Acta Dermatovenerol APA

Acta Dermatovenerologica
Alpina, Pannonica et Adriatica

2012;21:21-22
doi: 10.2478/v10162-012-0006-3

Bortezomib and bilateral herpes zoster

Nicola di Meo[1]✉, Serena Bergamo[1], Adina Dondas[1], Giusto Trevisan[1]

Abstract

Bortezomib is a proteasome inhibitor that has proven to be a very effective treatment for multiple myeloma. There is considerable debate about the potential for reactivation of the varicella zoster virus (VZV) in patients with multiple myeloma during treatment with bortezomib. This report describes the case of a 70-year-old patient with multiple myeloma that developed bilateral herpes zoster shortly after being treated with bortezomib. Furthermore, it emphasizes the importance of using an antiviral prophylaxis with acyclovir in these patients treated with bortezomib.

Received: 17 May 2011 | **Returned for modification:** 23 January 2012 | **Accepted:** 4 March 2012

Introduction

Bortezomib is a widely used proteasome inhibitor that has proven to be very effective in treating multiple myeloma. In patients treated with this drug, however, both the humoral immunity response and cell-mediated immunity are compromised. Several studies confirm that reactivation of the varicella zoster virus (VZV) commonly occurs in patients with multiple myeloma that are being treated with bortezomib. The incidence of VZV reactivation ranges between 10 and 60% in these patients.

This report describes the case of a 70-year-old male patient with multiple myeloma that was treated with bortezomib and subsequently developed bilateral herpes zoster reactivation along two separate dermatomes. A brief literature review is included to emphasize the importance of using the antiviral prophylaxis acyclovir in patients treated with bortezemib.

Clinical case

A 70-year-old male patient came to us because of the appearance of several vesicles grouped in bunches, bilaterally distributed on his back along the dermatome supplied by D1-D2 sensory innervation on the right and along the dermatome supplied by D9-D10 innervation on the left, respectively (Fig 1).

The patient reported intense pain localized along the areas where the vesicles appeared, as well as functional impairment of his movements. On physical examination, perilesional edema and erythema surrounding multiple clusters of vesicles was noted, which caused pain when palpated (Fig 2). Given the clinical aspect of the elementary lesions, their arrangement, and the overall symptomatology, the diagnosis of bilateral herpes zoster was made. Furthermore, the ELISA test for VZV IgG, IgM, and IgA was positive, confirming a virus reactivation. We subsequently received the results for the PCR analysis carried out on a sample of the vesicles on the lesions that provided direct confirmation of VZV.

Given that the herpetic manifestation was bilateral and this could imply that the patient was immunologically compromised, a careful patient history and clinical analysis was carried out.

The patient was diabetic, had chronic kidney disease, and had been suffering from multiple myeloma for nearly 1 year. After six cycles of VAD (vincristine, adriamycin, and dexamethasone) chemotherapy he obtained a good hematologic response. Recently, however, he had had a relapse, developing increased levels of Bence-Jones proteins in the urine as well as plasma cell infiltration and decreased kidney function. The patient had therefore started a new therapeutic regime with bortezomib (Velcade®), melphalan, and prednisone. The herpes zoster reactivation occurred during the second cycle of this treatment. Bortezomib had been given on days 1, 4, 8, and 11 of a 21-day cycle. Considering his clinical condition and the concurrent chronic kidney disease, and given that an intravenous treatment was necessary, the patient was admitted to the hospital, where he was treated with acyclovir 375 mg intravenously per day for 10 days, with a complete resolution of the cutaneous symptoms.

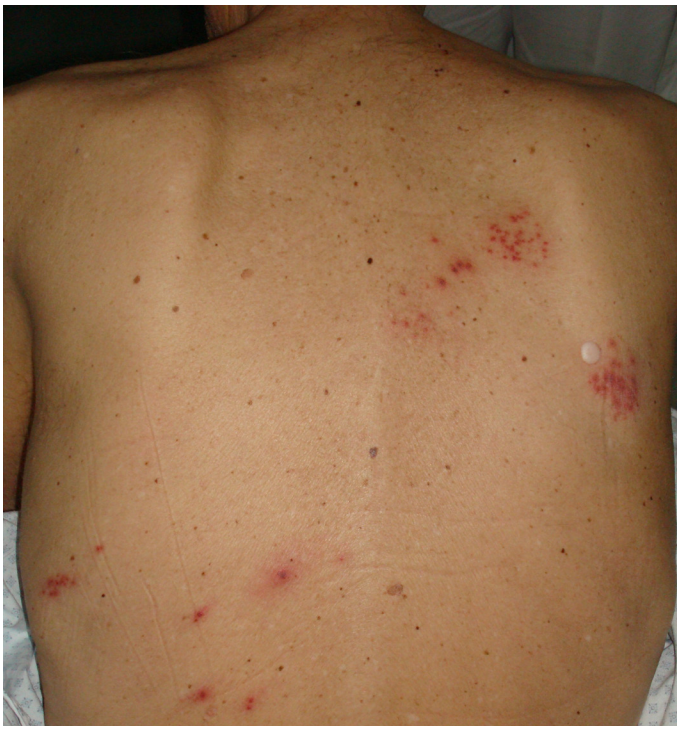

Figure 1 | Bilateral herpes zoster spreading over the patient back corresponding to D1-D2 and D9-D10 dermatomes.

[1]University of Trieste, Department of Dermatology and Venereology, Piazza ospedale 1, 34100 Trieste, Italy. ✉Corresponding author: nickdimeo@libero.it

Once he recovered from herpes zoster reactivation, the patient resumed VAD chemotherapy, with the addition of antiviral prophylaxis with acyclovir 200 mg daily. The dosage was calculated taking into account his kidney disease, and the patient presented no further viral reactivation.

Due to the progression of his disease, the patient developed severe anemia and died 6 months later.

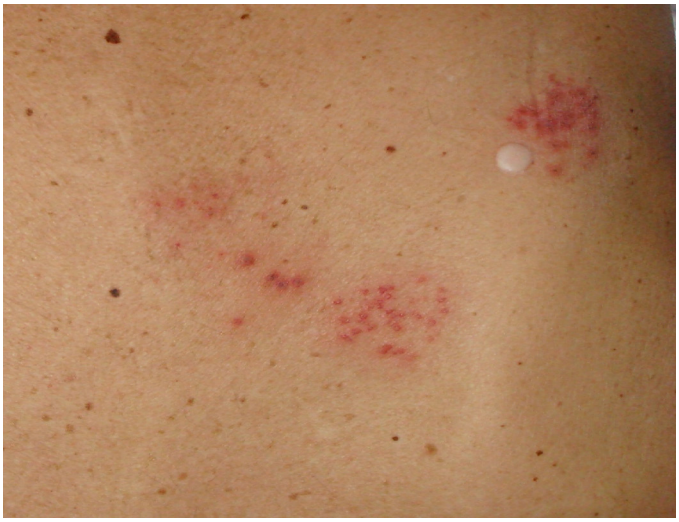

Figure 2 | Examination revealed localized, multiple, grouped vesicles, erosions over erythematous base with crusting.

Discussion

Bortezomib is a reversible and highly selective inhibitor of 26S proteasome. This drug can inhibit a group of proteins (known as proteasomes) that are needed by neoplastic cells to survive and multiply. The inhibition of such protein complexes, whose main function is to degrade unneeded or altered proteins (the proteasomes), changes the level of intracellular signals and regulating proteins that cause a cellular block and even apoptotic phenomena.

Since 2003, bortezomib has been FDA-approved for treating relapsed or refractory multiple myeloma (1). Several studies prove that the introduction of new drugs such as proteasome inhibitors has fundamentally changed the way multiple myeloma is treated. These drugs have been proven to change time to progression (TTP) and the overall survival (OS) (2) in patients.

Many clinical trials have shown that patients treated with bortezomib and patients treated with therapeutic regimes in which bortezomib was used have a higher risk of VZV reactivation. In a phase III trial (the APEX Study), which involved 663 subjects, a significantly higher incidence of VZV reactivation was reported in patients treated with bortezomib than in patients treated with dexamethasone (3).

VZV reactivation during a chemotherapy cycle with bortezomib has started becoming a relevant problem. The pathophysiology of this side effect is not yet well known. It is important to note, however, that patients on bortezomib treatment are at higher risk of herpes zoster reactivation than other infectious developments.

Considering two recent studies (4, 5), the use of prophylactic therapy with acyclovir seems to be useful in patients starting a treatment with bortezomib.

The first study emphasized the decreased incidence of VZV reactivation among multiple myeloma patients that received the antiviral prophylaxis. Furthermore, this study emphasizes that both the humoral immunity response and cell-mediated immunity can be compromised, especially in multiple myeloma patients undergoing treatment (4). In addition, a Japanese study demonstrated that there is a high VZV reactivation percentage (43%) among patients that do not receive any prophylactic treatment with acyclovir (5). Considering both these studies and our clinical case, the use of prophylactic therapy with acyclovir seems to be advisable in patients starting bortezomib treatment. Daily antiviral intake is proven to reduce VZV relapses. In patients suffering from multiple myeloma that are taking bortezomib, certain treatment regimes suggest an intake of acyclovir in a dosage of 200 or 400 mg daily (4, 5). Such prophylactic antiviral therapies are currently effective in preventing any reactivations, with excellent outcomes in close to 100% of cases.

References

1. Kane RC, Bross PF, Farrell AT, Padzur R. Velcade: U.S. FDA approval for the treatment of multiple myeloma progressing on prior therapy. Oncologist. 2003;8:508-13.
2. Palumbo A, Gay F. How to treat elderly patients with multiple myeloma: combination of therapy or sequencing. Hematology Am Soc Hematol Educ Program. 2009;566-77.
3. Chanan-Khan A, Sonneveld P, Schuster MW. Analysis of herpes zoster events among bortezomib-treated patients in the phase III APEX study. J Clin Oncol. 2008;26:4784-90.
4. Vickrey E, Allen S, Mehta J, Singhal S. Acyclovir to prevent reactivation of varicella zoster virus (herpes zoster) in multiple myeloma patients receiving bortezomib therapy. Cancer. 2009;115:229-32.
5. Aoki T, Nishiyama T, Imahashi N, Kitamura K. Efficacy of continuous, daily, oral, ultra-low-dose 200 mg acyclovir to prevent herpes zoster events among bortezomib-treated patients: a report from retrospective study. Jpn J Clin Oncol. 2011;41:876-81.