A 49-year-old male with multiple myeloma was receiving treatment with bortezomib at a dose of 1.3 mg/m² IV on days 1, 4, 8, and 11, after failed therapies including anakinra, dexamethasone, and thalidomide. During the first cycle of bortezomib, the patient developed bilateral periorbital edema. Over the second cycle skin toxicity progressed into angioedema and asymptomatic, erythematous papules–plaques measuring up to 1.0 cm on his face, neck, and upper trunk. A skin biopsy of one of the cutaneous lesions showed a dense neutrophilic, perivascular and periappendageal infiltrate in the dermis with focal areas of necrobiosis and leukocytoclastic vasculitis (Figure 1). The epidermis showed necrosis and focal ulceration.

The patient was admitted to the intensive care unit for airway observation and bortezomib was interrupted. He was given short course i.v. corticosteroids and diphenhydramine every 6 h for angioedema prophylaxis. The angioedema and cutaneous lesions resolved over subsequent days, and his third cycle of bortezomib was initiated in a controlled inpatient setting, with prior administration of 25 mg oral prednisone, without recurrence of facial edema or rash.

Bortezomib is the first proteasome inhibitor approved by the Food and Drug Administration. This potent, reversible inhibitor is indicated in patients with multiple myeloma refractory to at least one prior therapy. Its strong affinity for the 26S proteasome and disruption of signaling cascades vital for growth and survival promote apoptosis in malignant cells [1]. Notably, bortezomib blocks the activity of nuclear factor-kappa B, a transcription factor that induces the production of proteins that block cell death pathways, promote cell proliferation, and regulate the expression of cell surface adhesion molecules [1]. Blocking of cell surface adhesion molecules prevents myeloma cells from binding to bone marrow stromal cells and inhibits cell adhesion-mediated drug resistance [1]. This impedes the production of interleukin 6 and vascular endothelial growth factor, thereby inhibiting angiogenesis [2].

Skin toxic effects are well-described adverse events of bortezomib. Leukocytoclastic vasculitis and a folliculitis-like rash has been reported after second and third treatment cycles of bortezomib in patients with multiple myeloma [3]. In a recent study, 6 out of 47 (13%) multiple myeloma patients treated with bortezomib showed erythematous plaques measuring 0.5–2 cm on the trunk, neck, and limbs that resolved within 4–7 days after treatment with low-dose prednisone and/or antihistamines [4]. Analysis of skin biopsies indicated a range of dermatitis types, including perivascular, interstitial, and interface [4]. No biopsies showed neutrophilic infiltrates or vasculitis with vascular wall necrosis [4].

Conventional pharmacologic management of multiple myeloma includes the use of alkylating agents, glucocorticoids, and thalidomide. Positive response rates have been reported at 17%–47% with thalidomide and 25%–50% with VAD, a combination therapy of Vincristine, doxorubicin (Adriamycin) and high-dose Dexamethasone [5]. Bortezomib, representing a new class of drugs, appears to induce a positive response rate in 35%–38% of patients when used alone in patients with disease refractory to prior treatment [1, 5]. Rash development is not a contraindication for use. Prevention of rash is typically

**Figure 1.** Close-up of lesion (left panel) showing an erythematous plaque with no epidermal changes and dilated follicular openings. Biopsy (right panel) shows a perivascular neutrophilic infiltrate with nuclear dust and necrobiosis of collagen.
accomplished either by prophylactic oral prednisone administration or concurrent i.v. steroids, allowing for continuation of bortezomib therapy.

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funding

Robert H. Lurie Comprehensive Cancer Center.

references


doi:10.1093/annonc/mdm436