Multiple recurrent squamous cell carcinomas and utility of anticytokeratin immunohistochemistry

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Key words: aggressive; dermatologic surgery; immunohistochemistry; Mohs surgery; nonmelanoma skin cancer; recurrent; squamous cell carcinoma.

INTRODUCTION

Mohs micrographic surgery remains the gold standard for the treatment of cutaneous squamous cell carcinomas (SCCs) of the head and neck. However, for recurrent or aggressive SCCs, it can be challenging at times to ensure complete margin control on hematoxylin and eosin (H&E) frozen sections alone. The authors present a case of multiple recurrent SCC that was ultimately found to have occult foci of tumor identifiable only by anticytokeratin immunohistochemistry (IHC). Although a large volume of literature addresses the topic of IHC for melanocytic neoplasms treated by traditional Mohs and "slow Mohs," there is a relative paucity of commentary on its use in SCCs.[1] This unusual case highlights the importance of anticytokeratin IHC for SCCs, especially in tumors that are recurrent or have aggressive or atypical cytomorphology.

Abbreviations used:

AE1/AE3:	anti-pan cytokeratin 1/3
ART:	adjuvant radiation therapy
H&E:	hematoxylin and eosin
IHC:	immunohistochemistry
SCC:	squamous cell carcinoma

CASE REPORT

A 63-year-old woman with a medical history significant for 2 basal cell carcinomas, follicular lymphoma, and breast cancer presented for evaluation of an 8-mm infiltrative erythematous papule on the left lateral cheek near the angle of the mandible. There was no nerve pain, pruritus, or other clinical indicator of perineural invasion. A biopsy of the lesion found a well-differentiated invasive SCC (Fig 1), which was excised via the Mohs technique and repaired with a small advancement flap.

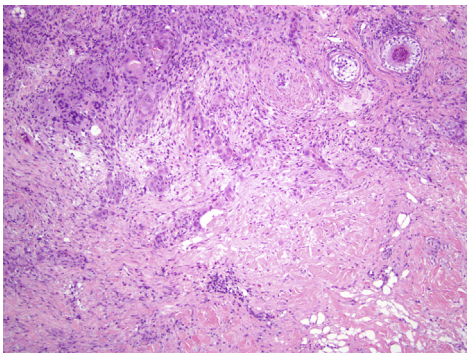

Fig 1. Original biopsy shows SCC infiltrating into the papillary dermis. (H&E stain; original magnification: ×10.)

Fifteen months later, the patient presented for evaluation of an infiltrative, scaly, telangiectatic 1-cm plaque immediately superior to and abutting the scar from the prior Mohs procedure without regional lymphadenopathy. Biopsy of the lesion found well-differentiated and invasive SCC in a background of scar and repair changes. The pathologists noted in their report that the specimen had architectural and

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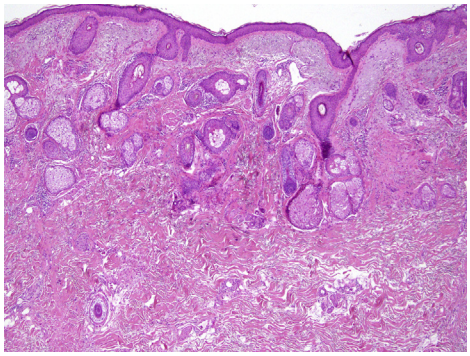

Fig 2. Permanent sections of the Mohs layer did not show SCC. (H&E stain; original magnification: ×4.)

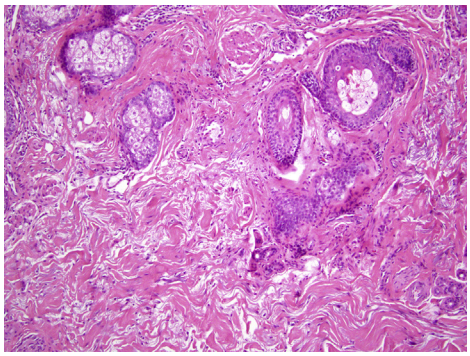

Fig 3. Permanent sections of the Mohs layer did not show SCC. (H&E stain; original magnification: ×20.)

cytological features consistent with an aggressive tumor, specifically noting marked nuclear pleomorphism and an infiltrative growth pattern. The tumor was re-excised using the Mohs technique. Given the aggressive histopathologic appearance, referral was also made to the radiation oncology department. Although recommended at that time to undergo a dedicated planning computed tomography scan in anticipation of adjuvant radiation, the patient declined both the computed tomography scan and the adjuvant radiation.

Two years later, the patient was again found to have a lesion suspicious for recurrence—this time a 7-mm firm, tender, erythematous papule within the scar. There was no regional lymphadenopathy. Biopsy and subsequent histopathologic examination found well-differentiated and invasive SCC at the site, with aggressive features as before, including marked nuclear pleomorphism and a highly infiltrative growth pattern. For this second recurrence, the patient was again treated with Mohs micrographic surgery, which was thought to be clear after 3 stages and closed with an advancement flap.

Eight months later, the patient noted a small area of ulceration within the inferior portion of the scar.

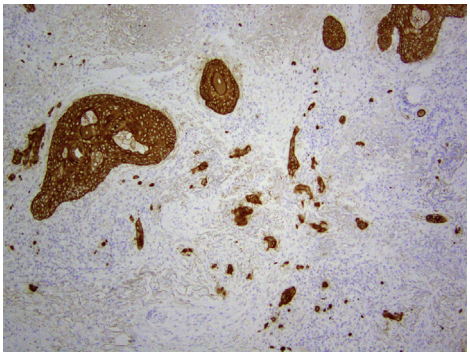

Fig 4. IHC using AE1/AE3 shows irregular infiltrating strands of SCC and scattered single atypical cells. (AE1/AE3 stain; original magnification: ×20.)

Rebiopsy found well-differentiated SCC again. At that time, a dedicated computed tomography scan of the face and neck/larynx with contrast found no radiographic evidence of tumor or lymphadenopathy. The patient subsequently underwent her fourth Mohs procedure, which was thought to be clear after 2 stages. However, this time, the final stages were sent for formalin-embedded permanent sections to be read by a dermatopathologist prior to definitive closure (Figs 2 and 3). This action was done because of the multiple recurrences of the tumor and an inflammatory infiltrate noted on frozen section potentially obscuring occult foci of tumor, a feature that had not been noted during any of the patient's previous Mohs procedures. On histopathologic examination, no residual SCC was identified on H&E, so the defect was then closed as planned. Given the unusual circumstances of the case and development of additional nonmelanoma skin cancers at other sites over the same period, the patient was started on acitretin. She was also evaluated by radiation oncology for a second time, but the patient remained reluctant to undergo any radiation therapy.

One year later, the patient had a suspicious lesion at the same site, and rebiopsy found well-differentiated invasive SCC again. At this time, given the unusual nature of the case, anticytokeratin staining (AE1/AE3) was performed on the block sent for frozen section from the most recent Mohs procedure 1 year prior. Despite no residual SCC identified on H&E by an experienced dermatopathologist, AE1/AE3 staining found a minute focus of infiltrating cells in the papillary dermis suspicious for residual SCC (Fig 4). Given the apparent impossibility of fully characterizing the tumor on H&E and its multiple recurrences, Mohs was no longer felt to be an appropriate treatment modality. The patient then was sent to the otolaryngology department for a wide local excision with parotidectomy and