Autologous Haematopoietic Stem Cell Transplantation for Refractory Rheumatic Diseases

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Recently Lee et al. [1] published an interesting article that the long-term outcomes of autologous peripheral blood stem cell transplantation (PBSCT) to treat refractory rheumatic diseases. They assessed 11 Korean patients who underwent PBSCT for refractory rheumatic diseases between 2002 and 2005 for outcomes including treatment response, adverse events, damage accrual, and survival. Overall 10-year survival rate was 70% with a 40% recurrence rate and 20% treatment-related mortality rate. Their overall prognosis was not substantially different from previous reports [2-4].

Hematopoietic stem cell transplantation (HSCT) has been proposed as an effective alternative treatment for refractory rheumatic diseases. The first treatment with autologous HSCT in a patient with rheumatic disease was described in 1996 [5]. Following the study, further autologous HSCT were performed, many under the framework of the European Society for Blood and Marrow Transplantation (EBMT)/European League Against Rheumatism autoimmune disease stem cell project [6]. The EBMT registry now comprises over 1,800 HSCT procedures performed to treat severe rheumatic diseases, including systemic sclerosis (SSc), systemic lupus erythematosus (SLE), rheumatoid arthritis, juvenile idiopathic arthritis, and Sjögren’s syndrome [7]. The aim of HSCT in autoimmune disease is the eradication of autoreactive immune cells and the regeneration of a naive, self-tolerant immune system [8]. To date, a variety of mechanisms have been proposed to explain the clinical effects (“immune reboot”) of autologous HSCT in severe autoimmune diseases. Whereas a “debulking of inflammation” is an instantaneous and predictable effect of any high-dose cytotoxic conditioning regimen, sustained clinical responses are best explained by long-term alterations in immune reconstitution via thymic and/or extrathymic pathways. Shifts in T- and B-cell subpopulations from memory to naive cell dominance, with restoration of polyclonal T-cell receptor (TCR) diversity, correction of immune gene expression abnormalities, and other changes in T cells, B cells, plasmablasts, and natural killer cells support immune re-education and tolerization with autologous HSCT [9]. HSCT renews the CD4+ T cell compartment and the Treg cell population, which is accompanied by an increase in the number of Treg cells and the re-establishment of TCR diversity and function. The thymus is likely to have an important role in restoring this immune balance. Also, following transplantation, the B cell compartment becomes naive and the number of autoreactive antibodies decreases [7]. Clinical remission in autoimmune disease after HSCT is the result of a true reconfiguration of the immune system instead of long-term immunosuppression.

There is now sufficient evidence that HSCT can result in significant improvement of skin thickness and functional ability in SSc [10], while the recently completed Autologous Stem Cell Transplantation International Scleroderma trial demonstrated that HSCT can also prolong survival in selected patients with diffuse cutaneous SSc when compared with IV pulse cyclophosphamide [11]. In patients with SSc, autologous HSCT results in increased treatment-related mortality within the first year but a considerable long-term, event-free survival benefit.
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minal reconfiguration of the adaptive immune system
[12]. This notion is reflected by a significant decrease or
or even disappearance of autoantibody levels (including an-
ti-dsDNA, anti-phospholipid and antinuclear antibodies),
where chronic immunosuppression had been ineffective.
Autologous HSCT is worth emphasizing in terms of its
curative potential for treatment. The advantage of autolo-
gous HSCT is the almost complete ablation of the autor-
eactive memory for the resetting of the immune system
becoming tolerant to self that can provide sustained re-
mission in the absence of chronic immunosuppression
[12]. Compared to continued insufficient or failed chron-
immunosuppression, early use of autologous HSCT has
the potential to protect against organ-failure and tox-
icity-related morbidity, improve quality of life and reduce

However, autologous HSCT requires a careful selection
of patients according to rheumatic diseases, consid-
eration of therapeutic alternatives, risks and benefits, and
the expertise of the transplantation team. The results of
autologous HSCT depend on better patient selection,
center effect, transplantation early in the disease course
and preemptive infection and other supportive therapies.

In addition to autologous HSCT, mesenchymal stem
cells (MSCs), might also have potential for rheumatic dis-
ease treatment. MSCs have potent immunoregulatory
and anti-inflammatory properties. The relative ease of
harvesting MSCs and their stable phenotype in culture
make the cells an attractive tool for cellular therapy in al-
loimmunity, autoimmunity, and inflammation [16]. This phenomenon has led to an increasing number of clinical
trials. Recently clinical trials with this goal are ongoing in
patients with rheumatic diseases. Further studies are nec-
essary to ascertain the concept of MSCs in order to estab-
lish the treatment strategy for use in rheumatic diseases.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article
was reported.

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