

# Collision tumor of microcystic adnexal carcinoma and squamous cell carcinoma discovered on Mohs sections



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## INTRODUCTION

Microcystic adnexal carcinoma (MAC) is an uncommon, locally aggressive tumor that typically extends far beyond the clinically evident lesion but has a low risk of regional or distant metastasis.<sup>1</sup> MAC is misdiagnosed about 27% of the time, most commonly as desmoplastic trichoepithelioma (DTE), morpheaform basal cell carcinoma (BCC), or syringoma when superficial biopsy techniques are used.<sup>2</sup> Less often, MAC is misdiagnosed as squamous cell carcinoma (SCC) because the superficial portion of MAC can have keratinaceous structures that resemble SCC.<sup>3</sup> Unfortunately, there are no routinely utilized immunohistochemical (IHC) stains that differentiate MAC from these mimics.

## CASE REPORT

An 83-year-old white man was referred for Mohs micrographic surgery (MMS) of an SCC on the right upper lip that had grown slowly over 1 year. He had a history of multiple nonmelanoma skin cancers, but none in this site. On clinical examination, there was an ill-defined, 2.6- × 1.4-cm, indurated plaque extending from the vermilion border of the right upper lip to the nasal vestibule. The degree of induration was concerning for full-thickness tumor involvement. There was no palpable head and neck lymphadenopathy.

After sharp debulking the clinically evident tumor, the patient underwent MMS. A portion of the debulked tissue was processed via frozen section

### Abbreviations used:

|       |                                |
|-------|--------------------------------|
| BCC:  | basal cell carcinoma           |
| CEA:  | carcinoembryonic antigen       |
| CK:   | cytokeratin                    |
| DTE:  | desmoplastic trichoepithelioma |
| IHC:  | immunohistochemical            |
| MAC:  | microcystic adnexal carcinoma  |
| MMS:  | Mohs micrographic surgery      |
| PNI:  | perineural invasion            |
| SCC:  | squamous cell carcinoma        |
| SLNB: | sentinel lymph node biopsy     |

(Fig 1) and showed keratinizing proliferations of atypical keratinocytes representative of SCC. The first 3 stages of MMS showed infiltrative cords of basaloid tumor cells with extensive perineural invasion (PNI) of small and medium-caliber nerves (Fig 2). The fourth stage achieved clear surgical margins resulting in a 6.8- × 4.4-cm full-thickness surgical defect (Fig 3). The patient had preoperatively scheduled reconstruction with a plastic surgeon, who performed a radial forearm free flap.

Given the extent of PNI and the presence of a population of basaloid, nonkeratinizing tumor cells on frozen sections that were unexpected for SCC, the remainder of the Mohs debulk was sent for permanent section evaluation. The debulk specimen (Fig 4) showed a large, poorly circumscribed, sclerosing epithelial tumor. Superficially there were atypical keratinocytes with extensive keratinization that extended from the epidermis into the superficial dermis, representing SCC. Histologically, the SCC

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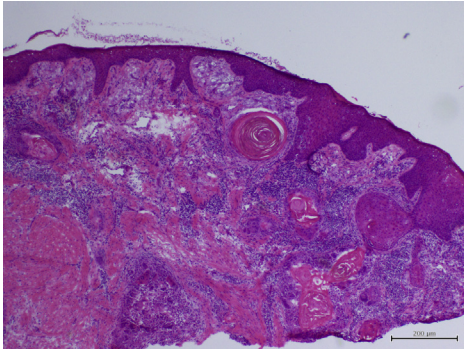
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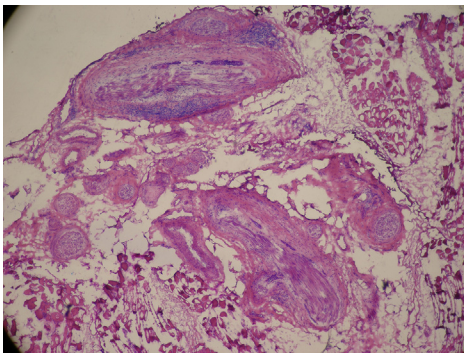
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**Fig 1.** Frozen section analysis of debulked tissue shows keratinizing proliferations of atypical keratinocytes extending to the epidermis, consistent with SCC.



**Fig 2.** Frozen section of MMS stage 2 with multifocal perineural infiltrating strands and cords of basaloid tumor cells.

was adjacent to a more predominant finding of cords and strands of basaloid and squamous tumor islands within a sclerotic stroma infiltrating the dermis and subcutis with ductal differentiation and PNI involving small nerves in the deep dermis, representing MAC. The MAC portion had a margin of zonation between the epidermis and dermal tumor component, not seen in the SCC. Overall, the findings were consistent with a collision tumor involving SCC and MAC.

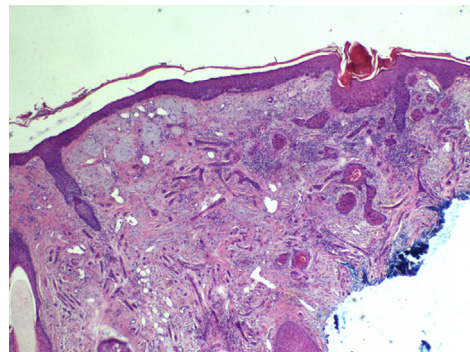
The initial biopsy was interpreted outside of our institution, and the microscopic description reported buds, cords, and larger irregularly shaped lobules of atypical keratinocytes extending to the depth of the specimen. These buds and cords stained positively for AE1/3 and CK5-6, leading to a diagnosis of SCC. Because the initial biopsy was superficial, sampling error likely contributed to the inability to identify MAC prior to tumor debulking.

## DISCUSSION

This case highlights the unique collision of a cutaneous SCC and MAC. There are similar, yet



**Fig 3.** Final surgical defect measuring  $6.8 \times 4.4$  cm after 4 stages of MMS.



**Fig 4.** Permanent section of MMS debulk. On the left side there are infiltrating strands and cords of basaloid tumor with a margin of zonation between the epidermis and the dermal tumor component. On the right side there are keratinizing proliferations of atypical keratinocytes, classic for SCC, extending to the epidermis.

different cases described in the literature: a case of both SCC and MAC existing within an ovarian cystic teratoma, a case of MAC-like SCC involving the facial nerve, and a case of SCC with MAC-like differentiation of the chin.<sup>4-6</sup> Additionally, there are reported cases of MAC initially misdiagnosed as SCC owing to shallow biopsy techniques.<sup>3</sup> Although most of our patient's lesion was characteristic of MAC, it represents a collision tumor given the distinct SCC and MAC histologic features.

Pathologists often use IHC stains to help differentiate tumor types. Although ductal elements of MAC stain positively for carcinoembryonic antigen (CEA), epithelial membrane antigen, and cytokeratins (CK), it does not have a specific, routinely utilized IHC profile. Ber-EP4, an antibody targeting epithelial cells, is typically diffusely positive in BCC but negative in SCC, making it a useful to differentiate these 2 tumors. Ber-EP4 is not useful for

differentiating MAC from BCC or DTE, as all tumors can stain positively.<sup>3</sup> Likewise, both MAC and SCC stain positively with CK, such as AE1/3 and CK5-6, both of which were used to evaluate the initial biopsy in this case.

AE1/3 stains both high and low-molecular-weight CK: AE1 recognizes CK10, 14, 15, 16, and 19, whereas AE3 recognizes CK1 through 8. Uniquely, CK15 alone has been shown to positively stain MAC and does not stain SCC or the infiltrative subtype of BCC.<sup>3</sup> CK15 is thought to be a relatively specific marker for hair follicle-related neoplasms.<sup>3</sup> In this patient, IHC with AE1/3 may have provided false reassurance that this tumor represented a single entity, SCC, as AE1/3 does not separate out CK15. CEA may also be a useful adjunct IHC stain to differentiate SCC from MAC, as CEA stains around 30% to 58% of MAC tumors and does not stain SCC.<sup>3</sup> However, CEA is more useful to distinguish between MAC and DTE, as DTE stains positive with CK15 and negative with CEA.<sup>2,3</sup>

Preoperatively differentiating MAC from tumors with higher metastatic potential, such as SCC, is helpful to appropriately counsel patients on the potential morbidity of surgical management of MAC, which typically extends several centimeters beyond the clinically apparent tumor, and the potential further management and staging of high-risk SCC including imaging and sentinel lymph node biopsy (SNLB). Adjuvant radiation after surgical management of MAC has some supportive evidence to improve local control of MAC in patients with positive surgical margins or PNI.<sup>2,7</sup> Given the low frequency of MAC nodal metastasis, SLNB biopsy is not recommended for MAC staging, and there is no evidence to support prophylactic nodal

radiotherapy, which is in contrast to SCC in which patients with Brigham and Women's Hospital stage T2b or higher may be considered for SLNB.<sup>2,8</sup>

In this case, given the presence of both MAC with extensive PNI and SCC, our institution's multidisciplinary team decided to pursue adjuvant radiation to both the tumor bed and nodal basins. It has been 4 years since the patient underwent MMS and adjuvant radiation, and he continues to have no clinical evidence of recurrence.

#### REFERENCES

1. Eisen DB, Zloty D. Microcystic adnexal carcinoma involving a large portion of the face: when is surgery not reasonable? *Dermatol Surg.* 2005;31(11):1472-1478.
2. Worley B, Owen JL, Barker CA, Behshad R, et al. Evidence-based clinical practice guidelines for microcystic adnexal carcinoma: informed by a systematic review. *JAMA Dermatol.* 2019. <https://doi.org/10.1001/jamadermatol.2019.1251>. [Epub ahead of print].
3. Hoang MP, Dresser KA, Kapur P, et al. Microcystic adnexal carcinoma: an immunohistochemical reappraisal. *Mod Pathol.* 2008;21(2):178-185.
4. Yoon HK, Park SM, Joo JE. Combined microcystic adnexal carcinoma and squamous cell carcinoma arising in the ovarian cystic teratoma—a brief case report. *J Korean Med Sci.* 1994;9(5):432-435.
5. Mueller SK, Iro H, Lell M, et al. Microcystic adnexal carcinoma (MAC)-like squamous cell carcinoma as a differential diagnosis to Bell's palsy: review of guidelines for refractory facial nerve palsy. *J Otolaryngol Head Neck Surg.* 2017;46(1):1.
6. Ibrahim YL, Lambert S, Kazakov DV, Kaya G. An unusual morphological presentation of cutaneous squamous cell carcinoma mimicking microcystic adnexal carcinoma: a diagnostic pitfall. *Dermatopathology.* 2018;5:64-68.
7. Pugh TJ, Lee NY, Pacheco T, Raben D. Microcystic adnexal carcinoma of the face treated with radiation therapy: a case report and review of the literature. *Head Neck.* 2012;34(7):1045-1050.
8. Fox M, Brown M, Golda N, et al. Nodal staging of high-risk cutaneous squamous cell carcinoma. *J Am Acad Dermatol.* 2019; 81(2):548-557.