The Prospect of Stem Cell Therapy in Multiple Sclerosis

Multiple sclerosis is a multifocal inflammatory disease of the central nervous system that generally affects young individuals, causing paralysis of the limbs, sensation, visual and sphincter problems. The disease is believed to occur by an autoimmune mechanism: the immune system produces antibodies and cells that attack the self myelin antigens, causing demyelination. Damage to this myelin sheath protecting the nerve cells in the brain and spinal cord leads to retardation, distortion, or loss of messages from the brain and presents as a relapse of neurological disability, a flare-up of symptoms lasting anywhere from 24 hours to several months. Damage or destruction of these important axons (nerve fibers) over time can also lead to irreversible neurodegeneration, causing progression of the disease and an increase in disability. Although current immunotherapies (like Copaxone and interferons) downregulate the autoimmune anti-myelin reactivity and reduce the rate of relapses, there is no effective means today to stop the progression of disability or induce rebuilding of the destroyed myelin (Mesenchymal Stem Cells for the Treatment of MS).

From what is currently understood about the interactions between stem cells and Multiple Sclerosis, there are two main functions for which stem cell therapies might be developed. In simple terms, these two are preventing immune damage to the nervous system and repairing the myelin sheath that has already been damaged. These therapies would serve to protect the nerve fibers in side of the myelin sheath. In the future, it is hoped that stem cells could be

used to rebuild lost nerve fibers although this seems a bit ambitious with the current status of stem cell research (Stem Cell Therapies in MS).

To achieve the two functions described above, many types of stem cells could be used. Currently, several types of stem cells have shown potential benefit after extensive study in Experimental Autoimmune Encephalomyelitis (EAE), an animal model that mimics MS. These types include Hematopoietic Stem Cells (HSCs), Mesenchymal Stem Cells (MSCs), Neural Stem Cells (NSCs), Embryonic Stem Cells (ESCs), and Induced Pluripotent Stem Cells (iPSCs). HSCs, adult stem cells found in bone marrow and blood, are being trialled in highly active forms of MS where it is thought that, through their immunomodulatory effects, they help prevent damage to myelin. MSCs, adult stem cells found in bone marrow, skin, and fat tissue, provide a similar immunomodulatory effect while also promoting the nervous system's endogenous remyelination mechanisms. NSCs are the cells primarily responsible for repairing myelin in the brain. Their loss of function in MS has prompted two possible solutions: develop drugs to improve endogenous NSC function or transplant new cells capable of completing the repairs the resident cells cannot. It is believed that NSCs have the same effects observed in studies with MSCs, but because of the difficulty of harvesting cells from the brain, fetal stem cells are used in clinical trials. ESCs can naturally produce any cell type in the body and iPSCs can be induced to do the same but it is currently controversial whether these cells can be used to treat MS as both have the potential to become tumors (Stem Cell Therapies in MS).

Because there are so many types of MS and so many possible stem cell treatments, shifting focus to a current clinical study concerning the potential of MSCs in treating Secondary Progressive Multiple Sclerosis will allow for a closer investigation of the applicability of stem cells in treating the disease. Within the last five years, the University of Cambridge, the Royan Institute, and the Hadassah Medical Organization have initiated a clinical study to query the efficacy of MSCs to induce immunomodulatory and neurogenerative effects. These bone marrow-derived stromal cells were shown to induce similar effects to NSCs in the EAE animal model and are clinically advantageous since they can be obtained from the patient's bone marrow (autologous transplantation), alleviating the worry concerning rejection of donor cells, and require no modification. The researchers also commented that, in addition, MSCs carry a safer profile and are less prone to malignant transformation than NSCs (Mesenchymal Stem Cells for the Treatment of MS).

Out of the three groups mentioned earlier to have started a clinical trial within the past five years, only the group working in Cambridge completed their trial. This group, along with publishing a paper on their results, established a protocol for extracting bone marrow cells from which they selected and assessed the identity of the MSCs. This protocol was in compliance with the guidelines set up by the European Group for Blood and Bone Marrow Transplantation developmental committee and the MSCs were characterized according to the International Society of Cellular Therapy recommendations (Connick et al 2011). Ten participants with Secondary Progressive Multiple

Sclerosis and eight healthy controls were recruited for the study and MSCs were successfully isolated, expanded, and characterized in vitro for all participants in the treatment arm. Participants received intravenous doses of autologous MSCs at a dose of 1-2 x 10^6 cells/kg for six months. Using clinical, neurophysiological, and imaging assessments, the group found that this dose is both safe and feasible as a treatment for MS. They also developed a model of the disease process in MS by looking at deficits in the anterior visual pathways. Deemd the "sentinel lesion" approach, the groups asserts this methodology is a novel detector of neuroprotective agents in MS. They look to further studies to test the efficacy of this regimen, as their sample size was too small to ascertain the protocol's efficacy without introducing bias (Connick et al 2011).

Although we are not yet at the point of understanding how stem cells might definitively be used clinically to resolve various diseases phenotypes, the research being conducted to learn which stem cells work to mitigate certain diseases is incrementally bringing us closer to that goal. The wealth of understanding in basic stem cell biology nominates many stem cell candidates to treat Multiple Sclerosis clinically, although few clinical trials have gone to completion and provided consistent results. Looking at a recently conducted clinical study in patients with Secondary Progressive Multiple Sclerosis, it seems the effects of bone marrow-derived MSCs are yet to be fully described, though their safety and feasibility might someday bring them to the bedside.

Works Cited

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