Severe onycholysis and eyelash trichomegaly in a patient treated with erdafitinib

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Key words: erdafitinib; fibroblast growth factor receptor inhibitor; onycholysis; oncodermatology; paronychia; trichomegaly.

INTRODUCTION

In the last 2 decades, persistent advancements in anticancer treatment have resulted in the development of an armory of targeted therapies that interfere with specific oncogenic molecular aberrations foundational to tumorigenesis. These individualized therapeutics improve overall patient outcomes through superior anticancer efficacy as well as maintained quality of life with minimization of generalized, morbid toxicities common to conventional chemotherapeutics. Representation of such success of a novel targeted agent was recently demonstrated by erdafitinib, a potent pan—fibroblast growth factor receptor (*FGFR*) inhibitor that prevents angiogenesis, cell proliferation, and antiapoptotic signaling in *FGFR* pathway—activated cancer cell lines.[1] In phase I studies, erdafitinib proved efficacious for the treatment of advanced or recurrent urothelial carcinoma and cholangiocarcinoma with clonal *FGFR* mutations.[2] The most common erdafitinib-related adverse events are hyperphosphatemia, dry mouth, and asthenia; however, dermatologic toxicities are also frequent and make up 11% of treatment-related adverse events. Skin toxicities include xerosis and hand-foot syndrome, whereas nail toxicities include onycholysis or nail dystrophy. Although common, dermatologic toxicities are almost exclusively grade 1/2 and only require conservative management.[2]

We present a case of erdafitinib-induced grade 3 dermatologic toxicities including onycholysis, nail bed superinfection, and paronychia as well as eyelash trichomegaly and eyebrow hypertrichosis that severely diminished quality of life and required temporary drug discontinuation and subsequent dose reduction. We hope this case brings awareness to the potential severity of *FGFR* inhibitor—associated dermatologic toxicities and encourages mindfulness of available prophylactic measures to limit their occurrences.

Abbreviation used:

FGFR: fibroblast growth factor receptor

CASE REPORT

The patient is a 71-year-old man with a history of recurrent, metastatic high-grade papillary urothelial carcinoma with an *FGFR3 Y373C* mutation. He was treated initially with pembrolizumab; however, because of immune-related arthritis he required alternative therapy. Because of the known *FGFR3* mutation, erdafitinib was initiated. The patient experienced abrupt relief of urinary symptoms and cancer-related pain; however, 8 weeks after therapy initiation he complained of nail, skin, and hair changes and was referred to the dermatology department. On examination, there was near-complete onycholysis of all fingernails and toenails with complete loss of 1 nail plate. Additional nail changes include malodorous, purulent drainage from multiple fingernails and paronychia (Fig 1). Hair changes included coarsening and curling of scalp hair, eyebrow hypertrichosis, and eyelash trichomegaly (Fig 2). Lastly, there was painful macular erythema on the palmar and dorsal surfaces of bilateral hands and feet.

The patient was started on metronidazole cream for suspected gram-negative infection of the nails and continued on doxycycline, which was previously prescribed by the ophthalmology department

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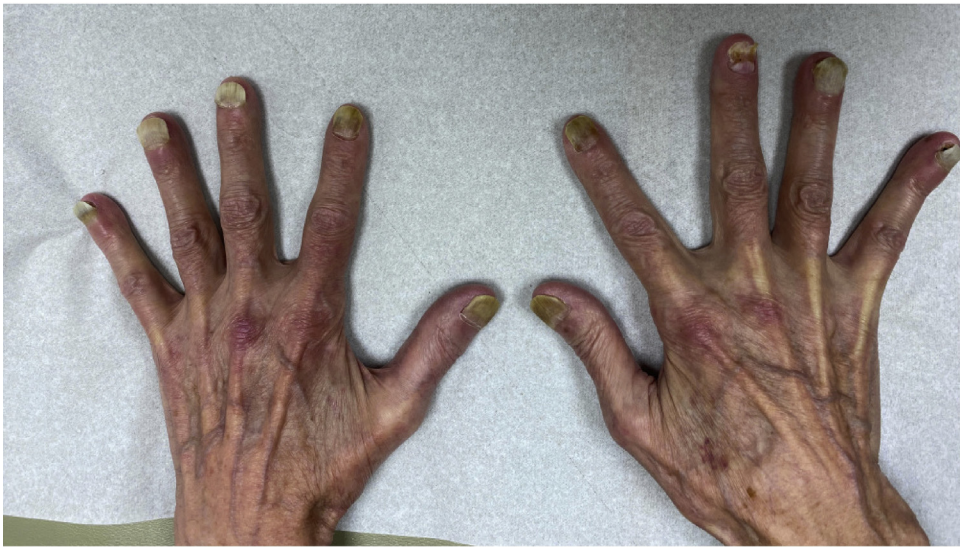

Fig 1. Severe onycholysis and nail bed infection of fingernails. Erythematous patches over metacarpophalangeal joint, distal interphalangeal joint, and periungual areas.

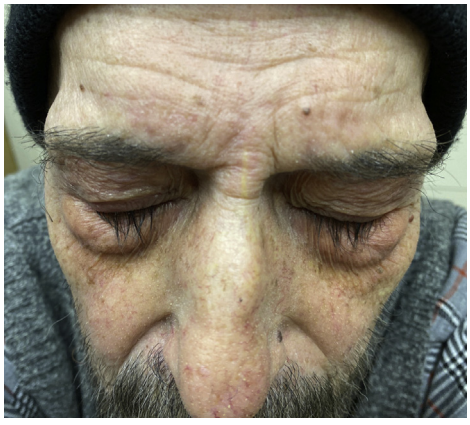

Fig 2. Coarse, thick, curled eyelashes (trichomegaly) and eyelash hypertrichosis bilaterally.

for bilateral squamous blepharitis. Daily antiseptic soaks were recommended for the fingernails and toenails, and triamcinolone cream was prescribed for the dermatitis on the hands and feet. Because of these dermatologic manifestations, as well as concurrent ophthalmologic toxicities, erdafitinib was discontinued and planned to reinitiate at a lower dose when toxicities resolved. A bacterial culture from nail bed drainage grew mixed flora. On follow-up with the dermatology department 2 weeks later, the patient had significant improvement in all nails with healthy regrowth and no remaining drainage or pain. Topical metronidazole was discontinued; however, the patient remained on doxycycline for blepharitis. The patient also continued with prophylactic daily antiseptic soaks of the nails.

DISCUSSION

Increasing use of *FGFR* inhibitors will likely be seen, as 7.1% of all cancer types harbor mutations in this pathway,[1] and knowledge of their class-specific side effects will be essential for optimized patient treatment. Fortunately, these toxicities are akin to those seen with other anticancer therapeutics, and management can be modeled as such. For instance, eyelash hypertrichosis, hirsutism, and trichomegaly are characteristic of targeted therapies such as epidermal growth factor receptor, B type rapidly accelerated fibrosarcoma kinase, and multikinase (MKI) inhibitors.[3] Although these changes typically regress after treatment termination, inward lash curling puts patients at risk for keratitis, and eyelash trimming may be required.[4] Interestingly, classical targeted therapy—associated nail changes such as paronychia and pyogenic granuloma are less archetypal of *FGFR*-induced nail toxicities, and these more closely resemble chemotherapy-related, specifically taxane-related, changes including onycholysis, onychomadesis, and nail bed superinfection.[5] Antiseptic soaks are recommended in both prophylaxis and management, with the addition of topical or systemic antibiotics or antifungals if superinfection is present.[4]

Aside from clinical trial data, to our knowledge, there are no similar reports of erdafitinib-induced dermatologic toxicities. However, 2 cases of patients on alternative *FGFR* inhibitors with analogous dermatologic manifestations have been described.[6] Additionally, a case of erdafitinib-induced hyperphosphatemia and resultant calcinosis cutis was reported,[1] and awareness of this drug-specific

cutaneous manifestation remains of equal importance. This case enriches the spectrum of dermatologic toxicities associated with targeted anticancer therapies and continued documentation of drug-specific manifestations remains important as use of erdafitinib increases.

REFERENCES

1. Arudra K, Patel R, Tetzlaff MT, et al. Calcinosis cutis dermatologic toxicity associated with fibroblast growth factor receptor inhibitor for the treatment of Wilms tumor. *J Cutan Pathol*. 2018;45(10):786-790.
2. Bahleda R, Italiano A, Hierro C, et al. Multicenter phase I study of erdafitinib (JNJ-42756493), oral pan-fibroblast growth factor receptor inhibitor, in patients with advanced or refractory solid tumors. *Clin Cancer Res*. 2019;25(16):4888-4897.
3. Freites-Martinez A, Shapiro J, Goldfarb S, et al. Hair disorders in patients with cancer. *J Am Acad Dermatol*. 2019;80(5):1179-1196.
4. Macdonald JB, Macdonald B, Golitz LE, LoRusso P, Sekulic A. Cutaneous adverse effects of targeted therapies: Part I: Inhibitors of the cellular membrane. *J Am Acad Dermatol*. 2015;72(2):203-218. quiz 219-220.
5. Lacouture M, Sibaud V. Toxic side effects of targeted therapies and immunotherapies affecting the skin, oral mucosa, hair, and nails. *Am J Clin Dermatol*. 2018;19(Suppl 1):31-39.
6. Betrian S, Gomez-Roca C, Vigarios E, Delord JP, Sibaud V. Severe onycholysis and eyelash trichomegaly following use of new selective pan-FGFR inhibitors. *JAMA Dermatol*. 2017;153(7):723-725.