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Single Case

### Nivolumab for Metastatic Cutaneous Squamous Cell Carcinoma

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#### Keywords

Nivolumab · PD-1 checkpoint inhibitor · Immunotherapy · Squamous cell carcinoma

#### Abstract

Nivolumab is a programmed death receptor 1 (PD-1) inhibitor. It is part of a group of drugs known as immune checkpoint blockers, which enable potent and durable T-cell responses against several tumors. We report the case of a patient with a metastatic squamous cell carcinoma, who is being treated with nivolumab. This patient achieved a complete response and continues treatment without progression signs, supporting the notion that PD-1 inhibition can induce long-term remission and is well tolerated in this type of patient.

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#### Introduction

Cutaneous squamous cell carcinoma (cSCC) is a frequent cancer type, but only 3–5% of all patients with this tumor develop extensive disease [1].

Nivolumab and pembrolizumab are programmed death receptor 1 (PD-1) inhibitors approved for the treatment of advanced melanoma, squamous cell carcinoma of the lung, and other types of cancer. They are part of a group of drugs known as immune checkpoint blockers, which enable potent and durable T-cell responses against several tumors. It is believed



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that cSCC has the clinical and molecular hallmarks of a tumor that is likely to be responsive to systemic immune therapy [2]. To our knowledge, very few patients have been reported so far confirming this fact in the clinical scenario [1, 3–5].

#### **Case Report**

A 77-year-old man presented in February 2017 suffering from a 24-mm skin lesion located in the scalp (Fig. 1). Regarding his previous medical history, he had been diagnosed with bladder cancer which was surgically treated in 2015. After the first evaluation, the scalp lesion was excised. The anatomopathological report described a poorly differentiated squamous cell carcinoma, with a depth of 7 mm. No perineural, lymphatic, or vascular involvement was reported, and resection margins were negative.

Ten months later the patient presented with bilateral neck lymph node enlargement. Bilateral neck SCC lymph node metastases were confirmed by CT and FNA. A bilateral neck lymph node dissection was performed, labeling the tumor as stage IV (T3N2cM0).

Following a multidisciplinary approach, the patient was also treated with chemotherapy with cisplatin and cervical radiation. Five months later, in March 2018, several infiltrated and ulcerated skin lesions appeared in the anterior thorax and were confirmed as skin metastases (Fig. 2). The patient was treated unsuccessfully with intravenous methotrexate.

In May 2018 a right parotid node was detected in a CT, confirmed as SCC invasion by FNA. Accordingly, nivolumab was started at 3 mg/kg/day every 2 weeks. The response was assessed after three cycles, parotid metastasis resolved in 5 months, and skin lesions improved quickly. In April 2019, the skin metastases were almost cured (Fig. 3). Ten months after the first dose of nivolumab, all target lesions have disappeared, and the patient continues the treatment. Drug tolerance has been good, since the patient has only experienced mild diarrhea and canker sores.

#### **Discussion and Conclusion**

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At present, advanced or metastatic cSCC portend a poor prognosis, with few available treatment options. Most of the literature is based on platinum therapy or cetuximab, with low overall response rates and high toxicity [6].

To date, only a very few papers have been published focusing on PD-1 inhibition for the treatment of advanced or metastatic cSCC. Earlier reports support the notion that this inhibition can induce long-term remission and is well tolerated in this type of patient [1, 3-5]. Consistently, in September 2018 the FDA approved cemiplimab, another anti-PD-1 antibody, for the treatment of advanced and metastatic cSCC. This approval was based on phase I and phase II studies with overall response rates around 50% [2].

We report a patient suffering from cSCC with parotid and skin metastases, who developed a complete response to nivolumab, which supports the abovementioned, without relevant toxicity. The anti-PD-1 antibody nivolumab is already part of the therapeutic armamentarium, facilitating its use in clinical practice. Probably, in the near future, PD-1 inhibitors will change the challenging management of disseminated cSCC. Several clinical trials are ongoing to better define the role of PD-1 inhibitors in advanced or metastatic cSCC.



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#### **Statement of Ethics**

The patient gave his written informed consent to publish his case, including publication of images. The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

#### **Disclosure Statement**

The authors have no conflicts of interest to declare.

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#### **Author Contributions**

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship of the manuscript, take responsibility for the integrity of the work as a whole, and gave final approval of the version to be published.

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Fig. 1. A 24-mm firm, hyperkeratotic, and ulcerated tumor in the scalp.



Fig. 2. Infiltrated and ulcerated tumors in the anterior thorax.

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Fig. 3. Superficial erosion in the anterior thorax.

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