**CASE REPORT**

**Avapritinib-induced photo-aggravated cutaneous reaction**

Farinoosh Dadrass, MS,a Joohee Han, MD,b Kevin J. Gaddis, MD,b and Marki Swick, MDb

Maywood, Illinois and Minneapolis, Minnesota

**Key words:** avapritinib; cutaneous eruption; cutaneous phototoxicity; drug reaction; gastrointestinal stromal tumor; photosensitivity; phototoxic reaction; sun exposure; tyrosine kinase inhibitor.

**INTRODUCTION**

Cutaneous phototoxicity is a nonimmunologic reaction resulting in direct cellular damage after sun exposure. This phenomenon occurs secondary to various drugs, including targeted oncologic therapies, in combination with UV-A or visible radiation. Currently, tyrosine kinase inhibitors are the treatment of choice for the majority of gastrointestinal stromal tumors (GISTs). Avapritinib, a type I tyrosine kinase inhibitors, was recently approved for patients with GISTs carrying the D842V mutation. To date, there is no documented literature on photosensitivity secondary to avapritinib. We report a case of phototoxic cutaneous eruption in a 56-year-old woman with a GIST on avapritinib.

**CASE REPORT**

A 56-year-old woman with Fitzpatrick skin type II and a history of a stage IV GIST presented with well-demarcated, edematous, brightly erythematous plaques with overlying ruptured bullae in photo-distributed areas on the bilateral shins (Fig 1, A-C). The rash initially appeared as a sunburn on the patient’s anterior shins and dorsal surface of her feet after prolonged sun exposure while she was wearing capri pants with the rest of her legs covered. Over the next 3 days, the rash worsened, with the development of bullae and pain.

Oral avapritinib (300 mg) daily for the patient’s GIST was initiated 5 months prior to presentation. Her prior treatment history for her GIST included trials of imatinib, sunitinib, and regorafenib. After the appearance of bullae, the patient presented to the emergency department and was discharged with cephalexin for 7 days in suspicion of possible cellulitis. She returned to the emergency department the next day with confusion, lethargy, worsening bilateral lower-extremity edema, and pain and was found to be febrile, hypoxic, and hemodynamically unstable. Blood cultures were drawn in the emergency department for possible hospital-acquired pneumonia and/or sepsis, and the patient was started on piperacillin/tazobactam. The patient was admitted and required 1 to 4 L of oxygen via a nasal cannula. Her chest X-ray imaging showed bilateral pulmonary infiltrates and small bilateral pleural effusions. Diuresis and diagnostic and therapeutic thoracentesis did not show any infection or malignancy. For the new-onset rash on her shins, dermatology was consulted. A punch biopsy of the right lower extremity was performed (Fig 2, A and B) and demonstrated marked papillary dermal edema and mixed inflammation with rare dyskeratotic keratinocytes.

Avapritinib was discontinued. On day 4 of her admission, the patient was able to wean off her oxygen requirement. She was discharged with oral furosemide 40 mg daily along with the recommendation for strict photoprotection and compression stockings, and 0.1% triamcinolone cream was initiated, with the improvement of the rash. The patient continued to improve and was never restarted on avapritinib, eventually starting ripretinib instead.
DISCUSSION

Most GISTs contain a constitutively active c-Kit receptor, which is why they are typically treated with tyrosine kinase inhibitors, such as imatinib, nilotinib, and dasatinib. These agents have been shown to cause various cutaneous toxicities that are dose-related and reversible following drug cessation. Cutaneous findings documented include edema, morbilliform eruption, pigmentary changes, alopecia, and inflammatory eruptions, such as erythroderma.\(^1\) In 2020, avapritinib was approved by the Food and Drug Administration for patients with advanced GISTs, and, as a result, potential adverse effects are being elucidated.\(^2\)

Photo-induced cutaneous toxicities have been reported secondary to multikinase inhibitors, such as vandetanib and pazopanib.\(^3,4\) Our patient’s well-demarcated erythematous plaques, along with the pathologic findings of dermal edema, mixed inflammatory infiltrates, rare dyskeratotic keratinocytes, and follicular interface, were consistent with photosensitivity secondary to avapritinib.

This patient’s photosensitive eruptions could be categorized as grade 3 due to the blistering that developed.\(^5\) The management consists of corticosteroid use and strict photoprotection, such as sun avoidance, photoprotective clothing, generous application of broad-spectrum sunscreen with UV-A–blocking agents, and UV-light–blocking window films.\(^5\) For phototoxities refractory to treatment with corticosteroids and strict photoprotection, 1
case report of vandetanib-induced phototoxicity demonstrated complete clearing following 8 weeks of oral supplementation with 240 mg of Polypodium leucotomos extract daily. 6

We report a photo-induced eruption occurring in the setting of avapritinib therapy. Our case emphasizes the importance of sun protective precautions and monitoring for cutaneous findings in patients on avapritinib for the treatment of GISTs.

Conflicts of interest
None disclosed.

REFERENCES
1. 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):203-220.
2. Martin-Broto J, Moura DS. New drugs in gastrointestinal stromal tumors. Curr Opin Oncol. 2020;32(4):314-320.
3. Doan HQ, Hu MI, Goldstein J, Piha-Paul SA, Subbiah V, Patel AB. Vandetanib photoinduced cutaneous toxicities. Cutis. 2019;103(5):E24-E29.
4. Udompanich S, Chanprapaph K, Rajatanavin N. Phototoxic reaction induced by pazopanib. Case Rep Dermatol. 2018;10(3):251-256.
5. Macdonald JB, Macdonald B, Golitz LE, LoRusso P, Sekulic A. Cutaneous adverse effects of targeted therapies: part II: inhibitors of intracellular molecular signaling pathways. J Am Acad Dermatol. 2015;72(2):221-238.
6. Korman AM, Reynolds KA, Nabhan F, Konda B, Shah MH, Kaffenberger BH. Vandetanib-induced phototoxic drug eruption treated with Polypodium leucotomos extract: a case report and review of the literature. J Clin Aesthet Dermatol. 2019;12(10):35-38.