CASE REPORT

Intravascular squamous cell carcinoma treated with cemiplimab

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INTRODUCTION
The management of patients with high risk of cutaneous squamous cell carcinoma (cSCC) is an emerging field of focus in dermatology. Despite standard treatment options, including Mohs micrographic surgery with or without adjuvant radiation treatment, some locally advanced or metastatic tumors are not amenable to surgery or radiation alone.1 Herein, we present a rare case of intravascular cSCC, which showed a tremendous response to cemiplimab. In the future, standard treatment options may more widely include cemiplimab for patients with inoperable cSCC or those who have substantial physical defects due to surgery.

CASE REPORT
A 64-year-old man presented for the evaluation of a purple area on his left cheek. The lesion appeared as a spot 3 years ago, which had grown to cover the entire cheek (Fig 1, A). There was no associated pain with the lesion, just a sense of fullness and tingling behind the ear. The patient denied experiencing fevers, chills, weight loss, or lymphadenopathy. The patient's past medical history was significant for squamous cell carcinoma (SCC) on the left temple 5 years ago, treated with excision and radiation. We were unable to review the pathology for clear margins because the procedure was performed at an outside institution.

Upon examination, an ill-defined, purple, bruise-like plaque associated with some fullness was present on the left cheek (Fig 1, A). The patient initially presented to a family medicine physician, who obtained a superficial shave biopsy (Fig 1, B), which led to the condition being misdiagnosed as basal cell carcinoma. Given the clinicopathologic disconnect, the patient was referred to the dermatology department, where several punch biopsies of the lesion were performed (Fig 2, A and B).

Microscopic examination of the punch biopsies at a low power (Fig 2, A) revealed some sparse perivascular and lymphohistiocytic infiltrate. Higher-power examination exhibited a collection of pleomorphic and hyperchromatic cells confined to the vessels. Multiple punch biopsies showed the lack of dermal or epidermal involvement. The staining of microscopic images yielded positive results for p40 antibody, consistent with SCC (Fig 2, B). It was concluded that the intravascular SCC in the initial shave biopsy result (Fig 1, B) was likely mistaken for the islands of basal cell carcinoma, with retraction.

A positron emission tomography/computed tomography scan was performed, which revealed no primary lesion and the absence of the facial nerve and parotid gland involvement (Fig 3, A). Additionally, the cheek was not F-fluorodeoxyglucose–avid.

A multidisciplinary tumor board recommended treatment with cemiplimab. After 10 months of...
treatment with cemiplimab, without any adverse event (Fig 3, B), there was clinical resolution of the lesion, with improvement in the sense of fullness and tingling behind the ear and 4 scouting punch biopsies showing histologic resolution of the carcinoma.

**DISCUSSION**

cSCC is the second most common skin cancer after basal cell carcinoma. Cases in the United States currently exceed 700,000 per year, and there is a 10% lifetime risk of the development of SCC in these cases. It typically presents as an ulcerative, red lesion with scales. cSCC has a recurrence and metastatic rate of 8% and 5%, respectively. Greater than 95% of patients can be treated with surgical procedures. However, some patients have inoperable tumors because of metastasis or tumor progression and are no longer amenable to the standard treatment. Although intravascular invasion has been reported to be associated with squamous cell carcinoma, to our knowledge, this is the first case of a purely intravascular recurrence, likely due to the patient’s previous SCC of the left temple.

Immunotherapy with cemiplimab received the United States Food and Drug Administration’s approval in 2018 for locally advanced and metastatic cSCCs. Cemiplimab is an immunoglobulin-G monoclonal antibody that binds to the programmed cell death protein 1 receptor on T cells, preventing T-cell inactivation by tumor cell receptor ligands programmed death-ligand 1and programmed death-ligand 2.
death-ligand 2. Without the inactivation by tumor cells, T cells can induce the apoptosis of tumor cells. Although other programmed cell death protein 1 monoclonal antibodies exist, cemiplimab became the first approved antibody for cSCC. The approval by the United States Food and Drug Administration for this drug was based on a trial that included 108 patients with advanced cSCC. The overall response rate was 47% for those with metastatic cSCC and 49% for those with locally advanced cSCC, with 61% of the responses durable for 6 months or greater. Given the high response rates seen in unresectable or metastatic cSCC, there are clinical trials ongoing to evaluate the role of neoadjuvant cemiplimab for resectable cSCC.

This case highlights an unusual presentation of intravascular SCC and shows that superficial biopsies may be mistaken for basal cell carcinoma. This rare case of intravascular cSCC was successfully treated with cemiplimab monotherapy.

Conflicts of interest
Dr Durkin serves on the speaker bureau for Sanofi-Genzyme. Sanofi-Genzyme had no role in the writing or editing of this manuscript. Dr Yilmaz and Author Rose have no conflicts of interest to declare.

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