 sebaceous neoplasm of the skin and 1 or more low-grade visceral malignancies.[22,23] Approximately 30% of sebaceous neoplasms associated with MTS will be sebaceous carcinoma, with the most common visceral malignancies colorectal (51%), genitourinary (25%), and breast (12%).[22,24-26]

PREOPERATIVE EVALUATION

Given the propensity for sebaceous carcinoma to occur in patients with MTS, the presence of the lesion should prompt an evaluation beyond that of the lesion itself. A thorough history can help with guiding further examinations. The baseline laboratory tests and imaging studies should include chest radiography, complete metabolic panel, complete blood count, and screening for visceral cancer, which can include a rectal examination, full colonoscopy, and barium enema.[13,22,24,25] Additionally, genetic counseling could be warranted, especially if the presence of MTS is strongly considered or confirmed, given the hereditary nature of the syndrome.[13] Imaging of the head and neck should be considered even for patients with negative findings from clinical examination of the neck. The use of lymphoscintigraphy with sentinel node biopsy has been advocated, given rate of metastatic potential of 20 to 25%.[12,27,28]

TREATMENT

In addition to the division according to an ocular or extraocular origin, staging is determined by the

location of the sebaceous carcinoma.[20,29] However, the role of TNM staging for extraocular sebaceous carcinoma for predicting the prognosis and determining the management has not been studied. The relationship between the TNM stage and disease progression for ocular sebaceous carcinoma was recently studied in a retrospective cohort study. That study showed that stage T2b disease or higher for ocular sebaceous carcinoma can be predictive of the presence of nodal metastasis, and T3a disease or higher can be predictive of cancer-specific mortality.[20,30] However, how such findings can translate into clinical decision making has not yet been clarified. Furthermore, it is unclear whether their findings translate to extraocular sebaceous carcinoma.

The treatment of choice for sebaceous carcinoma has been WLE or Mohs micrographic surgery (MMS). In addition, radiotherapy, topical mitomycin-C, neoadjuvant chemotherapy, and, possibly, targeted proteins have also been explored for periorbital disease.[31]

Patients who are unable or unwilling to undergo surgical excision could benefit from palliative radiation therapy, although studies have indicated that radiation therapy will not be as effective as surgical treatment.[13,32,33] In the reported data, the 4-year mortality rate for patients undergoing radiation therapy alone was 78% compared with 33% after simple tumor excision and 7% after WLE.[34] Radiation therapy has also been associated with local complications similar to those experienced by patients with other head and neck malignancies such as hair loss and pigmentation and skin changes. Topical mitomycin-C has been successful in the initial tumor control of periorbital sebaceous carcinoma with pagetoid invasion without tumor infiltration into the underlying epithelium but has not been studied in extraorbital sebaceous carcinoma.[13,35]

Antimetabolite 5-fluorouracil or cisplatin-based chemotherapy has been used for metastatic disease. However, currently, the data for these therapies have been limited to case reports and cannot be advocated for use in local disease.[34] The overexpression of proteins related to angiogenesis, inflammation, and cell proliferation has been demonstrated in sebaceous carcinoma but have not yet been investigated as an immunotherapy alternative for cure or adjunct to the current standard treatment of excision.[10,31] The poor differentiation of sebaceous carcinoma could be a factor in considering the need for adjuvant therapy.[11,13]

Recently, reported data have favored MMS instead of the standard WLE, because it resulted in lower recurrence and mortality with superior tissue conservation.[7,13,35,36] The incidence of sebaceous carcinoma recurrence after MMS has been reported to be ~12% compared with 29% after WLE.[12,32,37] The width of surgical margins has not been agreed on; however, many have chosen WLE with a surgical margin of 5 to 6 mm, slightly larger than that for BCC, and a 2-mm margin for MMS.[20,28,38] MMS might be advantageous because of sebaceous carcinoma having a tendency for intraepithelial spread, which could result in the final excision margins being significantly larger than the clinically visible margins.[13,32] It has been recommended that the margins for WLE should be evaluated in both permanent paraffin-embedded tissues and frozen sections.[13,35,39]

Cases of both ocular and extraocular sebaceous carcinoma have been known to metastasize to the regional lymph nodes. The preauricular and parotid lymph nodes have been the most common sites of metastasis.[8,12,39,40] Specifically, extraocular sebaceous carcinoma has been reported to have a metastatic rate of 20 to 25%.[12,27]

Sawyer et al[28] recommended sentinel node biopsy, given the potential aggressive behavior of extraocular sebaceous carcinoma. However, no consensus has been reached regarding cervical nodal treatment, whether via sentinel lymph node dissection, neck dissection, or close surveillance, despite the relatively high metastatic rate.

The poor prognostic factors have included a lesion size greater than 10 mm, delay in the diagnosis of longer than 6 months, multicentric origin, vascular, lymphatic, orbital, or pagetoid invasion, poor differentiation, and a highly infiltrative pattern.[13,27,35,39] A retrospective analysis of the Surveillance, Epidemiology, and End Results database for patients with a diagnosis of sebaceous carcinoma of the head and neck found that lymph node metastasis did not appear to be an independent prognostic factor.[41]

SURVEILLANCE

Although no specific guidelines for surveillance of these rare lesions have been generated, the reported data have supported extensive, long-term follow-up examinations because late relapses secondary to pagetoid, nodal, or distant spread have been reported 5 to 11 years after excision of the primary sebaceous carcinoma.[42-45]

In conclusion, sebaceous carcinoma is a rare entity of the nostril, with many cases that resemble common skin lesions such as BCC. Although the data are limited, the worse outcomes and difficult diagnosis warrant further attention from surgeons treating skin cancers of the head and neck, such as OMSs. Additionally, surgeons should investigate for possible underlying MTS, given the strong association between sebaceous carcinoma and underlying visceral malignancies.

Biopsy and histopathological assessment is required for the diagnosis of sebaceous carcinoma. Prompt evaluation, accurate diagnosis, and appropriately aggressive treatment of these lesions are essential for good outcomes. Surgical excision, either through WLS or MMS, remains the treatment of choice. Given the metastatic potential of these lesions to the regional and distant lymph nodes, neck disease must be ruled out, and the role of sentinel lymph node biopsy and computed tomography studies of extraocular sebaceous carcinoma should be considered.

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