Sir,

A 62-year-old male presented with fever, skin rash, and oral erosions of one-week duration. He was a known case of metastatic carcinoma urinary bladder with bilateral DJ stent in situ, on regular oncology follow-up. He received injection enfortumab 1.25 mg/kg on days 1 and 8 of the first cycle. Skin rashes started 3 days after the first infusion of enfortumab given on October 19, 2020; no dose modification was required as these were of grade 1. However, skin rashes worsened after the second infusion which was given a week later. Past treatments included four cycles of gemcitabine and cisplatin and eight cycles of pembrolizumab. His medical history was significant for hypertension, coronary artery bypass grafting in 2006, and chronic liver disease. On examination, the patient was febrile, drowsy, with tender, macular, reticulate erythematous rash over neck, axillae, forearms, flanks and groin folds, proximal thighs, lower trunk, and feet. Erosions over lips and palate, multiple scattered follicular pustules over scalp, and crusting over nasolabial folds were also observed. Conjunctival erythema over palms and soles without target lesions or blisters were present.

Investigations revealed hemoglobin 8.8 g/dL, total leucocyte count 2.3 × 10^9/L, with 58.9% neutrophils, 29.9% lymphocytes, 10.2% monocytes, and 0.8% eosinophils and platelet count 90 × 10^9/L. Serum creatinine was 2.9 mg/dL and total and direct bilirubin level were 3.1 and 2.3 mg/dL, respectively. Serum albumin was 2.5 mg/dL, and serum transaminases were normal. Urine routine, chest X-ray, ECG, and thyroid profile were normal. A diagnosis of enfortumab-induced symmetrical flexural and intertriginous exanthem (grade 4 skin rash, Common Terminology Criteria for Adverse Events) was considered.

Patient was treated with antibiotics, systemic and topical corticosteroids, and other supportive care. Gradually over the next 2 days, he remained febrile with extreme difficulty in swallowing and the erythema persisted with development of erosions over trunk. His urine output decreased; serum creatinine increased to 4.9 mg/dL with worsening leucopenia (total leucocyte count 100 × 10^9/L, absolute neutrophil count 1 × 10^9/L) and thrombocytopenia, platelet count of 26 × 10^9/mm^3. Total and direct bilirubin increased to 5.9 and 5.1 mg/dL. Blood and urine cultures showed no growth. Chest X-ray and ultrasound abdomen were normal. Arterial blood gas analysis showed lactic acidosis. Continuous renal replacement therapy was planned after nephrology review, while transfusion of fresh frozen plasma and platelets was continued.

On day 5, peeling of skin occurred at sites of removal of micropore tape, corresponding to positive pseudo-nikolsky sign [Figure 4]. The skin over erythema over palms and soles without target lesions or blisters were present.

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In 2019, the United States Food and Drug Administration approved the drug as a third-line treatment for patients who had failed in previous trials of programmed cell death protein 1 and platinum-based chemotherapeutic agents in patients of metastatic urothelial carcinoma.[1] The drug has demonstrated to have a significant response rate in early phase trials and is known for its tolerable side-effect profile.[3] The most common adverse reactions include fatigue, peripheral neuropathy, decreased appetite, nausea, dysgeusia, diarrhea, dry eyes, rash, alopecia, pruritus, and dry skin.[3]

Cutaneous adverse reactions can be observed with enfortumab vedotin and are generally low grade and manageable, often demonstrating a maculopapular and diffuse appearance.[1] Skin rashes have been reported in 54% of patients given enfortumab, of which 26% presented with maculopapular rash while 30% had pruritus.[3] Grades 3–4 skin reactions occurred in 10% patients and included symmetrical drug-related intertriginous and flexural exanthem (SDRIFE), bullous dermatitis, exfoliative dermatitis, and palmo-plantar erythrodysesthesia.[3]
Enfortumab vedotin is a new drug on the horizon for metastatic urothelial carcinoma. We are reporting this case from India to highlight the risk of severe cutaneous adverse reactions from this drug. Skin biopsy helps in differentiating from other possible entities though TEN is mainly a clinical diagnosis. Consent for skin biopsy was refused in our patient by his family because of his critical condition. On initial evaluation, in our patient, morphology of rash resembled SDRIFE; however, rapidly progressing erosions and worsening mucosal involvement occurred. In the absence of skin biopsy, it remains inconclusive whether the rash of SDRIFE progressed to TEN or it was a case of atypical presentation of TEN.

Physicians using this molecule should remain extremely vigilant since most of the patients are elderly, have comorbidities, and on multiple other drugs. Two patients of enfortumab-induced TEN with fatal outcome have been reported previously\textsuperscript{[4,5]} and our would be third such patient.

**Abbreviations**

SDRIFE: Symmetrical drug-related intertriginous and flexural exanthem.

TEN: Toxic epidermal necrolysis.

**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.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

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