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LETTER TO THE EDITOR

Rapid complete remission in multiple myeloma with bortezomib/thalidomide/dexamethasone combination therapy following development of tumor lysis syndrome

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To the editor

We describe a myeloma patient who achieved a rapid complete remission after the onset of tumor lysis syndrome after the first dose of bortezomib. A 62-year-old woman was diagnosed to have plasmacytoma of the right femur in 2003 presenting with pathological fracture. She received three cycles of VAD followed by local irradiation in Mainland China. She was in complete remission with absence of monoclonal gammopathy in the serum or urine since then. She defaulted follow-up but presented in late 2006 to our hospital, complaining of backache and malaise. Serum protein electrophoresis was negative but serum immunoglobulins G, A and M were all suppressed. Serum-free lambda light chain measured 6,320 mg/L (normal: 5.71–26.3 mg/L) with kappa/lambda ratio of 0.0021 (normal: 0.26–1.65), and urine protein electrophoresis showed monoclonal gammopathy. Serum creatinine was within normal limits and serum calcium measured 2.85 (normal: 2.24–2.63 mmol/L). Serum lactate dehydrogenase (LDH) was 320 U/L (normal < 400 U/L) and urate measured 340 μmol/L (normal: 220–520 μmol/L). Bone marrow examination showed 66% of plasma cells. Skeletal survey and magnetic resonance imaging (MRI) of the bone showed multifocal bone lesions, consistent with Durie Salmon stage III lambda light chain multiple myeloma. In view of relapsed light chain multiple myeloma, she received bortezomib (1.3 mg/m^2 on days 1, 4, 8 and 11), thalidomide 200 mg/day and dexamethasone 20 mg/day (days 1–4 and 8–11). She was admitted after the first dose of bortezomib because of fever of 38°C 8 h after bortezomib infusion. Blood culture was negative. Serum biochemistry showed mildly deranged renal function with elevated creatinine from 50 μmol/L (normal: 45–82 μmol/L) prior to bortezomib to 98 μmol/L. Serum urate level rose from 340 to 694 μmol/L and LDH from 320 to 4619U/L. (Fig. 1). Her creatinine and LDH gradually returned to normal level within 1 week, and the chemotherapy of bortezomib, thalidomide and dexamethasone was administered as scheduled. Two weeks after commencement of bortezomib, serum-free lambda light chain dropped to 21 mg/L (normal 5.71–26.3 mg/L) with normalization of kappa/lambda ratio (Fig. 1). Immunofixation of urine showed absence of M-protein. She has completed three cycles of bortezomib, thalidomide and dexamethasone. She remained in complete remission (CR) with reassessment showing normal free light chain levels, normal kappa/lambda ratio, absence of monoclonal protein in serum and urine by immunofixation, and repeat bone marrow examination showed 3% plasma cells only.

Recent clinical trials confirmed the efficacy of bortezomib in multiple myeloma (MM) [1]. The efficacy of bortezomib in refractory and relapsed MM was demonstrated in both phase II (summit trial) and phase III trial (Apex Trial) [2]. More recently, a very high CR and near CR rate of 43% was reported in elderly patients using bortezomib in combination with melphalan and prednisolone as first line treatment [3], thereby attesting the superior efficacy of bortezomib in less-heavily treated or untreated patients. Therefore, bortezomib is not only effective in patients with relapsed/refractory MM, it is also more effective in previously untreated patients.

MM is characterized by a low proliferative index with less than 1% plasma cells engaging in cellular proliferation

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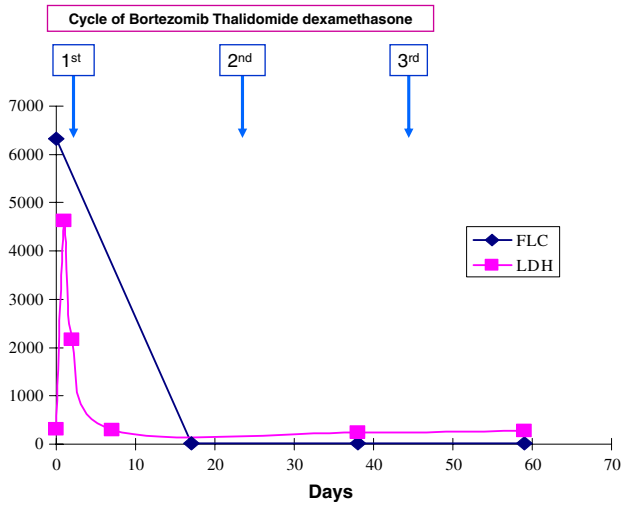

Fig. 1 Figure showing rapid decline and surge of serum-free light chain (FLC; mg/L) and serum lactate dehydrogenase (LDH; U/L) levels after the first bortezomib infusion. The timing of first, second and third cycles of bortezomib combinations was charted

[4]. Therefore, tumor lysis syndrome (TLS) has been rarely encountered during chemotherapy treatment of MM.

TLS is rare in myeloma patients receiving conventional alkylator therapy, which might be explained by the low proliferative activity of the plasma cells. In general, less than 1% tumor cells in MM are engaged in cellular proliferation [4]. However, TLS has been reported occasionally with the use of bortezomib in myeloma patients with high tumor load or aggressive extramedullary disease [5, 6]. This disparity might be explained by the fact that chemotherapy targets proliferating tumor cells while bortezomib targets tumor cells with constitutively activated NF-κB that occurs in myeloma plasma cells [7]. Moreover, tumor lysis might be enhanced by the combined use of bortezomib, thalidomide and dexamethasone. Therefore, tumor lysis prophylaxis is warranted in patients with high tumor load treated with bortezomib in combination with other therapeutic agents.

Finally, ours is the first case showing immunifxation-negative CR (based on the normalization of serum-free light chain levels and negative immunofixation of urine) after the first cycle of bortezomib.

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