Use of autologous stem cell transplantation in adult patients with idiopathic inflammatory myopathies: a case-report and review of the literature

Sirs,

Idiopathic inflammatory myopathies (IIM) are systemic autoimmune diseases with extremely variable and complex therapeutic approaches. Haematopoietic stem cell transplantation (HSCT) may be an option in clinical cases refractory to conventional and biological therapy (1, 2).

We report the use of HSCT in a refractory IIM adult patient and review the literature using the MEDLINE database.

A 59-year-old Caucasian female patient diagnosed with juvenile dermatomyositis age 9 years was treated successfully with steroids and several imunosuppressive drugs including methotrexate and azathioprine. She re-presented in July 2000 after 10 years of disease quiescence. Her skin rash had reappeared and her proximal muscle weakness had recurred, grade 4/5 on Medical Research Council (MRC) scale, the creatine kinase (CK) rose from normal to 332 IU/l (normal range 26–140 IU/l), the erythrocyte sedimentation rate was 37 mm/h (normal <20 mm/h), the c-reactive protein was 17 mg/l (normal <5.0 mg/l) and her immunology remained negative. The upper limb electromyography showed myopathic features without neurogenic changes. The upper arm and upper leg magnetic resonance imaging demonstrated diffuse and moderate inflammatory changes and muscle biopsy confirmed the diagnosis. She was started on steroids and methotrexate, but changed to azathioprine after two years, because of a decrease in response. In April 2004, given the clinical deterioration, intravenous immunoglobulin (IVIG) was prescribed but there was no improvement. Rituximab (1gx2) with methylprednisolone was then administered. Although no real change in her CK was observed, she felt stronger for a period of about 2 years. Tacrolimus was then started with moderate benefit. In November 2010, after further deterioration and CK increase to 656 IU/l, the use of HSCT or cyclophosphamide were discussed with the patient, who opted to try HSCT. Based on local protocols, granulocyte-colony stimulating factor at 10 mcg/kg/day for 4 days was used for peripheral blood stem cells (PBSC) mobilisation and after BEAM myeloablative conditioning regimen (carmustine, cytarabine, melphalan, etoposide), $3.5x10^6$ CD34+ autologous stem cells/kg collected by apheresis were infused. Severe sepsis due to *Escherichia coli and Streptococcus salivaris* and exuberant oropharyngeal candidiasis developed and was managed with appropriated antimicrobial therapy. The patient was discharged with complete blood count recovery and was subsequently assessed by clinical history, muscle strength grade and laboratory tests. A muscle strength improvement (grade 5/5 on MRC scale) and normalisation of the CK and inflammatory markers was noted. However, a year later, a recurrent clinical deterioration and progressive increase CK to 562 IU/l led to tacrolimus prescription with moderate benefit.

Thus, assessing the clinical history, the clinical examination and the laboratory tests, we report a clinical case with a different outcome to the four described in the literature (Table I) (3-6). Regardless of sample heterogeneity and the paucity of data in the published reports, it seems that older patients may have a worse prognosis. We did not find any significant difference in the immunosuppressive drugs used before HSCT. There seems to be little difference in outcome comparing high (patient 1, 4 and 5) and less (patient 2 and 3) intensive conditioning regimens, although the numbers reported so far are small. However, it is possible that regimens containing cyclophosphamide may be associated with beneficial outcome. Complications were common and severe.

Although many therapeutic "possibilities" exist, alternative strategies in the management of refractory disease are still required. Further studies on autologous stem cell transplantation in adult patients with IIM are needed to identify eligibility criteria, the best mobilisation and conditioning regimen and some outcome predictors.

Table I. Characteristics of adult patients with idiopathic inflammatory myopathy who have had autologous peripheral blood stem cell transplantation.

	Age (yrs)	Sex	Diagnosis	Auto antibodies	Drugs used before HSCT	Mobilisation regimen	Conditioning regimen	Complications	Outcome (follow-up)	Reference
1	28	F	PM	Jo-1	Steroids, AZA, MTX, CYC,	CYC Etoposide, G-CSF	Busulphan, CYC, ATG	ARDS, Haemorrhagic cystitis, CMV reactivation	Improved (15 months)	3
2	38	F	PM	Jo-1	Steroids, AZA, CYC, IVIG, CsA, Plasmapheresis	CYC, G-CSF	CYC	MAC subcutaneous abscess	Slowed progression (24 months)	4
3	54	F	DM	–	Steroids, CsA, CYC	CYC, G-CSF	CYC	Listeriosis, CMV reactivation	Improved (12 months)	5
4	32	M	PM	SRP	Steroids, AZA, CsA, MMF, IVIG, CYC, Alemtuzumab, Infliximab	CYC, G-CSF	CYC, TBI	–	Improved (36 months)	6
5	59	F	JDM	–	Steroids, MTX, AZA, IVIG, RTX, Tacrolimus	G-CSF	BEAM	Severe sepsis, Candidiasis (12 months)	Not improved	This report

ARDS: acute respiratory distress syndrome; ATG: anti-thymocyte globulin; AZA: azathioprine; BEAM: carmustine, cytarabine, melphalan, etoposide; CMV: cytomegalovirus; CsA: cyclosporine; CYC: cyclophosphamide; DM: dermatomyositis; F: female; G-CSF: granulocyte colony stimulating factor; HSCT: hematopoietic stem cell tranplantation; IVIG: intravenous immunoglobulin; JDM: juvenile dermatomyositis; M: male; MAC: Mycobacterium avium complex; MMF: mycophenolate mofetil; MTX: methotrexate; PM: polymyositis; RTX: rituximab; SRP: signal recognition particle; TBI: total body irradiation.

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Competing interests: none declared.

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