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Successful treatment of recurrent advanced cutaneous squamous cell carcinoma with cemiplimab

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Abstract

A 90-year-old man presented for evaluation of an incompletely excised squamous cell carcinoma above the right brow, with pathology demonstrating tumor extending to resection margins with perineural invasion. A cord of tumor was noted to extend past the orbital rim and towards the posterior orbit. Mohs excision versus coordinated resection and reconstruction with colleagues in the head and neck surgery and craniofacial plastic surgery departments were considered. Multidisciplinary consensus was to proceed with radical resection in the operating room followed by adjuvant radiation therapy. One year later, the patient presented to our Mohs unit with a 3cm eroded multinodular plaque. Following an in-depth discussion regarding the options of further surgery versus systemic treatment, the patient and his family opted to pursue consultation with a medical oncology consultant to discuss restaging and potential systemic therapy. A PET scan with concurrent CT revealed a hypermetabolic right temporal scalp mass without evidence of bony invasion or extension into the nodal basin. Immunotherapy with cemiplimab was started at a dose of 350mg IV every three weeks. After 7 cycles, the patient demonstrated complete clinical resolution with a repeat PET scan showing interval near resolution of abnormal metabolic activity.

Keywords: cutaneous squamous cell carcinoma, cemiplimab, immunotherapy

Introduction

With an estimated annual mortality ranging from 3,900 to 8,700 patients a year, cutaneous squamous cell carcinoma accounts for approximately 20% of all skin cancer related deaths in the United States [1]. In most cases, early stage disease can be cured by surgery. However, a small percentage of patients go on to develop advanced disease, no longer amicable to curative surgery or radiation. Cutaneous squamous cell carcinoma not amenable to surgery has historically been difficult to treat with a dismal overall survival of only 10.9 months [2]. Herein, we report a patient with recurrent and locally advanced cutaneous squamous cell carcinoma with a dramatic clinical and radiologic response to cemiplimab.

Case Synopsis

A 90-year-old man presented for evaluation of an incompletely excised squamous cell carcinoma above the right brow. Squamous cell carcinoma had been treated in this area with wide local excision (WLE) by his dermatologist three years prior to presentation. Approximately one month prior to presentation, the patient had undergone a second WLE by his dermatologist, with pathology demonstrating tumor extending to resection margins with perineural invasion (**Figure 1**). Incidentally, the patient had experienced a traumatic event to the right eye in the 1960s requiring enucleation.

At the time of presentation, a cord of tumor was noted to extend past the orbital rim and towards the posterior orbit. Mohs excision versus coordinated resection and reconstruction with colleagues in head and neck surgery and craniofacial plastic surgery were considered. Multidisciplinary consensus was to proceed with radical resection in the operating room

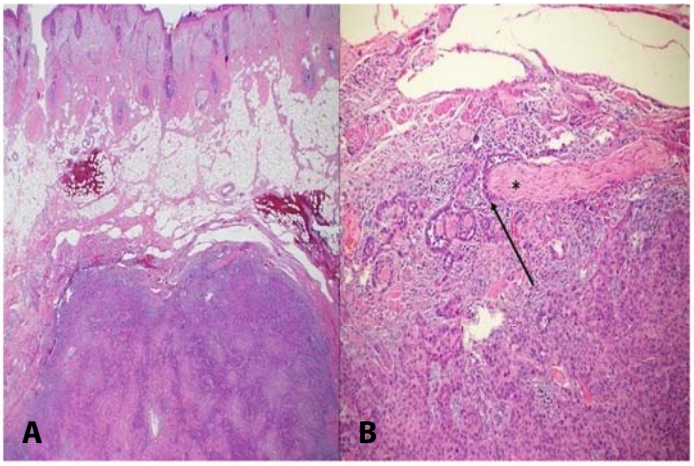

Figure 1. ***A)*** *At low power, large nodular aggregate nests and lobules of squamous cell carcinoma are visible within the subcutaneous tissue.* ***B)*** *At higher power, perineural tumor infiltration (arrow) is noted in relation to a 0.21mm caliber cutaneous nerve (*). H&E,* ***A)*** *10×,* ***B)*** *40×.*

followed by adjuvant radiation therapy. The patient tolerated treatment well, with only a small focus of exposed bone along the superior orbital rim at follow up. This was believed to be the sequelae of radiation treatment.

One year later, the patient presented to our cutaneous oncology unit with a 3cm eroded multinodular plaque, fixed to the underlying tissues on the right temple and temporal scalp (**Figure 2A**). Following an in-depth discussion regarding the options of further surgery versus systemic treatment, the patient and his family opted to pursue consultation with a medical oncology consultant to discuss restaging and potential systemic therapy.

A PET scan with concurrent CT revealed a hypermetabolic right temporal scalp mass without

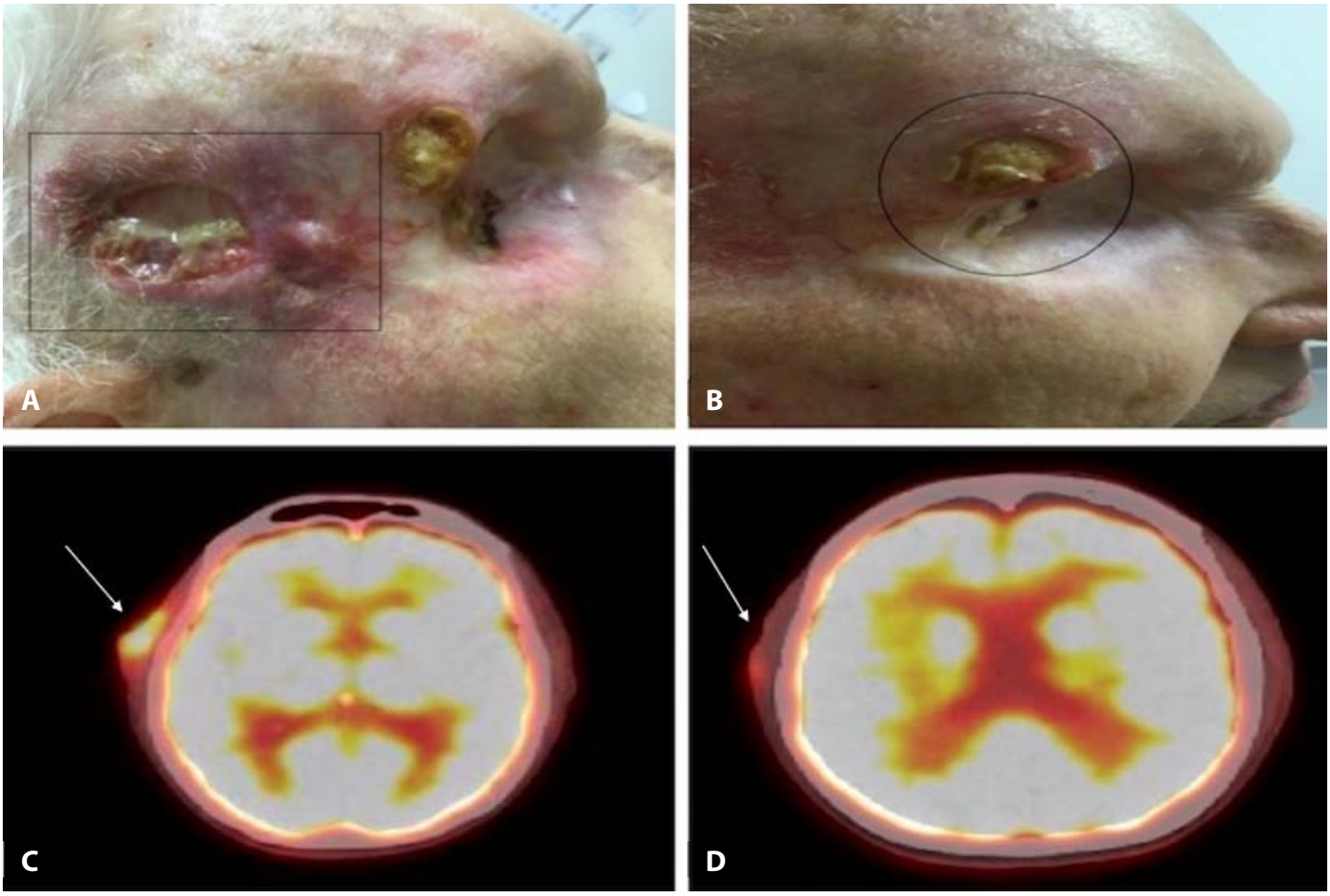

Figure 2. ***A)*** *Large 3cm eroded multinodular plaque with deep tumor fixation clinically (rectangle).* ***B)*** *Complete clinical resolution following 7 cycles of cemiplimab. Of note, the crusted plaque on the right lateral orbit from previous eye was desiccated bone related to previous radiation therapy and not bony invasion at this site (circled).* ***C)*** *Initial PET scan showing a hypermetabolic right temporal scalp mass.* ***D)*** *Repeat PET scan showing interval near resolution of abnormal metabolic activity demonstrating radiologic evidence of a positive response to therapy.*

evidence of bony invasion or extension into the nodal basin (**Figure 2C)**. Per the 8th edition of the American Joint Committee on Cancer (AJCC) his tumor was staged as T3N0M0 [3]. Utilizing the Brigham and Women's Hospital (BWH) alternative staging, his tumor was categorized as stage T2b with multiple high-risk features including tumor diameter ≥2cm and perineural invasion greater than 0.1mm [4]. Immunotherapy with cemiplimab was started at a dose of 350mg IV every three week. After 7 cycles, the patient demonstrated complete clinical resolution (**Figure 2B)** with a repeat PET scan showing interval near resolution of abnormal metabolic activity (**Figure 2D)**.

Case Discussion

Advanced, surgically unresectable squamous cell carcinoma can be particularly difficult to treat with a recent retrospective analysis showing only a 20-30% response to all classic therapeutic regimens including chemotherapy, radiation, and first generation immune therapeutic agents such as cetuximab [2]. In September 2018, the U.S. Food and Drug Administration approved cemiplimab, a novel high affinity, fully human monoclonal antibody, for the treatment of both metastatic and locally aggressive cutaneous squamous cell carcinoma. This approval followed the results of a pivotal phase 1 cohort expansion and phase 2 clinical trial that showed an impressive 50 % and 47% response rate for unresectable advanced and metastatic cutaneous squamous cell, respectively. The study also showed durable responses exceeding 6 months in more than 50% of the study patients and an estimated probability of progression-free survival at 12 months of 53% and overall predicted survival at 12 months of 81% [1].

The programmed cell death protein 1, commonly referred to as the PD1 receptor is found on T cells. It binds to its ligands (PDL1 or PDL2), an interaction that results in the deactivation of T cells, thereby reducing the host's anti-tumor immune surveillance. Increased PD1 and PDL1 expression levels have been associated with high-risk cutaneous squamous cell carcinomas, in particular those noted to have perineural invasion as well as tumors in the organ transplant population [6]. The PD1 inhibitors are a more recent addition to a growing list of immunotherapeutic agents, with several other PD1 inhibitors such as nivolumab and pembrolizumab already approved for the treatment of other malignancies such as melanoma, non-small cell lung cancer, renal cell carcinoma, and several other solid organ and hematologic malignancies [7].These agents work by binding PD1 on activated immune cells to disrupt the PD1 interaction with its ligands, thereby attenuating the inhibitory signals and augmenting the host antitumor response [7].

Conclusion

With a variable clinical presentation and lack of standardized guidelines, the management of advanced locally aggressive cutaneous squamous cell carcinoma remains clinically challenging [5]. Immunotherapy with cemiplimab, a recently approved PD1 inhibitor, is an important addition to the cutaneous oncology armamentarium that may be considered in patients with advanced disease not amenable to surgery. Our patient is of particular interest as to our knowledge, there have been no reports of advanced recurrent cutaneous squamous cell carcinoma treated successfully with cemiplimab since its approval by the FDA.

Potential conflicts of interest

The authors declare no conflicts of interests.

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