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LETTER TO THE EDITOR

Atypical bortezomib-induced neutrophilic dermatosis

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Dear Editor,

A 76-year-old man was treated with prednisone-melphalan and sub-cutaneous injections of bortezomib for an IgG kappa multiple myeloma (MM). On day 25 of the first chemotherapy cycle, the patient presented with painless red-to-purple edematous, bullous, or ulcerated, and hemorrhagic plaques, involving the forehead, the dorsal face of fingers, and both ankles (Fig. 1a, b). The complete blood count was normal. Skin biopsy revealed an infiltrate of neutrophils located within the dermis with partially destroyed hair follicles, but without vasculitis, dermal edema, or any type of tumor cell (Fig. 1c). Echocardiography, microbiological skin samples, and blood cultures were normal. Considering the histologic features and the patient's clinical and drug history, we hypothesized bortezomib-induced neutrophilic dermatosis (ND).

Bortezomib is a proteasome inhibitor, and its main adverse events include gastrointestinal disorders, peripheral neuropathy, and hematological complications. Skin adverse events occur in up to 24% of the patients, with various clinical presentations [1, 2]. The commonest is an acute eruption associating papules and nodules. The histological features of these lesions are heterogeneous, and include perivascular dermatitis, interface dermatitis, and leukocytoclastic vasculitis. Skin manifestations generally occur in the third or fourth treatment cycle. Bortezomib-induced Sweet's syndrome (also known as acute febrile neutrophilic dermatosis [3]) and Sweet-like lesions are also well-known [4–10]. Unlike classic bortezomib-induced cutaneous adverse side effects, Sweet's syndrome and Sweet-like affections generally occur in the first or second cycle of chemotherapy. The usual presentation of this bortezomib-induced Sweet's syndrome involves fever and asthenia, with typical painful round erythematous and edematous plaques on the head, neck, or trunk. Skin biopsy classically reveals a dermal infiltrate consisting of mature or immature neutrophils. Walker et al. proposed 5 criteria for typical drug-induced Sweet's syndrome [9]: (1) acute onset of painful erythematous plaques or nodules; (2) dermal neutrophilic infiltrate without evidence of vasculitis on histopathological examination; (3) pyrexia > 38 °C; (4) temporal relationship between drug ingestion and clinical presentation, or recurrence after rechallenge; (5) resolution of lesions after drug withdrawal or treatment with systemic corticosteroids. Although our case meets 3 of these five criteria, it differs from previously reported bortezomib-induced ND on account of the lack of systemic symptoms and the painless, ulcerated, hemorrhagic lesions, and their atypical localization on the extremities and forehead, sparing the trunk. The histology is characteristic of ND, but the absence of dermal edema and vasculitis respectively excludes usual Sweet's syndrome and erythema elevatum diutinum. Therefore, this observation broadens the spectrum of bortezomib-induced ND. The pathophysiology of these manifestations is still poorly understood: an imbalance of pro-inflammatory cytokines induced by bortezomib may lead to a chemotactic migration of neutrophils toward the dermis. In our case, bortezomib was discontinued and prednisone was started at 1 mg/kg/day, leading to a complete regression of the skin lesions. The standard regimen of prednisone and melphalan was continued without reappearance of the lesions. Reintroduction of bortezomib after a first episode of DN has been associated with a relapse of skin lesions, supporting a strong implication of the drug in the pathophysiology of DN [7, 10].

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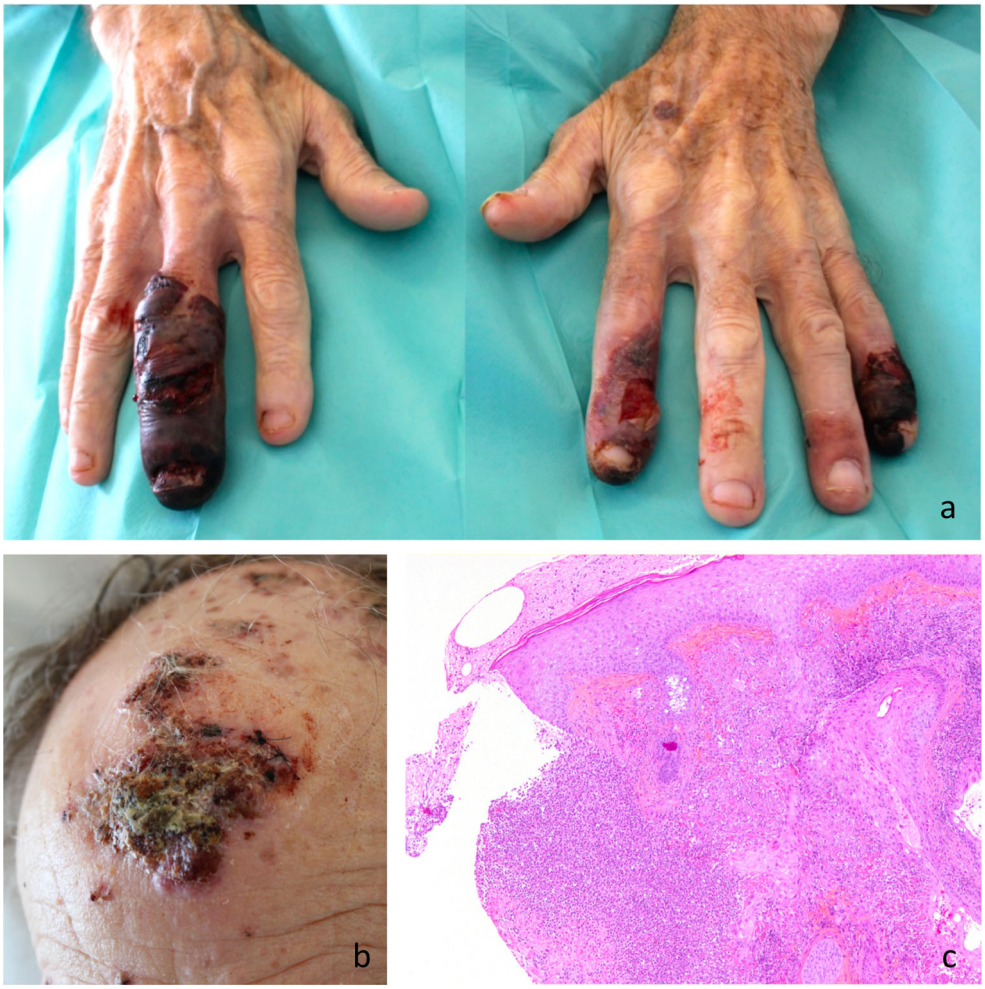

Fig. 1 **a**, **b** Painless red-to-purple edematous, bullous, or ulcerated, and hemorrhagic plaques, involving the forehead, the dorsal face of fingers, and both ankles. **c** Marked and diffuse dermal neutrophilic infiltrate with necrotic changes around hair follicles on skin biopsy. No evidence of vasculitis neither edema was shown. No evidence of micro-organism (HES stain, × 10)

Considering the initial severity of the skin lesions, bortezomib was not re-introduced in our case.

Authors' contribution All of the authors participated in the preparation of the manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they no conflict of interest.

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