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A Clinical Case of a Right Eyelid Multilobulated Lesion: Invasive Sebaceous Carcinoma Masquerading as Chalazion

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ABSTRACT

Sebaceous carcinoma (SC) is a rare and aggressive malignancy of the sebaceous glands, most commonly arising from the eyelid. The general presentation of SC varies, resulting in delayed identification and frequent misdiagnosis. Clinicians should include SC in a differential diagnosis when a patient presents with an eyelid lesion. Undiagnosed and untreated SC can have detrimental outcomes; therefore, early diagnosis and treatment are imperative to decrease mortality and morbidity.

This is the case of a 71-year-old male referred by his primary care physician to the ophthalmologist for an inflamed, multilobulated lesion on his right upper eyelid. The patient was initially diagnosed with chalazion and prescribed Vigamox. A shave biopsy was obtained and sent to pathology, which revealed the diagnosis of invasive SC. The patient was subsequently referred to oncology and general surgery for multidisciplinary management. This case report highlights a unique account of invasive SC initially misdiagnosed as chalazion, underscoring the importance of thorough evaluation and awareness of this rare presentation.

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KEYWORDS

sebaceous carcinoma; chalazion; invasive sebaceous carcinoma

INTRODUCTION

Sebaceous carcinoma (SC), a rare and aggressive malignancy, arises from the oil-producing cells within the skin. Specifically, SC arises most commonly from the Meibomian glands and less commonly from the sebaceous glands of Zeiss and sebaceous glands in the ocular caruncle.[1] Although SC can occur wherever sebaceous glands reside, extra-orbital lesions are considered less aggressive than periorbital lesions.[1] Up to 80% of SCs present on the head and neck, with 40% presenting on the eyelids. The upper eyelid is more commonly affected due to the increased number of sebaceous glands.[1,2]

Irregular, asymmetric sebaceous lobules histopathologically identify these cancers, with cells displaying significant pleomorphism, mitotic activity, and nuclear atypia.[1] They are then placed into 1 of 4 categories: papillary, lobular, comedocarcinoma, and mixed.[1] SC risk factors include Muir-Torre Syndrome, prior radiation exposure to the head/neck region, ultraviolet exposure, immunosuppression, and age. However, most are due to sporadic mutation in the LEF-1 gene.[1,3,4] Muir-Torre syndrome, a nonpolyposis colorectal cancer syndrome, is a type of Lynch Syndrome involving variants of DNA mismatch repair genes (MSH2, MSH6, MLH1) that have been identified in nearly 30% of those diagnosed with SC.[3] Those affected are at an increased risk of developing malignancies of the skin and of gastrointestinal/genitourinary origin. The highest incidence is associated with non-Hispanic whites at least 80 years old.[3]

CASE PRESENTATION

This is the case of a 71-year-old male with a past medical history of myopia, facial dermatitis, astigmatism, cataracts, and dry eyes who was referred by his primary care physician to the ophthalmologist with the complaint of an inflamed lesion on his right upper eyelid. He stated the lesion had been present for "weeks" and that he kept "squeezing it out." On physical exam, he was alert and oriented times 3. A multilobulated lesion was on the right upper eyelid (Figure 1). Upon eye examination, gross visual fields were full to confrontation, pupils were equal in size and reactive to light bilaterally, and there was total ocular motility. The iris was normal in appearance. Vitreous was clear and quiet. The patient was initially diagnosed with chalazion and prescribed Vigamox until chalazion surgery 1 week later. A shave biopsy was obtained from the right upper eyelid and sent to pathology. Follow-up was scheduled for approximately 2 weeks later.

The pathology report of the right upper eyelid shave biopsy revealed sections showing invasive carcinoma, comprising sheets and a nest of tumor cells with vacuolated cytoplasm (Figure 2). The gross pathology of the specimen consisted of 2 gray-tan irregular pieces of soft tissue measuring 0.5 cm and 0.6 cm in greatest dimension.

Immunostains for cytokeratin (CK) 5/6, pancytokeratin, and p63 reacted with lesional cells (positive). Ki-67 had a very high proliferation index of

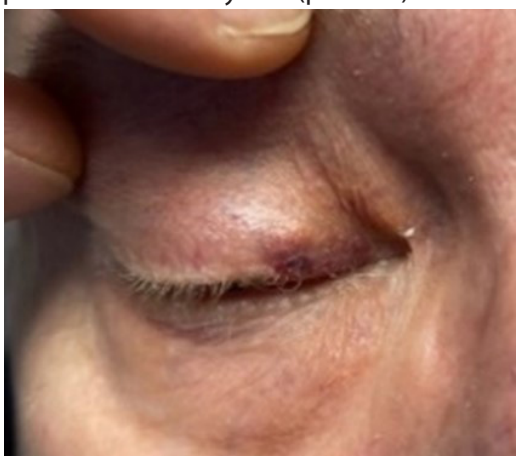

FIGURE 1. Right upper eyelid lesion.

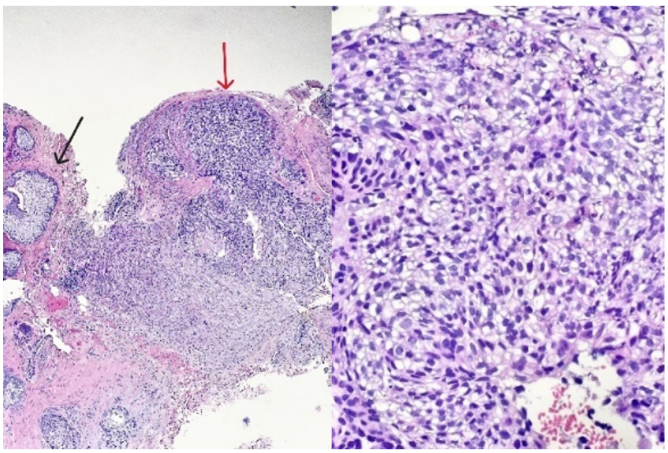

FIGURE 2. Hematoxylin and eosin (H&E) 20X showing non-neoplastic sebaceous glands (black arrow) adjacent to areas of invasive sebaceous carcinoma (red arrow). H&E 400X showing a high-powered view of pleomorphic cells of sebaceous carcinoma.

approximately 40%, and the CD45 highlight revealed a nonspecific scattering of leukocytes. Additional immunostains for epithelial membrane antigen (EMA) and adipophilin were positive, supporting the diagnosis of invasive SC (Figure 3).

The results were discussed with the patient upon follow-up, and he was referred to oncology and general surgery for multidisciplinary team management.

DISCUSSION

Sebaceous carcinoma (SC) is a rare malignancy, and the general presentation may vary from a small, painless, gradually enlarging lump to an inflamed and thickened sore.[1] These presentations may cause SC to be mistaken for a chalazion or blepharitis. SC may also invade nearby ocular and periorbital structures, leading to worsening symptoms.[1] Additional findings that may suggest an underlying malignancy include diffuse inflammation of the eyelid, loss of cilia, failure to respond to standard treatment, or recurrence following excision. Atypical presentations of SC include a pedunculated lesion or mass within the eyebrow or lacrimal gland.[5]

The propensity of SC to masquerade as other benign and malignant lesions contributes to frequent misdiagnosis.[5] Moreover, SC of the eyelid often presents in very late stages. A biopsy should be obtained for every skin lesion that appears suspicious or fails to resolve after therapy.[5,6] Benign conditions often confused with SC include chalazion, blepharitis, conjunctivitis, and Churg-Strauss syndrome.[5] Chalazion and blepharitis remain the most common benign etiologies in the differential diagnosis of SC. Chalazion tends to occur in younger patients presenting with pain and is not likely to cause loss of cilia.[5] Additionally, chalazion may be distinguishable from SC through the use of noninvasive meibography, aiding in timely diagnosis of suspicious eyelid lesions caused by SC.[7] SC may also be mistaken for other malignancies that appear similarly, including basal cell carcinoma (BCC), squamous cell carcinoma (SCC), melanoma, Merkel cell carcinoma, and lymphoma.[5]

In an older patient with atypical or recurrent chalazion, the lesion should be biopsied to rule out SC or other malignant tumors.[5] In a retrospective case series, Shields et al.[5] found that the accurate initial pathologic diagnoses of SC were made in only 50% of cases, highlighting a discrepancy between clinical suspicion and histopathologic

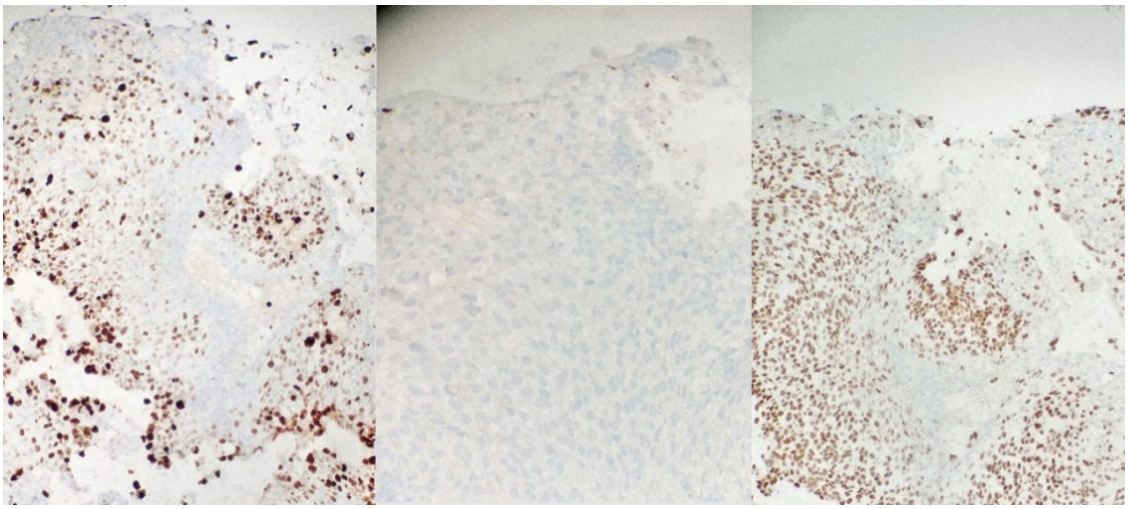

FIGURE 3. Ki-67 Immunohistochemistry highlighting an increase in mitotic activity within tumor cells (left), S100 Immunohistochemistry negative within neoplastic cells (middle), and a p63 Immunohistochemical stain showing positivity within neoplastic cells (right).

confirmation. As exemplified by this case, the initial presentation of a painless right lobular lesion was thought to be a chalazion, a common benign eyelid pathology. However, due to suspicion of a more severe diagnosis, an excisional skin biopsy was performed. The histopathology report confirmed invasive SC. Within 2 weeks of the first presentation to the ophthalmologist, the patient was referred to oncology and surgical services, demonstrating timely diagnosis and management commencement.

Immunohistochemistry may be an excellent aid in differential diagnosis between SC and other neoplasms. In a study comparing the pathologic differences between eyelid SC and BCC (102 and 175 confirmed cases, respectively), Zhang et al.[8] demonstrated several markers that can be utilized to differentiate them, including shelterin subunit levels, P53 mutation rates, Siah1 mRNA expression, levels of senescent cells, Ki-67, and Bcl-2. As seen in this study's patient, levels of Ki-67 were remarkably high, with a proliferation index of 40%, which strongly suggested the diagnosis of SC. In another case series, Sinard9 suggested that combining the 3 markers anti-EMA, BRST-1, and Cam 5.2 can help discern between SC, SCC, and BCC. Current research suggests that SC's most indicative immunohistochemistry markers include androgen receptor, adipophilin, and epithelial membrane antigen (EMA).[9,10] As in this case, the patient's sample was positive for adipophilin and EMA, further supporting the diagnosis of SC.

Management for SC depends on the progression and stage of the disease. When diagnosis is made at an early stage, surgical intervention with wide excision is often sufficient.[5] However, advanced cases are more likely to have complications after surgery, and if metastasis has been confirmed, chemotherapy will be necessary under the supervision of an oncologist.[5] SC prognosis significantly depends on staging at diagnosis, emphasizing the importance of early detection and treatment. Studies show that SC tumors classified as stages T1, T2, or T3 in the tumor, node, metastasis (TNM) system generally had favorable prognoses with no deaths attributable to the tumor, indicating a cause-specific, 5-year survival rate of 100%.[11] In contrast, tumors classified as stage T4 led to significantly worse prognoses, with a cause-specific, 5-year survival rate of 42.9%.[11] This disparity underlines the critical role of clinicians in the early detection and intervention of SC to mitigate the risk of invasion and metastasis. Moreover, some authors have suggested that combining the T category with other factors could help better predict metastasis-free survival. Notably, Gu et al.[12] developed a nomogram to assess the risk of nodal metastasis in patients with SC by evaluating factors such as diffuse pattern, orbital invasion, perineural invasion, and Ki-67 index. Outcome prediction was shown to be more successful than traditional TNM staging, suggesting a potential benefit to future SC treatment management.[12]

CONCLUSION

SC is a rare malignancy of the sebaceous glands and is often misdiagnosed as a benign skin pathology. Clinicians should include SC in a differential diagnosis when a patient presents with an eye lesion. Undiagnosed and untreated SC can have detrimental outcomes. Therefore, early diagnosis and treatment preceding invasive disease can decrease mortality and morbidity.

INFORMED CONSENT

Standard consent was obtained by the treating facility at the time of registration.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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