Skin lesions induced by bortezomib

We report on six cases of skin lesions induced by bortezomib in patients treated for relapsed multiple myeloma. The folliculitis-like rash appeared in the second cycle of bortezomib therapy. Therapy with prednisone led to rapid resolution of the skin lesions. Prednisone 10 mg before each infusion of bortezomib was necessary to prevent recurrence of the rash while antihistamines alone were ineffective.

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Bortezomib has been shown to be highly efficient in the treatment of relapsed multiple myeloma (MM) (1). Between December 2004 and July 2005 we treated 25 MM patients with bortezomib. The patients were treated with standard dosage schedule (intravenous infusions of bortezomib 1.3 mg per square meter of body area on days 1, 4, 8, 11 of a 21-day cycle).

In six of 25 patients (24%), rash developed during the second treatment cycle (Figure 1A). All six patients had relapsed after autologous peripheral blood stem cell transplant. The first cycle of bortezomib was well tolerated in all cases. Of these six patients, four had IgA MM (of 9 IgA MM patients in the group; 44%) and two patients had IgG type (of 16 IgG patients in the group; 13%). But the incidence skin toxicity of bortezomib was not significantly higher in IgA M (Fisher exact test p=0,142). Skin biopsy was done in first three patients , in all cases perivascular lymphoid infiltrates were found.

The rash resolved rapidly in all cases after treatment with prednisone 20 mg/day (Figure 1B). Two patients were treated with prednisone and cetirizine (10 mg/day). After resolution of rash, prednisone was discontinued, but the rash recurred with the next bortezomib infusions despite continued treatment with cetirizine. To prevent the recurrence of the rash, it was necessary to administer corticosteroids (10 mg prednisone) prophylactically before every administration of bortezomib. Two patients with bortezomib-associated rash were treated with dexamethasone together with bortezomib from 3rd cycle onwards due to minimal treatment response. In these patients, rash resolved and did not recur. The rash did not lead to discontinuation of bortezomib treatment in any of the patients. Rash is a relatively common toxicity seen in MM patients treated with bortezomib. Where reported, its incidence in clinical trials ranged from 8 to 18%.[1,2,3] In our report as well as in that by Agterof and Biesma[4] lesions infiltrated by lymphocytes seem to be the most typical after bortezomib. In conclusion, according to our clinical experience, corticosteroids are useful for the prevention and treatment of bortezomib-associated rash while maintenance treatment with antihistamines alone is not effective.

Figure 1. A 53-years old male with IgA multiple myeloma had relapsed 45 months after autologous peripheral blood stem cell transplant. On the 9th day of the second treatment cycle, folliculitis-like exanthema not associated with fever or pruritus developed on the patient's trunk, back and neck (Figure 1A). The patient was treated with 20 mg of prednisone per os (p.o.) and cetirizine 10mg p.o. daily, and the rash resolved after three days of treatment (Figure 1B). Treatment with prednisone was discontinued but cetirizine was given further as a maintenance therapy. The rash recurred with the subsequent cycle (9th day of the third cycle). The patient was again treated with 20 mg of prednisone and the rash resolved. After that, prednisone 10 mg p.o. was prophylactically administered before every infusion of bortezomib and the skin rash did not reappear.

References

1. Richardson PG, Sonneveld P, Schuster MW, Irwin D, Stadtmauer EA, Facon T, et al. Assessment of Proteasome Inhibition for Extending Remissions (APEX) Investigators. Bortezomib or high-dose dexamethasone for relapsed multiple myeloma. N Engl J Med. 2005 Jun 16;352:2487-98.
2. Wu KL, van Wieringen W, Vellenga E, Zweegman S, Lokhorst HM, Sonneveld P. Analysis of the efficacy and toxicity of bortezomib for treatment of relapsed or refractory multiple myeloma in community practice. Haematologica. 2005 Jul;90:996-7.
3. Richardson PG, Barlogie B, Berenson J, Singhal S, Jagannath S, Irwin D, et al. A phase 2 study of bortezomib in relapsed, refractory myeloma. N Engl J Med. 2003 Jun 26;348(26):2609-17.
4. Agterof MJ, Biesma DH. Images in clinical Medicine. Bortezomib-induced skin lesions. N Engl J Med. 2005 Jun 16;352:2534.

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