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Follicular spiny hyperkeratosis induced by sorafenib

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ABSTRACT

Introduction: Follicular spiny hyperkeratosis is a rare dermatosis, usually related to multiple myeloma. Some cases associated with drug use have been reported.

Case Report: A 60-year-old male patient with a history of papillary thyroid cancer started treatment with sorafenib. Ten days later, he presented with a dermatosis affecting the scalp and forehead, characterized by thick interfollicular scaling and spiny hyperkeratosis. Dermoscopy revealed tubular scaling along the hair shaft. A skin biopsy was performed, revealing a spine of compact parakeratotic material, leading to the diagnosis of follicular spiny hyperkeratosis.

Conclusion: Follicular spiny hyperkeratosis can develop after exposure to sorafenib. Recognizing it allows for timely identification of causality and optimal individualized management.

Keywords: Follicular spicules, Follicular spiny hyperkeratosis, Sorafenib, Tyrosine-kinase inhibitors

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INTRODUCTION

Follicular spiny hyperkeratosis is a rare dermatosis characterized by small hyperkeratotic spicules in a follicular distribution [1]. Most cases have been associated with multiple myeloma, while some are secondary to the use of drugs, mainly B-Raf serine-threonine kinase (BRAF) inhibitors and cyclosporine [2]. Idiopathic cases have also been reported [3].

We present the case of a patient treated with sorafenib for papillary thyroid cancer who developed follicular spiny hyperkeratosis.

CASE REPORT

A 60-year-old male with a five-year history of systemic arterial hypertension, managed with losartan and hydrochlorothiazide, and benign prostatic hyperplasia, treated with tamsulosin and finasteride, was diagnosed in August 2023 with conventional papillary thyroid carcinoma with oxyphilic features, deemed unresectable. He subsequently received radiotherapy and systemic treatment with lenvatinib. In June 2024, treatment with sorafenib 800 mg per oral was initiated. Ten days later, he reported scalp pruritus associated with scaling, prompting a dermatology consultation.

On examination, a dermatosis localized to the head affecting the scalp and forehead was observed, characterized by thick inter and perifollicular scaling and spiny hyperkeratosis (Figures 1–3). Trichoscopy showed tubular scaling along the hair shaft (Figure 4). Suspecting a psoriasiform reaction to sorafenib, we performed a skin biopsy, which revealed a basket-weave stratum corneum with slight regular acanthosis, mild spongiosis, and lymphocyte exocytosis, a dilated follicle with a compact spiny/digitate follicular hyperorthokeratosis and

parakeratosis. There was a sparse superficial perivascular infiltrate of lymphocytes and some histiocytes, confirming the diagnosis of follicular spiny hyperkeratosis (Figure 5).

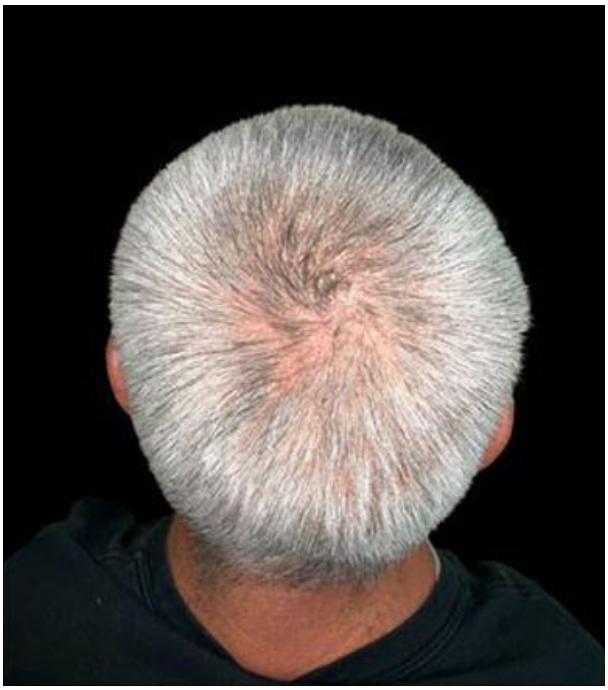

Figure 1: Thick and white scaling observed on the patient's scalp.

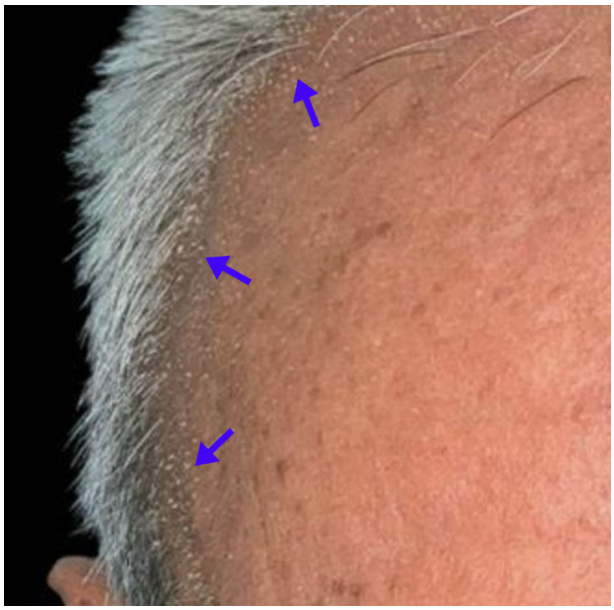

Figure 2: A close-up of the forehead showed spiny hyperkeratosis, represented as small white spines adhered to the skin (blue arrows).

DISCUSSION

Sorafenib is a multikinase inhibitor initially approved by the FDA for advanced renal cell carcinoma in 2006 [4]. It works by inhibiting vascular endothelial growth factor receptor (VEGFR) 1, 2, and 3, platelet-derived growth factor receptor, FMS-like tyrosine kinase 3, c-kit, and RAF-1, which are involved in tumor cell signaling,

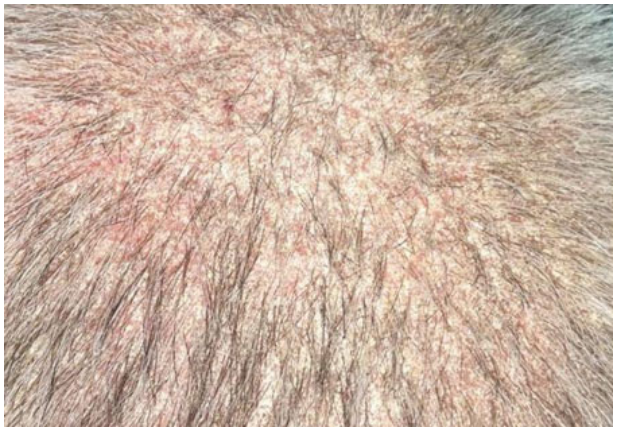

Figure 3: Close-up of the scalp characterized by thick white interfollicular and perifollicular scaling.

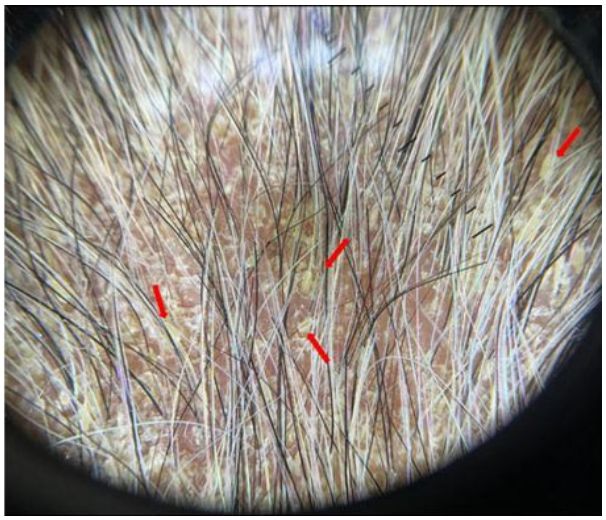

Figure 4: Trichoscopy image. Red arrows indicate tubular scaling along the hair shaft.

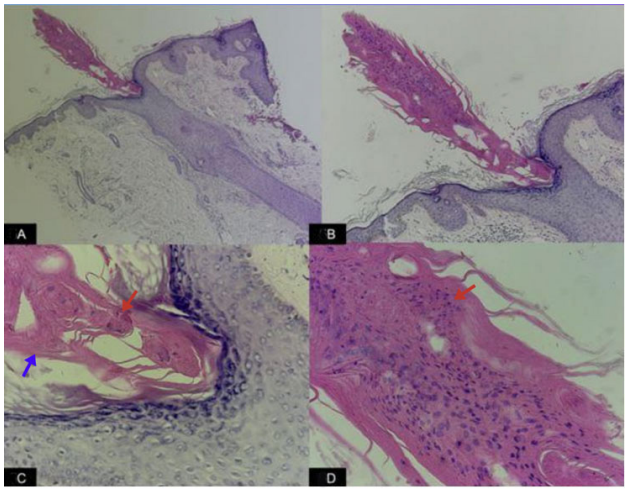

Figure 5: (A) Punch biopsy with basket-weave stratum corneum with slight regular acanthosis and a dilated follicle at the center, with a compact follicular hyperorthokeratosis. Discreet superficial perivascular infiltrate of lymphocytes in dermis. (B) Compact follicular parakeratotic material on a digitate disposition. (C) Infundibulum filled with compact keratin and nuclei (parakeratosis—red arrow and hyperorthokeratosis—blue arrow). (D) Nuclei retention in the keratin (parakeratosis—red arrow).

proliferation, angiogenesis, and apoptosis [5]. Cutaneous adverse effects occur in approximately 70% of cases. In 2010, Franck et al. reported the first association of follicular spiny hyperkeratosis with sorafenib use in 9 patients [3].

Follicular spiny hyperkeratosis, also known as hyperkeratotic spicules, filiform hyperkeratosis, parakeratotic horns, and follicular hyperkeratosis [3], is a rare benign skin reaction characterized by hyperkeratotic spicules on the head and trunk [6]. It is considered a rare but characteristic cutaneous manifestation of multiple myeloma [7]. To date, there are few reported cases associated with drug use, and the pathophysiological mechanism remains poorly understood. Angiogenesis is thought to play a role in follicular growth and size, and vascular endothelial growth factor (VEGF) increases keratinization, which explains why the inhibition of these mechanisms may lead to follicular spiny hyperkeratosis [3].

In the case of sorafenib, the development of follicular spiny hyperkeratosis has been reported to occur between 9 and 164 days after exposure. In our patient, the onset of lesions 10 days after starting sorafenib allowed us to establish causality more easily. Discontinuation of the drug is considered the best intervention for resolving the lesions; however, in some cases, dose reduction is sufficient [4], and the dermatosis is not currently considered a criterion for discontinuing treatment [3].

In our patient's case, we initiated treatment with high-potency topical steroids and keratolytic shampoo, with partial response. In the following weeks, he developed hand-foot syndrome, prompting the oncology team to discontinue sorafenib and resume radiotherapy sessions. One week after stopping sorafenib, both dermatoses resolved.

CONCLUSION

In conclusion, we want to highlight the importance of recognizing follicular spiny hyperkeratosis and its association with sorafenib use in order to promptly identify the dermatosis and tailor the management without initially discontinuing oncological treatment.

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Author Contributions

Marianne Thérèse Signoret-Bravo – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree 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

Genaro Briseño-Gascon – Conception of the work, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree 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

Maria Fernanda Figueroa-Hernández – Interpretation of data, Drafting the work, Final approval of the version to be published, Agree 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

Cristina Berumen-Glinz – Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree 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

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Guarantor of Submission
Cristina Berumen-Glinz is the guarantor of submission.

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Consent Statement
Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.