Hair Loss in Patients Treated with Vismodegib: A Single-Center Retrospective Study

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Keywords

Alopecia · Hair loss · Vismodegib · Basal cell carcinoma · Skin cancer

Abstract

Locally advanced basal cell carcinoma had always represented a form of skin cancer which had been difficult to treat until the hedgehog inhibitor vismodegib was approved. This small molecule acts by inhibiting the hedgehog signaling pathway that plays a critical role in the process of tumorigenesis. Although several trials have demonstrated the high efficacy of this drug, different adverse events have been described. Muscle spasms, dysgeusia, weight loss, and alopecia are the adverse events most frequently reported. The objective of this study was to report the incidence of alopecia arising in patients treated with vismodegib, assessing its characteristics, grade of severity, and time of onset.

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Introduction

Basal cell carcinoma (BCC) is the most common type of skin cancer, accounting for 80% of non-melanoma skin cancers. Treatment choice depends on BCC clinical characteristics and patients' personal history, with surgery rep-

resenting the first-line treatment. However, a small subset of BCCs can progress to an advanced or, very rarely, to a metastatic state, posing a challenge for clinical management. Vismodegib, a hedgehog pathway inhibitor, was approved in 2012 for the treatment of advanced BCCs ineligible for surgery and/or radiotherapy [1, 2]. It acts by inhibiting the hedgehog signaling pathway that plays a critical role in the embryonic development and in the regulation of maintenance of various tissues, including muscle, hair, taste buds, and the reproductive system [3]. Although trials and clinical studies have demonstrated the high efficacy and safety of vismodegib, several adverse events (AEs) have also been reported. Muscle spasms, dysgeusia, weight loss, and alopecia are the reversible AEs most frequently described [4]. Our objective was to report the incidence of alopecia arising in patients treated with vismodegib, assessing its characteristics; grade of severity, using the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.0); and time of onset.

Materials and Methods

This retrospective study was conducted at one referral center for skin cancer diagnosis and management from November 2016 to February 2020. The approved dosage of vismodegib was 150 mg per day. For each patient, clinical and demographic variables were registered, whereas follow-up visits occurred every month, including AEs recording and therapeutic response assessment.

Fig. 1. **a** Diffuse hair loss in a 74-year-old man after 6 months of vismodegib treatment. **b** Diffuse hair loss with visible hair thinning in a 63-year-old woman after 7 months of vismodegib treatment.

Results

Seventy-four patients (52 males and 22 females) with a median age of 76.32 years were included in the study. Seventy-two patients had a locally advanced BCC and 2 patients had metastatic BCCs, all histologically confirmed. The median duration of treatment was 7.2 (range 1–18) months. Overall, 19 of 74 patients (25.7%) reported complete remission of the disease, 39 (52.7%) reported partial remission of the disease, and 16 patients (21.6%) discontinued treatment for major AEs. Alopecia was observed in 54 (male: 42; female: 12) of 74 patients (72.9%), resulting one of the AEs most frequently described with a median time of AE onset of 127.5 days. In particular, 11 patients (20%) experienced a severity of grade 1, 18 patients (33%) of grade 2, 17 patients (31%) of grade 3, 5 patients (9%) of grade 4, and 3 patients (7%) of grade 5. Regarding clinical findings, all 54 patients showed a diffuse pattern of hair loss, varying in extent. Moreover, 48 patients presented an involvement of >50% of the scalp area, and only 6 patients reported the involvement of smaller areas (<50% of the scalp). Hair loss was associated with hair thinning but did not follow the pattern of androgenetic alopecia (Fig. 1a, b). No scales, erythema, or itching was reported.

Discussion

In agreement with what has been previously reported, alopecia is one of the AEs most frequently observed in patients with advanced BCCs treated with vismodegib, usually occurring after the first 3 months of treatment with a

higher severity grade [5]. This AE is usually reversible after vismodegib discontinuation, and several strategies, such as the use of topical or oral minoxidil, could be used to reduce the diffuse hair loss, which usually impacts on patients' quality of life. In conclusion, this study provided important additional clinical data regarding alopecia as a related AE in patients treated with hedgehog inhibitors. Limitations of the study were the retrospective design and the lack of randomization. Further analysis on a larger sample size is needed to better characterize this AE.

Statement of Ethics

This article is based on previously conducted studies and does not contain human participants or experiments involving animals performed by any of the authors. Ethics approval was not required.

Conflict of Interest Statement

Alessia Villani, Gabriella Fabbrocini, Claudia Costa, and Massimiliano Scalvenzi have nothing to disclose.

Funding Sources

No funding or sponsorship was received for this study or the publication of this article.

Author Contributions

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

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