

Autologous PBSCT in patients with cardiac amyloidosis

We read with interest the recent review by Gertz *et al*,¹ expressing concern about patient selection and toxicity of high-dose therapies (HDT) for patients with primary amyloidosis. Whilst we agree on many points, we would argue that measures taken to modify treatment-related morbidity and mortality, as illustrated in our following case report, may extend the applicability of HDT to poor risk patients.

Our patient, a 57-year-old male, presented with symptomatic cardiac failure which required treatment with diuretics and angiotensin converting enzyme inhibitor for 3 months prior to autologous HDT. A cardiac biopsy showed amyloid and echocardiography showed poor diastolic function as indicated by a left ventricular end diastolic pressure of 28 mmHg. His ejection fraction was 37%. A serum IgG lambda paraprotein (total IgG 18.3 g/l) was present as were trace amounts in the urine (urine protein 0.01 g/l) but a bone marrow aspirate and trephine biopsy did not show increased plasma cells or evidence of amyloidosis. Renal function was normal. Asymptomatic hepatomegaly was present with a raised bilirubin (50 $\mu\text{mol/l}$, normal <21) and a raised alkaline phosphatase (262 IU/l, normal <120) and hepatic biopsy confirmed amyloidosis. No gastrointestinal or neurological symptoms were present and biopsies of these and other organs were not performed. These features were diagnostic of primary amyloid with predominant cardiac manifestations but involvement of at least two major organ systems, predictive of both a poor prognosis without specific treatment and of high morbidity and mortality following HDT. Our patient was also a low priority candidate for cardiac allograft and we proceeded to autologous HDT

following advice from Dr Comenzo that we should consider elective patient admission to our intensive therapy unit.

Our patient was mobilised with G-CSF alone, requiring two attempts at doses of 10 $\mu\text{g/kg}$ and 16 $\mu\text{g/kg}$ with multiple aphereses collecting in total 3.5×10^6 CD34⁺ cells/kg. On day -3 the patient was admitted to ITU where a Swan-Ganz catheter was inserted to measure atrial filling pressure and cardiac output. As atrial distension is a potential cause of supraventricular tachycardias we used atrial filling pressures as a guide for intravenous fluid administration. After an intravenous fluid challenge of 500 ml over 1 h high-dose melphalan (200 mg/m²) was given fractionated over 2 days (days -3, -2) with 3 litres of fluid per day, as recent reports have questioned the need for forced diuresis after high-dose melphalan therapy.^{2,3} This was tolerated well and it was planned to fractionate DMSO cryopreserved stem cell infusions (9 bags per day) over 2 days on days 0, +1, after prophylactic amiodarone administration and modified fluid intake of 3 litres per day. However, 20 min after stem cell infusion on day 0 our patient developed cardiogenic shock which was recognised promptly and managed by discontinuation of amiodarone and treatment with dobutamine, midazolam and morphine infusions, the patient recovering slowly over the next 24 h. In view of this experience, the second planned stem cell infusion was abandoned and to hasten neutrophil recovery (CD34⁺ cells infused = $1.7 \times 10^6/l$), G-CSF 300 $\mu\text{g/day}$ was given from days +4 to +14. The Swan-Ganz catheter was removed on day +1 and the patient transferred to the bone marrow transplant ward, where the post-transplant course was marked by fluid overload responsive to diuretic therapy, severe nausea, vomiting and a single episode of uncomplicated neutropenic fever associated with Gram-positive bacillus infection. Neutrophils reached $0.5 \times 10^9/l$ on day +12 and plate-

lets reached $50 \times 10^9/l$ on day +23. The patient was discharged on day +22 and remains alive and well 3 months post HDT. An assessment at 11 weeks post HDT showed little change in performance status: Hb 102 g/l, WBC $4.2 \times 10^9/l$, neutrophils $3.1 \times 10^9/l$ and platelets $83 \times 10^9/l$ and minimal reduction in liver function tests with bilirubin 45 $\mu\text{mol/l}$ and ALP 202 U/l. However, he is starting to show evidence of haematological response with disappearance of Bence Jones proteinuria and marked reduction of his M band (total IgG 15.8 g/l).

We suspect our patient would not have survived the episode of cardiogenic shock following cryopreserved stem cell infusion had he been on our general ward. Saba *et al*⁴ report high treatment-related mortality in their series of autologous transplants for amyloidosis and recognise the 48 h following commencement of stem cells infusion as a high risk period. We would suggest that measures to limit DMSO exposure as well as those to reduce hydration with high-dose melphalan infusions combined with intensive cardiovascular monitoring with available inotropic support may reduce the high transplant-related mortality of patients with cardiac amyloid undergoing autologous HDT. It remains uncertain whether such patients will improve following high-dose melphalan but the ability to offer HDT more safely will permit the question to be answered.

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