

BRIEF ARTICLE

Alopecia Areata: Hair and Nail Findings in a Patient Undergoing Talquetamab Therapy for Multiple Myeloma

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ABSTRACT

Redirecting T cell-mediated killing of GPRC5D-expressing myeloma cells, talquetamab is a novel chemotherapeutic humanized bispecific antibody increasingly used for treatment of relapsed or refractory multiple myeloma. While skin-related adverse events, including nail disorders, were common in the initial clinical trials, hair pathology was not reported. We present a case of a 74-year-old female undergoing talquetamab therapy presenting with a one-year history of alopecic patches in addition to nail changes, glossitis, and keratoderma. Scalp punch biopsy revealed alopecia areata later found to be responsive to betamethasone dipropionate gel. This case highlights a spectrum of adverse cutaneous manifestations of talquetamab therapy likely secondary cross reactivity to GPRC5D-expressing keratinized structures. Deeper investigation is warranted to clarify the pathogenesis underlying these findings and optimal treatment modalities for this patient cohort undergoing talquetamab therapy.

INTRODUCTION

Emerging as a novel chemotherapeutic for treatment of relapsed or refractory (R/R) multiple myeloma (MM), talquetamab is a humanized bispecific antibody that targets G protein-coupled receptor family C group 5-member D (GPRC5D) and CD3, acting to redirect T cell-mediated killing of GPRC5D-expressing myeloma cells.¹ In a phase I study of two cohorts with either weekly or biweekly subcutaneous dosing regimens of talquetamab, 67% and 70% of subjects experienced skin-related adverse events.¹ Preliminary results from an additional phase I trial reported skin-related adverse events in

75% of treated patients, 18% of which were nail disorders.^{2,3} One recent report of a patient undergoing talquetamab therapy for R/R MM presented with acquired onychomadesis and palmoplantar keratoderma, a PubMed search of the English language literature using the terms “alopecia”, “hair”, and “talquetamab” revealed no prior cases of adverse events involving the hair.² We seek to highlight a case of alopecia areata with associated nail changes in a patient undergoing talquetamab therapy for R/R MM.

CASE



Figure 1. Nail findings of onychorrhexis, onycholysis, and trachyonychia in a patient undergoing talquetamab therapy.



Figure 2. Alopecia areata on the frontal (A) and vertex (B) scalp.

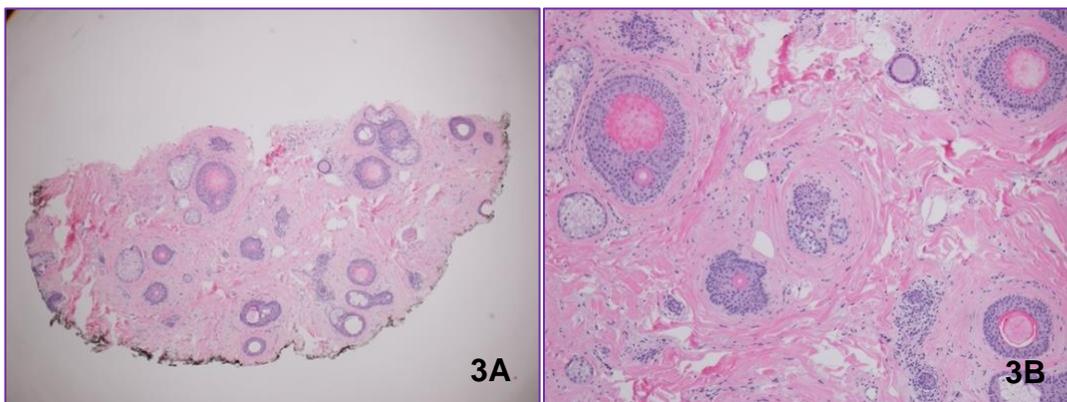


Figure 3. Low power horizontal section (A) and medium power (B) demonstrating follicular miniaturization and numerous catagen hair follicles with lymphocytic peribulbar inflammation around some of the bulbs.

A 74-year-old female presented to dermatology clinic for patchy loss of scalp hair and persistent nail changes. The patient first noted these concerns roughly one year prior to presentation, aligning with the initiation of talquetamab therapy for her R/R MM. She reported experiencing a total loss of her fingernails shortly after starting this therapy. After complete loss of her nails, regrowth was abnormal, with marked thinning and breakage of the nails. She also noted thickened skin of the hands and painful dermatitis of the distal fingertips.

Physical exam revealed, onychorrhexis, thinning of the nail plates, and longitudinal ridging consistent with trachyonychia of all nails of the bilateral hands (**Figure 1**). The patient's palmar skin was thickened with mild erythema and scale most pronounced at the distal digits. Examination of the oral cavity revealed a bright red tongue. Isolated patches of alopecia were observed on the frontal and vertex scalp, as well as loss of the eyelashes (**Figure 2**). Dermoscopy noted exclamation point hairs without white perifollicular cuffing or erythema.

A punch biopsy from the scalp demonstrated a reduced number of terminal anagen hair follicles with marked follicular miniaturization

keratoderma in a patient undergoing talquetamab therapy notes that GPRC5D is additionally thought to be expressed in Langerhans cells of palmoplantar skin.² Recently, a dose-escalation study administered GPRC5D-targeted chimeric antigen receptor (CAR) T-cell therapy to a cohort of patients and found toxic effects in hard keratinizing structures of the skin, manifesting as grade 1 nail changes and nail loss (65%) regardless of dosage, grade 1 rash (18%), and grade 1 dry mouth or dysgeusia (12%).⁵ The median time from infusion initiation to nail changes was 3.3

and numerous catagen hair follicles. A peribulbar lymphocytic inflammatory infiltrate was seen, consistent with the clinical impression of alopecia areata (**Figure 3**).

At 10 week follow up patient's keratoderma improved with betamethasone dipropionate ointment. Alopecia had started to respond to betamethasone dipropionate gel and intralesional triamcinolone at 5mg/ml to the affected areas was added with plans for further treatment at follow up.

DISCUSSION

In addition to its expression in malignant myeloma cells and plasma cells, GPRC5D is expressed in cells that produce hard-keratinized structures such as cortical cells of the hair shaft, the upper nail matrix and keratogenous zone of the nail, and the filiform papillae of the tongue.⁴ GPRC5D is expressed only during the mid to late anagen phase of the hair cycle.⁴ The disruption of hard keratinization by GPRC5D suggests a possible mechanism for skin appendage effects including keratoderma, glossitis, trachyonychia, and onychomadesis seen with this therapy.² A prior report of onychomadesis and palmoplantar

months, with spontaneous resolution of changes in 91% of patients.⁵ The propensity for therapies targeting this receptor family to trigger onychomadesis suggests acute injury to the nail. While the mechanism is unknown, as Naraya et al posit, targeting of GPRC5D in the differentiating cells of the nail matrix likely leads to nail matrix arrest.² Of note, the late-onset nail manifestations in our patient of trachyonychia and onychorrhexis are nail findings that are also commonly seen in alopecia areata.^{6,7}

While nail changes have been the most frequently reported cutaneous manifestation of talquetamab therapy, the development of alopecia areata in MM patients undergoing this therapy has not been reported. The hair follicle is regarded as an immune-privileged site, with increasing evidence demonstrating that a collapse in immune privilege is involved in the pathogenesis of autoimmune hair loss disorders.⁸ This breakdown in immunity may be associated with talquetamab's effect on GPRC5D resulting in cessation of nail and hair growth. Given consideration for the expression of GPRC5D in Langerhans cells of palmoplantar skin, it warrants further investigation for a pathogenic role of GPRC5D and talquetamab in antigen presenting cells within the hair follicle.²

Our case highlights the spectrum of adverse cutaneous manifestations of talquetamab therapy, including keratoderma, glossitis, nail dystrophy and the novel finding of alopecia areata. Further studies are needed to clarify the pathogenesis underlying these findings and optimal treatment modalities for this patient cohort undergoing talquetamab therapy for R/R MM.

Conflict of Interest Disclosures: None

Funding: None

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