doi:10.36849/JDD.2020.5184

Rapid Evolution of a Squamous Cell Carcinoma In Situ to Locally Invasive With Perineural Involvement

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ABSTRACT

We present a case of rapidly progressing squamous cell carcinoma in situ (SCCis) with progression to aggressive SCC. An elderly gentleman with multiple medical comorbidities presented with a left zygomatic tumor initially diagnosed as SCCis with adnexal extension on histology. After a period of approximately 10 weeks, the patient underwent Mohs micrographic surgery (MMS) with evidence that the tumor was now consistent with a well-differentiated SCC, with perineural involvement. MMS was stopped after two stages and the patient was sent to head and neck surgical oncology for further evaluation and management.

It has been reported in the literature that 3–5% of SCCis will progress to invasive SCC; although the inciting event to cause such progression is unknown, it is thought that mutations in key oncogenes or tumor suppressor genes such as *TP53* may play a role. In addition, as many as 31% of SCCis may have a component of invasive SCC that is missed on initial histology due to sampling bias. This case reminds us that sampling bias can occur during biopsy, SCCis can rarely progress to invasive SCC, and highly aggressive SCCs may prove to be therapeutically challenging requiring a multidisciplinary approach.

J Drugs Dermatol. 2020;19(11):1110-1111. doi:10.36849/JDD.2020.5184

INTRODUCTION

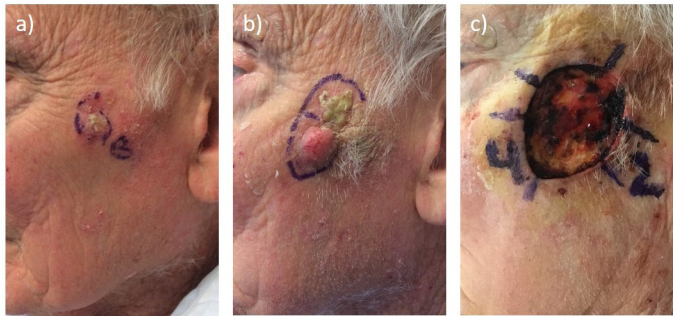
Non-melanoma skin cancers (NMSCs) are one of the most common type of cancer worldwide. When diagnosed early, basal cell and squamous cell carcinomas (BCC and SCC, respectively) are easily treated with local destruction or surgical excision. However, delay in detection or treatment can result in NMSCs becoming locally destructive, invasive and even metastatic. SCC in situ (SCCis, also known as Bowen or Bowen's disease) is a superficial form of SCC in which cancerous cells have not invaded through the full-thickness epidermis. The presence of atypical basaloid cells is associated with progression of pre-cancerous skin lesions to invasive SCC.[1]

There is a reported 3%–5% rate of SCCis progression to invasive SCC;[2] however, occult invasion of SCCis has been reported in as many as 10% of cancers subsequently removed by surgical excision or Mohs micrographic surgery (MMS).[3] Due to sampling bias, it has been reported that 31% of SCCis diagnosed on biopsy can have a component of invasive SCC which is discovered on the final pathology of the surgically excised specimen.[4] In this report, we describe a case of a rapidly progressive SCCis to invasive SCC with perineural involvement resulting in a therapeutic and diagnostic conundrum.

CASE

A 91-year-old man with an extensive medical history including multiple NMSCs, colon cancer, severe heart disease requiring a pacemaker, and multiple orthopedic fractures secondary to osteoporosis presented to clinic with a biopsy-proven SCCis with adnexal extension on the left zygoma. The patient was subsequently scheduled for MMS, however suffered a hip fracture requiring admission to a rehabilitation facility for eight weeks. The patient was offered radiotherapy, however refused, and MMS was scheduled upon patient's discharge from the rehabilitation center. The patient underwent MMS 10 weeks after initial diagnosis of the SCCis.

FIGURE 1. A case of a 91-year-old man with a (a) SCCis at initial biopsy, (b) SCC with perineural invasion at MMS 10 weeks later, and (c) the surgical defect after two stages of MMS. Although the tumor extended deep to the surgical defect, the patient ultimately decided to discontinue treatment and the area was closed with a graft performed by head and neck surgical oncology.



By this time of surgery, the tumor had significantly increased in size to clinically measure 4.7 x 2.3 cm. First layer histology revealed an aggressive, well-differentiated SCC extending deep into fat with perineural involvement. A second layer was taken; given the extensive involvement of the deep tissue, it was decided to stop MMS, consult head and neck surgical oncology, and leave the current surgical defect open, which measured almost 6 cm.

Upon workup, computed tomography (CT) of the head and neck revealed no underlying bony defects or evidence of regional metastatic disease, and although the CT of the chest demonstrated granulomatous disease, there was no evidence of metastatic disease either. Head and neck surgical oncology had a long discussion with the patient and his wife regarding further management of the SCC – watchful waiting, re-excision under general anesthesia with cardiology clearance, or radiotherapy. Given his age, comorbidities, and further risks associated with continued treatment, the patient opted for closure of the surgical site with a delayed skin graft and watchful waiting.

Three months after MMS, the patient presented to his primary care doctor with a well-healed graft site over the left cheek. No local recurrence of the SCC was noted at this time. The patient did not demonstrate evidence of metastatic disease to regional lymph nodes.

DISCUSSION

SCCs arise secondary to clonal expansion of keratinocytes harboring ultraviolet-induced DNA mutations, specifically the *TP53* gene. Further "hits" to keratinocyte DNA affect genes important for cell proliferation, adhesion, and migration causing locally invasive (perineural and/or perivascular), as well as possible metastatic disease. SCCis is an early, superficial carcinoma that can be treated using a multitude of techniques including liquid nitrogen, topical chemotherapeutics, curettage with or without electrodessication, photodynamic therapy, local radiation, laser therapy, and excision. However, with invasion, therapeutic options become limited – depending on the anatomic location, medical practitioners will often favor surgical techniques including wide local excision or Mohs micrographic surgery.[2]

Progression from SCCis to invasive SCC is relatively rare, with a reported 3%–5% conversion rate.[2] Mutations in key oncogenes or tumor suppressor genes may have resulted in the rapid progression of our tumor. Future advancements in whole genome sequencing may allow for characterization of the initial SCCis lesion versus the subsequent SCC to reveal specific DNA mutations associated with an increased risk of invasion and perineural involvement. Given recent developments in molecular characterization of melanomas in the outpatient setting, it is possible that sequencing of NMSCs is right around the corner. It is also possible that sampling bias during the initial biopsy may have contributed to misdiagnosis.[4]

As authors, we feel that this case is important to present to the dermatologic community, as it embodies the therapeutic and diagnostic challenges dermatologic surgeons encounter when faced with an aggressive, invasive carcinoma. Given our tumor's size on presentation for MMS, perineural extension and patient comorbities, this aggressive SCC proved a therapeutic challenge requiring a multidisciplinary approach with input from ENT, head and neck surgical oncology, and radiology. Although ultimately it was decided to discontinue further treatment and close the surgical defect with a graft, in other cases where patients are younger or have less comorbid disease, additional therapy with surgery and/or radiation may be warranted for locally invasive SCC.

DISCLOSURES

The authors received no funding for this research.
The authors have no relevant conflicts of interest to disclose.

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