High-Dose Melphalan and Autologous Bone Marrow Transplantation for Systemic AL Amyloidosis With Cardiac Involvement

To the Editor:

There is no clear effective therapy for primary systemic AL amyloidosis.1 When the disease involves heart with clinical symptoms of congestive heart failure, the median survival is terrifically short, evaluated to 6 months.2 Alkylating agent-based conventional chemotherapy for AL has been evaluated and seems beneficial in a subset of patients.3 Recently van Buren et al4 reported a clinical remission in a 32-year-old patient with AL amyloidosis after high-dose therapy including total body irradiation and cyclophosphamide followed by syngeneic bone marrow transplantation (BMT), suggesting that such procedure should improve the prognosis of this disease.4 We here report a prolonged survival and prolonged response in a 46-year-old patient with biopsy-proven AL amyloidosis, clinical symptoms of congestive heart failure, and disseminated disease treated with high-dose melphalan (HDM) and autologous (ABMT).

CASE REPORT

In August 1992, a 45-year-old female without evidence of any history of family amyloidosis and any inflammatory process presented with muscular weakness of arms and shoulders with muscular atrophy and elevated creatine kinase levels. Surgical muscular biopsy showed AL amyloidosis deposition, a type. No therapy was introduced and in January 1993, she described increased fatigue with symptoms of congestive heart failure with dyspnea and mild pretibial oedema. The chest X-ray showed general enlargement of the heart. Cineangiography showed hypokinesia of the anterolateral area of the myocardium, and echography a considerable left ventricular hypertrophy. Systolic left ventricular function was impaired with an ejection fraction of 52%. An endomyocardial biopsy specimen taken from the left ventricle showed diffuse amyloid deposition, a type. No hepatomegaly was palpable. BM investigations revealed 6% plasma cells with small amyloid deposits, but no monoclonal protein spike was detectable in the serum. Free monoclonal light chain a type was detectable in the urine, with a 24-hour protein loss evaluated to 0.5 g/d. Creatinine level was normal and no renal biopsy was performed. Hemoglobin level was normal, as well as platelet and white blood cell counts. Calceemia level was normal and there was no evidence of myeloma bone diseases.

Given the rapid progression and the poor prognosis of the disease, she received as first-line therapy in May 1993 200 mg/m² IV melphalan followed by reinfusion of ABMT procured and cryopreserved 3 weeks before, containing 10 × 10⁹ colony forming unit-granulocyte macrophage/kg. Granulocyte-colony stimulating factor was infused from day 1 posttransplantation to reduce the duration of aplasia. During hospitalization she experienced fever of unknown origin resolutive with IV broad spectrum antibiotics. The duration of neutropenia < 1,000/mm³ was 6 days, and platelet count < 50,000/mm³ 7 days, respectively. The follow-up after ABMT is now 17 months. She observed a considerable improvement of performance status with reduction of exercise-induced dyspnea and normalization of muscular strength 12 months after ABMT. She was able to work without any restriction 12 months after high-dose therapy. BM biopsy and BM aspirate were normal 3 months after ABMT, with disappearance of monoclonal λ chains and proteinuria on serial evaluations 3, 6, 12, and 17 months after ABMT. Nevertheless, despite considerable clinical improvement, left ventricular hypertrophy on echocardiogram and amyloid deposition on endomyocardial biopsy still persist 17 months after ABMT.

DISCUSSION

There are not many reported cases of regression of primary AL systemic amyloidosis with cardiac involvement. Sudden death has been reported with a doxorubicin-containing chemotherapy protocol.5 On the contrary, a recent communication has described two cases of reduction of the thickness of the interventricular septum with a new anthracyclin 4'-iodo-4'-deoxydoxorubicin among a series of eight patients with biopsy-proven AL.6 In this setting, heart transplantation seems to be ineffective.7 The team from the Mayo Clinic (Rochester, MN) suggest that alkylating agent-based conventional chemotherapy may be an interesting option but only in a very small subset of patients.7 In their experience, 5 out of 34 patients (15%) with amyloid cardiomyopathy responded to conventional doses of melphalan plus prednisone, and 2 of these 5 were alive 10 years after diagnosis. Moreover, such therapy, prolonged during more than 1 year after response, carries the risk of subsequent myelodysplastic syndrome or acute leukemia. Recently van Buren et al4 on the basis of a dose-response curve observed in plasma-cell dyscrasia, reported a clinical remission after syngeneic BMT in a patient with AL amyloidosis. Mariette et al8 also reported a complete response after high-dose therapy and autologous stem cell transplantation in a patient with light-chain deposition disease associated with multiple myeloma (MM).9 Our case is similar, and to our knowledge the first one with cardiac AL deposition treated with high-dose therapy and ABMT. Although amyloid deposits persist on endomyocardial biopsy,5 clinical remission is undoubtful with a follow-up superior to 16 months. Two hundred mg/m² IV melphalan followed by stem cell transplantation is now routinely performed in patients with MM.9 Given his low toxicity and the poor prognosis of AL amyloidosis, such therapy should be systematically considered in patients with evolutive AL disease under the age of 60.

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REFERENCES


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