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Single Case

Advanced Squamous Cell Carcinoma Developed on Chronic Hidradenitis Suppurativa, Successfully Treated with Cemiplimab: A Case Report

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Keywords
Squamous cell carcinoma · Hidradenitis suppurativa · Cemiplimab

Abstract
Hidradenitis suppurativa (HS) is an inflammatory skin disease showing a chronic-remitting course. It has been rarely reported that long-term inflammation in HS could lead to serious complications like cutaneous squamous cell carcinoma. Cemiplimab is a fully human antibody immunotherapy that inhibits programmed cell death protein-1, approved for the treatment of locally advanced squamous cell carcinoma, or metastatic squamous cell carcinoma, in patients not eligible for curative surgery or radiotherapy. Herein, we report the case of a 56-year-old patient developing an invasive SCC on longstanding and unresponsive HS lesions successfully treated with cemiplimab.

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Introduction

Hidradenitis suppurativa (HS) is an inflammatory skin disease showing a chronic-remitting course [1]. Even if HS pathogenesis is still unproven, many studies hypothesized genetic background triggered by various environmental factors [1]. Typical complications linked with longstanding HS include pustules, fistulas, or scarring [1–4]. It has been rarely reported that long-term inflammation in HS could lead to serious complications like cutaneous squamous cell carcinoma (CSCC) [1]. However, despite the reports of SCC occurring on

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pre-existing HS lesions, the link between HS and SCC has yet to be studied and integrated [2, 5–7]. Cemiplimab is a fully human antibody immunotherapy that inhibits programmed cell death protein-1, resulting in the stimulation of anticancer response. It received the US FDA and EMA approval for the treatment of locally advanced CSCC or metastatic CSCC in patients not eligible for curative surgery or radiotherapy [7]. Herein, we report the case of a 56-year-old patient developing an invasive SCC on longstanding and unresponsive HS lesions successfully treated with cemiplimab.

Case Report

A 56-year-old Caucasian male referred at our outpatient clinic with a 6-year history of chronic remittent HS characterized by painful nodules and abscess of the inguinal, perineal, and scrotal regions. His medical history was negative. Previous HS treatments included several cycles of systemic antibiotics and intralesional corticosteroids, which resulted in only temporary improvements. Moreover, he referred that due to the appearance of new scrotal painful necrotic lesions, he had undergone diagnostic skin biopsy of the scrotal region in which histological examination was diagnostic for hypertrophic lichen. Hence, he had been treated with systemic corticosteroid showing only partial clinical improvements. When he came at our observation, dermatological examination revealed the presence of voluminous ulcerated inflammatory lesions extending from the scrotum to the orifice of the anal canal (Fig. 1a). The ulcerated area showed necrotic background with voluminous nodular lesions. Skin ultrasound examination revealed diffuse thickening and inhomogeneous hyper-echogenicity of the scrotal bursae, and the presence of a 37 × 40 mm hyper-echogenic formation with indistinct margins, which was compatible with a chronic phlogistic process. However, due to long-lasting and unresponsiveness to previous treatments, and in the suspect of malignancy, we performed an MRI, and CT scan of the lower abdomen, which showed hyper-vascularized skin-subcutaneous thickening of the scrotal bursa and perianal region, a diffuse subcutaneous imbibition, and bilateral reactive lymphadenopathies. A perilesional biopsy skin, at the bottom of the ulcerated area, was diagnostic for well-differentiated (G1) initially invasive SCC. Due to the inoperability of the lesion, cemiplimab treatment (350 mg every 3 weeks intravenously) was started. After 18 weeks, the patient showed a huge improvement of the lesions (Fig. 1b), resulting eligible for surgical treatment.

Discussion

Even if the exact pathogenesis of HS is still unknown, recent studies have proposed that it may be caused by the combination of both hereditary and environmental factors [8]. A dysregulation in T cells' cytokine production has been found to play a key role in HS. Particularly, HS skin has shown an over-expression of mRNA levels of interferon and interleukin-(IL)-17, which have been linked to a higher T-helper activity [9–11]. IL-17 is essential for TGF-induced inflammation in premalignant skin lesions. Moreover, TGF is also required for Th17 cells to differentiate from naïve T cells, and higher TGF levels in the skin are linked to increased Th17 cell infiltration in premalignant lesions [10, 11]. In SCC progression, IL-17 production is suppressed and the number of invading Th17 cells reduces [9]. Mutagen-induced SCC causes higher amounts of secreted TGF in the tumor microenvironment, accelerating tumor progression by causing the establishment and progression of premalignant lesions, as well as metastasis. SCC is a promising immunotherapy target because it has a high mutational load, which is one of the determinants of an immune checkpoint blockade

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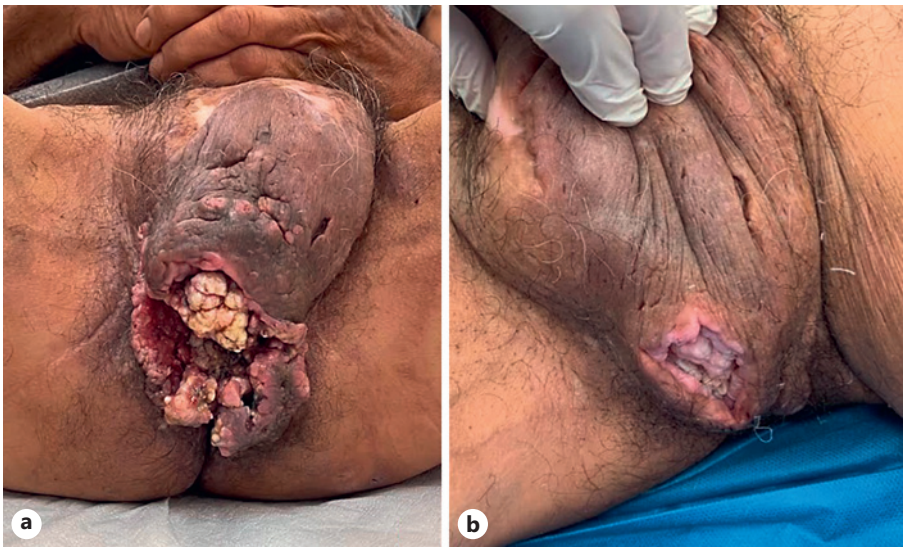

Fig. 1. Ulcerated squamous cell carcinoma of the scrotum developed on chronic hidradenitis suppurativa, before (**a**) and after 18 weeks of cemiplimab treatment (**b**).

response [9]. Because painful and inflammatory HS lesions can be difficult to differentiate from malignant development, diagnosing SCC in chronic HS still represents a challenge in dermatology [8]. Hence, a skin biopsy is frequently required to better define these conditions [12, 13].

Notch is a key protein for normal follicle growth and immune response modulation; thus, genetic or acquired abnormalities in notch pathway may play a role in HS pathogenesis [13]. Indeed, the hyper-activation of notch receptors, physiologically expressed by epidermal keratinocytes, may result in aberrant hair development, epidermal cysts, and finally follicle rupture and an inflammatory immune response [14]. Notch has also been demonstrated to act as a tumor suppressor in skin cancers other than melanoma. TNF-alpha, IL-1, and IL-12/23 inhibitors have all been studied as promising treatments in HS management, showing contrasting clinical outcomes [8]. Because there have been reports in the literature of SCC occurring following therapy with infliximab, more data are needed to determine the influence of immunosuppressants on the transformation of HS to SCC [15]. Most of CSCC can be treated with surgery alone; however, some patients may need adjuvant therapies. Around 10% of cases progress to advanced CSCC [15], in which surgery or radiotherapy is linked with severe patients' morbidity [15]. Cemiplimab was the first FDA treatment approved for advanced CSCC [16]. Traditional chemotherapy drugs (bleomycin, doxorubicin, and platinum-based drugs) have shown limited success and high toxicity. Cemiplimab, a fully human IgG4 monoclonal antibody, acts by tying up with programmed cell death protein-1 receptor, preventing it from the interaction with PD-L1, resulting in an increased immune system's anticancer activity, with direct tumor cell death by upregulated cytotoxic T cells [16]. There were no authorized systemic treatments for advanced CSCC previously. Cemiplimab was found to be effective and well tolerated in patients with advanced CSCC, showing a response rate of 50% [16]. In a phase II study, 47% of patients with metastatic CSCC improved after treatment, showing a long-term disease control in 61% of patients [16]. Due to promising results reported with immunotherapy, it may become one of the most important treatment choices in the management of advanced CSCC [16]. In our case, cemiplimab was started as first-line treatment due to ineligibility of the patient to surgery. Our results confirmed the promising results of cemiplimab even in advanced CSCC arising on areas chronically affected

by HS. However, more studies are needed to confirm our data and to better clarify the possible key role of cemiplimab in the management of these patients.

Statement of Ethics

All procedures adopted in the present study were in respect to the ethical standards in the World Medical Association Declaration of Helsinki. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Ethical approval was not required for this study in accordance with local/national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Angelo Ruggiero, Wanda Lauro, Chiara Miano, Alessia Villani, Gabriella Fabbrocini, and Claudio Marasca made substantial contributions to the conception or design of the work, or acquisition, analysis, and interpretation of data for the work, gave the final approval of the version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; Angelo Ruggiero, Wanda Lauro, and Chiara Miano: drafting and revising the work critically for important intellectual content.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Ruggiero A, Fabbrocini G, Megna M, Monfrecola G, Marasca C. Hidradenitis suppurativa in a patient affected by mayer-rokitansky-küster-hauser syndrome: insight into the role of hormones in HS. Skin Appendage Disord. 2020 Nov;6(6):366–9.
2 Lee SJ, Lim JM, Lee SH, Chung KY, Roh MR. Invasive cutaneous squamous cell carcinoma arising from chronic hidradenitis suppurativa: a case report of treatment by slow mohs micrographic surgery. Ann Dermatol. 2021; 33(1):68–72.
3 Megna M, Ruggiero A, Di Guida A, Patrì A, Fabbrocini G, Marasca C. Ixekizumab: an efficacious treatment for both psoriasis and hidradenitis suppurativa. Dermatol Ther. 2020 Jul;33(4):e13756.
4 Ruggiero A, Fabbrocini G, Cinelli E, Megna M. Efficacy and safety of guselkumab in psoriasis patients who failed ustekinumab and/or anti-interleukin-17 treatment: a real-life 52-week retrospective study. Dermatol Ther. 2021 Jan;34(1):e14673.

5 Napolitano M, Patruno C, Ruggiero A, Nocerino M, Fabbrocini G. Safety of dupilumab in atopic patients during COVID-19 outbreak. J Dermatolog Treat. 2022 Feb;33(1):600–1.
6 Villani A, Megna M, Scalvenzi M, Fabbrocini G, Ruggiero A. Teledermatology and chronic skin diseases: real life experience in a Southern Italian Dermatologic Centre. Dermatol Ther. 2020 Nov;33(6):e13839. Epub 2020 Jul 7.
7 Chapman S, Delgadillo III D, Barber C, Khachemoune A. Cutaneous squamous cell carcinoma complicating hidradenitis suppurativa: a review of the prevalence, pathogenesis, and treatment of this dreaded complication. Acta Dermatovenerol Alp Pannonica Adriat. 2018 Mar;27(1):25–8.
8 Ruggiero A, Martora F, Picone V, Marano L, Fabbrocini G, Marasca C. Paradoxical hidradenitis suppurativa during biologic therapy, an emerging challenge: a systematic review. Biomedicines. 2022 Feb 16;10(2):455.
9 Strait AA, Wang XJ. The role of transforming growth factor-beta in immune suppression and chronic inflammation of squamous cell carcinomas. Mol Carcinog. 2020 Jul;59(7):745–53.
10 Marasca C, Ruggiero A, Megna M, Annunziata MC, Fabbrocini G. Biologics for patients affected by hidradenitis suppurativa in the COVID-19 era: data from a referral center of Southern Italy. J Dermatolog Treat. 2022 Feb; 33(1):592.
11 Marasca C, Fornaro L, Martora F, Picone V, Fabbrocini G, Megna M. Onset of vitiligo in a psoriasis patient on ixekizumab. Dermatol Ther. 2021 Sep;34(5):e15102.
12 Wolk K, Warszawska K, Hoeflich C, Witte E, Schneider-Burrus S, Witte K, et al. Deficiency of IL-22 contributes to a chronic inflammatory disease: pathogenetic mechanisms in acne inversa. J Immunol. 2011 Jan 15;186(2): 1228–39.
13 Jourabchi N, Fischer AH, Cimino-Mathews A, Waters KM, Okoye GA. Squamous cell carcinoma complicating a chronic lesion of hidradenitis suppurativa: a case report and review of the literature. Int Wound J. 2017;14(2): 435–8.
14 Panelos J, Massi D. Emerging role of Notch signaling in epidermal differentiation and skin cancer. Cancer Biol Ther. 2009;8(21):1986–93.
15 Verdelli A, Antiga E, Bonciani D, Bonciolini V, Volpi W, Caproni M. A fatal case of hidradenitis suppurativa associated with sepsis and squamous cell carcinoma. Int J Dermatol. 2016;55(1):e52–3.
16 Ahmed SR, Petersen E, Patel R, Migden MR. Cemiplimab-rwlc as first and only treatment for advanced cutaneous squamous cell carcinoma. Expert Rev Clin Pharmacol. 2019 Oct;12(10):947–51.