Editorial

Emerging value of stem cell therapy in rheumatic diseases

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Rheumatic Diseases (RDs) including Rheumatoid Arthritis (RA) and osteoarthritis, are characterized by immune dysregulation and chronic progressive inflammation that leads to irreversible joint damage[1]. Recently, research has focused on Mesenchymal Stem Cells (MSCs) application in RDs due to their low immunogenicity and immunomodulatory properties[2]. MSCs have been widely investigated in RDs not only for their immunomodulatory action but also owing to their regenerative properties and therapeutic potency[1]. Activated T lymphocytes play an important role in the pathogenesis of RD. MSCs possess immunoregulatory activities but such functions of MSCs from bone marrow of Systemic Lupus Erythematosus (SLE), Systemic Sclerosis (SSc), and Ankylosing Spondylitis (AS) patients are impaired. Adipose tissue-derived MSCs are an optional pool of therapeutically useful MSCs, but biology of these cells in RD is poorly known[3].

Mesenchymal stem cells have a therapeutic potential in Rheumatoid Arthritis (RA) due to their immunomodulatory and differentiation effects[4]. Circulating interferon-γ (IFN-γ) was found to improve the clinical efficacy of MSC therapy in patients with RA[5]. Moreover, there was a sufficient immunoregulatory effect of autologous MSCs on regulatory T cells in patients suffering from refractory RA[6].

In the last years, a considerable progress has been made in the treatment of spondyloarthritides. Nonetheless, there remains a considerable number of patients who are unresponsive to all current therapies[2]. As MSCs can dampen inflammation and play an effective role in osteoarthritis, it was expected to be a potential solution for numerous human conditions. However, in RA and Spondyloarthritis (SpA), subsets of MSCs might conversely fuel synovitis and enthesitis[7].

Stem cell therapy has been proved to be an effective therapeutic approach to treat Systemic Lupus Erythematosus (SLE), the detailed underlying mechanisms are not fully understood[8]. Intra-renal injection of human bone marrow derived mesenchymal stem cells is a promising route for treatment of lupus nephritis in mice[9].

Haematopoietic Stem Cell Transplantation (HSCT) can cure Chronic Granulomatous Disease[10] and MSC infusion might be a potentially successful therapy for intractable drug-resistant Behcet disease patients with concomitant leg ulcer[11].

In Systemic Sclerosis (SSc), determined tissue repair leads to progressive fibrosis of the skin and internal organs. The key roles of Mesenchymal Stem Cells (MSCs) include initiating and regulating tissue repair[12]. MSCs represent a promising therapeutic advance due to their trophic and pleiotropic properties. MSCs display anti-fibrotic, angiogenic, and immunomodulatory actions that are imperative in the treatment of SSc[13]. The diversity in extent, severity, and progression of skin and internal organ involvement gives rise to challenges in determining optimal therapeutic options for SSc as disease modifying anti-rheumatic drugs (DMARDs) are lacking. In this scenario, it is not surprising that SSc was one of the first autoimmune diseases challenged with high-dose immunosuppressive treatment and stem cell therapy[14]. Since stem cell-based treatments have developed as a novel approach to rescue from several autoimmune diseases, it seems that stem cells, especially MSCs as a powerful regenerative tool can also be advantageous for SSc treatment via their remarkable properties including immunomodulatory and anti-fibrotic effects[15]. MSCs are characterized by a broad availability and no or low acute toxicity[16].

Mesenchymal Stem Cells (MSCs) have been demonstrated to exert great potential in the treatment of various autoimmune diseases. Although MSCs is an effective therapeutic approach for Sjögren Syndrome (SS), the underlying mechanisms are still elusive17. MSCs have been revealed to suppress CD4 + T cell activation and autoimmunity in both mouse models and patients with primary SS[18].

MSC-based cell therapy is a relatively safe treatment that holds great potential for Osteoarthritis (OA), evidenced by a positive effect on pain and knee function for a short term[19,20]. Using low-dose (25 million) and adipose-derived stem cells is likely to achieve better results[19]. In spite

that using stem cell therapy for knee osteoarthritis helps in pain improvement, but its effect on cartilage regeneration has not yet been explored[21].

In the near future, MSC therapy may be considered a potentially promising therapeutic option added to the management armamentarium of many rheumatic diseases.

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