Dear Editor,

Newer personalized, genotype directed therapy has revolutionized the treatment strategy for advanced malignancies given its specificity, superior efficacy, and less toxicity. Crizotinib is a multi-targeted tyrosine kinase inhibitor and is the first anaplastic lymphoma kinase (ALK)-positive inhibitor used clinically for advanced ALK+ non-small cell lung carcinoma (NSCLC). Herein we report a rare case of severe photosensitive dermatitis developed in an NSCLC patient who otherwise had a good response in disease status with crizotinib.

A man in his 60s presented to our dermatology outpatient clinic with intensely itchy reddish plaques on photo-exposed parts of two weeks duration [Figure 1a]. History of exposure to direct sunlight while doing gardening a day prior to the skin eruption was given by the patient. He was a non-smoker diagnosed with stage-4 NSCLC six months back and was started on crizotinib. He had a dramatic improvement in his tumor burden after starting the drug as evidenced on his repeat PET scan. He was tolerating the drug well and had no systemic adverse effects other than recent dermatologic rash that developed after 6 months of drug initiation. Due to persistence of the troublesome rash, the drug was planned to be discontinued for a while, for which the patient was not keen due to fear of worsening disease status.

Muco-cutaneous examination revealed, brightly erythematous crusted plaques on his forearm, lips and bald scalp [Figure 1b]. No seborrheic distribution was noted. Oozing was also noted from some of the lesions. The lesions were confined to the photo-exposed parts and skin creases were spared. No dusky erythema or target-like lesions were noted, and no lesions were noted in his oral mucosa. There was no regional lymphadenopathy. Histopathology showed parakeratosis, epidermal spongiosis [Figure 2a], and dermal inflammation predominated by lymphocytes [Figure 2b]. No basal cell vacuolization or apoptotic keratinocytes were noted. A diagnosis of photosensitive dermatitis probably due to crizotinib (Naranjo score, 5) was made.

The patient was prescribed oral prednisolone (40 mg/day) and oral antihistamines along with clobetasol cream and a sunscreen with sun-protection factor 30. He was also advised to follow strict photoprotection—to avoid unnecessary direct exposure to sunlight, wearing full sleeve garments, and broad-brimmed hats. He had a marked improvement in his symptoms and signs within two days of starting oral steroids which were tapered and stopped within 10 days. He had occasional flares of photosensitive rash for the next 3 months which were self-limiting. At one-year follow-up visit, his disease was in remission with ongoing crizotinib and there was no recurrence of the rash.

Cutaneous adverse effects are rare but game-changing events in patients on advanced antineoplastic agents. Such adverse events may necessitate withdrawing rewarding anti-neoplastic agents despite its systemic tolerability or positive effects on tumor load. In clinical trials, the common side effects reported with crizotinib are visual disturbances, gastrointestinal intolerance, and pitting edema. The cutaneous complaints were reported in 11% population in clinical trials and were non-significant.[1] However, in the real world scenario, we could find only four case reports of cutaneous adverse events due to crizotinib (erythema multiforme,[2] photosensitive dermatitis,[3] lichenoid drug eruption,[4] and oral lichenoid lesions).[5]

In a previous single report of severe photosensitive rash due to crizotinib, the drug had to be discontinued owing to the relapse of rash on re-challenge.[1] In our case also, the oncologist had to advise the patient to stop the well-performing crizotinib owing to the severity of the itchy cutaneous lesions. The rash in the patient was only photosensitive dermatitis; unlike the toxic epidermal necrolysis which shows cutaneous necrosis and may worsen on continuation of the culprit drug. We...
reiterate the need for a meticulous cutaneous examination for better characterization of the cutaneous lesion before contemplating withdrawal of a well-performing newer antineoplastic agent in such a scenario.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgment
Authors are indebted to Dr. K. K. Nejima, MD for the histopathological diagnosis of the rash.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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Access this article online

| Website: | www.idoj.in |
| Quick Response Code: | 10.4103/idoj.IDOJ_291_20 |

How to cite this article: Afra TP, Nair PP, Thanseer NT, Razmi TM. Crizotinib-induced severe photosensitive dermatitis in a carcinoma lung patient. Indian Dermatol Online J 2021;12:188-9.

Received: 23-Apr-2020. Revised: 20-Jun-2020. Accepted: 17-Jul-2020. Published: 28-Sep-2020.