

Bortezomib plus melphalan and prednisone (VMP regimen) as the initial treatment for IgE multiple myeloma: a case study

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Abstract Patients with IgE multiple myeloma have poor prognosis. Due to the rarity of this condition, no standard treatment has been developed. As the VMP regimen (bortezomib plus melphalan and prednisone) has been reported to be highly effective in the treatment of other types of myeloma, we treated a patient with newly diagnosed IgE myeloma using the VMP regimen. Her myeloma responded well to VMP regimen. The results of this case report thus suggest that physicians may consider VMP regimen for use as the initial treatment for IgE myeloma.

Keywords Multiple myeloma · IgE · Bortezomib · VMP regimen · Initial treatment

Introduction

VMP regimen (bortezomib plus melphalan and prednisone) has been reported to be highly efficacious in treating multiple myeloma [1, 2]. However, no standard treatment has been developed for IgE multiple myeloma, a rare disorder with a poor prognosis. Here, we report the case of a patient with newly diagnosed IgE myeloma who was successfully treated with the modified VMP regimen as the initial treatment.

Case report

A 70-year-old previously healthy woman was admitted to our hospital because of lumbago and subsequent neck pain.

The roentgenogram of her spinal column showed a compression fracture of the 11th thoracic vertebra and destruction of the fifth cervical vertebra. Magnetic resonance imaging of the spine showed multiple bone lesions with low T1-weighted and high T2-weighted signal intensities. In analysis of the patient's laboratory data, we found that serum IgG, IgA, IgM, and IgD were suppressed to 514, 66, 15, and <0.6 mg/dL, respectively. In contrast, IgE was increased above the upper detection limit in a fluorescence-enzyme immunoassay (FEIA), and immunoelectrophoresis of serum showed the presence of M-protein of the IgE- λ type (Fig. 1). Bone marrow examination showed that atypical plasma cells increased to 31.8 % of nucleated cells with no chromosomal abnormalities in conventional G-banding, and immunohistochemistry revealed that plasma cells were positively stained with anti-IgE and anti- λ antibody, but negatively with anti- κ antibody (Fig. 2). Therefore, we diagnosed the patient with IgE- λ myeloma with normal karyotype. On the basis of the existence of multiple bone lesions and other laboratory data (hemoglobin: 10.6 g/dL, serum albumin: 2.7 g/dL, β 2-microglobulin: 4.1 mg/L, creatinine: 1.0 mg/dL, and corrected calcium: 12.9 mg/dL), her disease status was diagnosed as stage 3A according to the Durie/Salmon staging system and stage 2 according to the International staging system.

We started the modified VMP regimen consisting of bortezomib (1.3 mg/m² intravenously on days 1, 8, 15, and 22), melphalan (9 mg/m² per os on days 1–4), and prednisolone (60 mg/m² per os on days 1–4) every 6 weeks. Then, her bone pain, anemia, and hypercalcemia improved rapidly. Her serum M-protein could not be measured because FEIA is an extremely sensitive technique with an upper detection limit (16,000 IU/mL) equal to 3.84 mg/dL. Although immunoelectrophoresis of urine showed the presence of Bence Jones protein, her urine M-protein value

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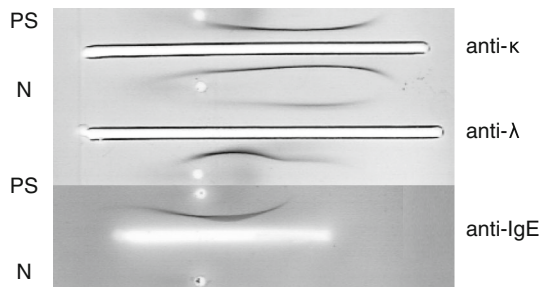


Fig. 1 Immunoelectrophoresis of the patient's serum compared to normal serum. Abnormal precipitin arcs with antisera to IgE (anti-IgE) and antisera to the λ light chain (anti- λ) were detected in the patient's serum. *N* normal serum, *PS* patient's serum

could also not be measured because her urine protein level was below 200 mg/24 h. However, she exhibited extremely high initial serum free light chain (FLC) λ value (1,410.0 mg/L) and rapid decline in the value responded to the regimen. The κ/λ ratio of her serum FLC, although extremely low (0.005) initially, also gradually increased after initiation of the regimen. After two courses of VMP regimen, her serum FLC value decreased to 83.4 mg/L and κ/λ ratio increased to 0.080, achieving a partial response (PR) according to international uniform response criteria [3]. Six courses of VMP regimen not only normalized her serum FLC value (23.9 mg/L) and bone marrow plasma cell count (1.2 %), but also resulted in the disappearance of M-protein in immunofixation electrophoresis, achieving a complete response (CR). Because the κ/λ ratio increased temporarily to a maximum value of 0.248, but fluctuated

thereafter and was still lower than normal just after the completion of all nine courses over 12 months, we are continuing maintenance therapy with biweekly bortezomib. She has maintained CR for over 10 months at the time of writing (Fig. 3). No serious treatment-related toxicities were observed throughout all courses of VMP regimen.

Discussion

IgE myeloma is a rare subtype that accounts for <0.01 % of all myeloma cases [4]. It is characterized by a high frequency of anemia, hepatomegaly and/or splenomegaly, and plasma cell leukemia, and by a rarity of severe renal failure [5–10]. Osteosclerotic and osteoblastic lesions are more likely to occur in this type of myeloma, although osteolytic lesions remain the most common type [5, 10–12]. It has no specific characteristics in terms of its microscopic appearance, but cytogenetically, it was reported that t(11;14)(q13;q32) or IgH-CCND1 was the hallmark of this type of myeloma [13]. Our case had anemia, but no hepatomegaly, splenomegaly, renal failure, or osteosclerotic lesions. Additionally, plasma cells were absent in peripheral blood and cytogenetic analysis of bone marrow showed normal karyotype.

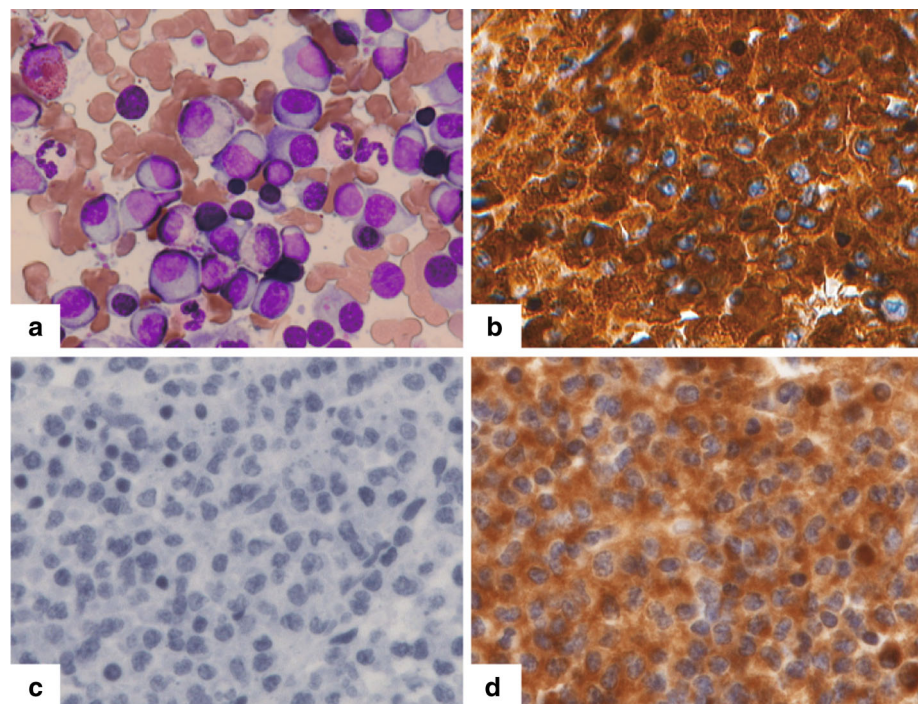
Some reports have suggested that the prognosis for IgE myeloma is worse than that for other types of multiple myeloma, since the mean survival of patients with IgE myeloma is only 12.5 months in the pre-bortezomib or

Fig. 2 a Bone marrow atypical plasma cells stained with May–Giemsa stain.

b Immunohistochemical staining with anti-IgE antibody.

c Immunohistochemical staining with anti- κ antibody.

d Immunohistochemical staining with anti- λ antibody



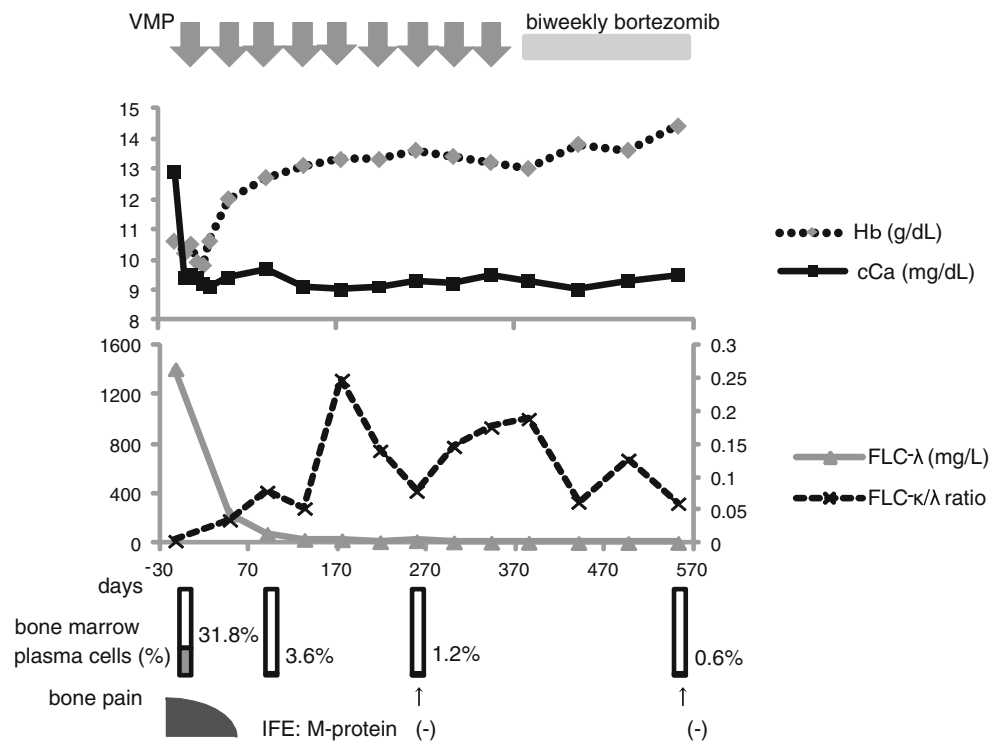


Fig. 3 The clinical course. Clinical symptoms including bone pain, anemia, and hypercalcemia improved rapidly. After two courses of VMP, free light chain-λ value also decreased, achieving a partial response. After six courses, bone marrow plasma cells decreased and

M-protein disappeared in immunofixation electrophoresis, achieving a complete response that has persisted until the time of writing. *IFE* immunofixation electrophoresis

immunomodulatory drug era [7]. Moreover, the overall survival of patients with IgE myeloma is reported to be shorter than that of patients with other types of multiple myeloma, even if they receive autologous hematopoietic stem cell transplantation [14].

As for novel agents in IgE myeloma, only six reports have described cases treated with a bortezomib-based regimen and four reports with a lenalidomide-based regimen [10, 15–19]. However, because most patients were treated with bortezomib or lenalidomide after the myeloma had become refractory to the initial regimen, the treatment often had no effect. Only 2 cases out of 7 treated with thalidomide were reported to be controlled over the long term [9, 10, 15, 16, 19–21]. However, because one of them was consolidated by high-dose therapy and autologous hematopoietic stem cell transplantation [20], and the other was treated with an anthracycline-based regimen concurrently [9], it is difficult to assert that thalidomide played a key role in their treatment. On the other hand, no reports of IgE myeloma have described treatment with VMP regimen, and there is only one report of IgE myeloma treated with a bortezomib-based regimen as the initial treatment, which had multiple extramedullary involvements and achieved only very short-term efficacy [19].

In patients with newly diagnosed multiple myeloma who were ineligible for high-dose therapy, the original VMP regimen, which uses bortezomib at 1.3 mg/m² on days 1, 4, 8, 11, 22, 25, 29, and 32 every 6 weeks, was reported to be superior to the melphalan–prednisone (MP) regimen, the standard treatment for multiple myeloma until recently [1]. Additionally, some studies have reported that the modified weekly VMP regimen used in our case and the original VMP regimen are equally effective, with the former treatment causing less toxicity than the latter [22, 23].

Although the efficacy of maintenance therapy in newly diagnosed transplant-ineligible multiple myeloma patients is controversial, there have been two randomized control trials that showed the possible efficacy of maintenance with bortezomib. One of these trials, which administered bortezomib combined with thalidomide or prednisone as maintenance after induction with a VMP or bortezomib–thalidomide–prednisone regimen, showed that the CR rate increased from 24 % at the end of induction up to 42 % after a median follow-up of 38 months [24]. The other trial, comparing a VMP plus thalidomide regimen followed by maintenance with bortezomib–thalidomide to a VMP regimen without maintenance, did not show a significant increase in 3-year overall survival after a median follow-up of 23.2 months [22], but did show a significant increase in

5-year overall survival after a median follow-up of 54 months [25]. Although maintenance therapy following VMP regimen has not been established yet as standard of care for elderly patients, these results suggested the possibility of the efficacy of bortezomib-containing maintenance therapy.

Because of the poor prognosis of the disease and the efficacy and tolerability of the regimen in patients with other types of myeloma, we hypothesized that administration of the modified VMP regimen as the initial treatment for a patient with IgE myeloma was reasonable. Although our current patient experienced a favorable outcome by treatment with VMP regimen, further studies are required to form definitive conclusions on the ability of this therapeutic regimen to prolong the survival of patients with IgE myeloma.

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

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