LETTER TO EDITOR

Optimal dosing of high-dose melphalan prior to autologous hematopoietic stem cell transplantation in a patient with AL amyloidosis and a solitary kidney

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High-dose melphalan with autologous hematopoietic stem-cell transplantation (HDM/SCT) prolongs survival and induces hematologic and clinical responses in selected patients with light-chain (AL) amyloidosis \cite{1}. The optimal dosing of melphalan in patients with a solitary functioning kidney (SFK) and preserved glomerular filtration rate (GFR) is unknown.

A 56-year-old Caucasian woman underwent left total nephrectomy in 2007 due to complications of pyelonephritis. She was found to have an M-protein spike during routine health screening in 2008 and was diagnosed with IgG-lambda monoclonal gammopathy of unknown significance. In 2012, she developed easy bruising, leg swelling, and periorbital ecchymosis, followed by macroglossia, enlarged submandibular glands, and orthostatic hypotension. Further investigation revealed nephrotic range proteinuria (5.9 g/d). Kidney function measurements were: creatinine 0.82 mg/dL, creatinine clearance (CrCl) 94.9 mL/min by Cockcroft-Gault method, GFR 72.1 mL/min/1.73 m\textsuperscript{2} by Modification of Diet in Renal Disease method, and 24-h urine CrCl 87 mL/min. Periorbital skin- and fat-pad biopsies stained positive for Congo red, confirming AL amyloidosis with renal, soft tissue, autonomic nervous system, and early cardiac involvement.

The patient was treated with three cycles of CyBorD (cyclophosphamide, bortezomib, dexamethasone) leading to hematologic partial response. After comprehensive evaluation, the patient underwent stem cell mobilization with granulocyte-colony stimulating factor 16 \textmu g/kg/d × 4 days

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and $5.0 \times 10^6$ CD34$^+$ cells/kg were collected. The patient received 200 mg/m$^2$ of Melphalan IV over 2 days, in divided doses on Days -3 and -2, and stem cell infusion on Day 0. The post-SCT period was complicated by Grade 4 neutropenia, thrombocytopenia, anemia, and Grade 3 febrile neutropenia (toxicities graded according to National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0). Neutrophil engraftment and platelet engraftment was achieved at Day +10 and Day +13, respectively. Renal function parameters remained stable until Day +22 (Figure 1).

At 6 months, a very good partial hematologic response was achieved. Proteinuria had improved (4.7 g/24 h) and renal function parameters at 6 and 12 months post-HDM/SCT were at baseline (Figure 2).

This is the first report detailing the renal outcome of a patient with AL amyloidosis and a SFK who underwent HDM/SCT with melphalan 200 mg/m$^2$. Kidney function was maintained throughout the peritransplantation period and 12 months after treatment. The patient tolerated treatment well and adverse effects resolved by time of engraftment.

The optimal dose of melphalan as conditioning regimen in patients with a SFK is unknown. Patients with renal insufficiency suffer from more adverse effects. In multiple myeloma patients with renal failure, melphalan 140 mg/m$^2$ may

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**Figure 1** (a) Trend of creatinine clearance (CrCl), Cockroft-Gault method during peri-transplant period. (b) Trend of glomerular filtration rate (GFR), MDRD method, during peri-transplant period.

**Figure 2** Creatinine clearance (CrCl) and GFR (MDRD) at 0, 6, and 12 months.
have similar efficacy to 200 mg/m² [2]. However, multivariate analysis of a large AL amyloidosis series demonstrated that patients who received 200 mg/m² melphalan had better survival rates relative to those receiving lower doses [3].

Acute kidney injury (AKI) occurs in 20% of patients undergoing HDM/SCT for AL amyloidosis [4]. This rate is higher than in patients with multiple myeloma. There is lack of evidence that having a SFK is a risk factor for developing AKI in HDM/SCT. Nooka et al. [5] reported three multiple myeloma patients with SFK who safely received 200 mg/m² melphalan [5]. In AL amyloidosis, older age, heavy proteinuria, hypoalbuminemia, diuretic use, and a high urine sediment score before treatment were risk factors for kidney injury [4]. Renal dysfunction should not preclude patients from HDM/SCT, which can be effective and tolerable in selected patients with end-stage renal disease, albeit with more toxicity [6].

HDM/SCT is associated with improved survival in AL amyloidosis. This case suggests that 200 mg/m² melphalan is safe and effective in patients with a solitary kidney and preserved function.

Conflicts of interest

The authors declare no conflicts of interest.

References