Success With Stem Cell Transplant in Myasthenia Gravis

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Seven patients with severe myasthenia gravis who received autologous hematopoietic stem cell transplants have experienced long-term remission that has been symptom and treatment free for many years.

"We are always reluctant to talk about this type of disease being cured, but these patients have all been disease free without any maintenance therapy since the procedure, which is very encouraging," one of the treating physicians, Harold Atkins MD, University of Ottawa, Ontario, Canada, toldMedscape Medical News.

Dr Atkins and colleagues describe their findings in a paper[published online](http://archneur.jamanetwork.com/article.aspx?articleid=2506781) in JAMA Neurology.

"While autologous hematopoietic stem cell transplants have been successfully used in other autoimmune conditions, such as multiple sclerosis, this is the first time this treatment has been described in myasthenia gravis, to our knowledge," Dr Atkins said.

"The key point with stem cell transplant is that we are not just globally suppressing the immune system, as is the case with usual drug therapies for autoimmune condition. We are instead wiping out the malfunctioning immune system and allowing a new one to grow that is functioning properly by using the patient's own stem cells, which have not yet developed the autoimmune memory," he explained.

The procedure has been associated with remarkable results. Since the current paper was submitted, another patient has been treated, bringing the total to eight. All eight have remained completely symptom free on no further treatment, and the first patient treated is now at 13 years post-procedure.

**"A Grueling Procedure"**

However, despite these impressive results, this therapy is not suitable for mainstream use.

"It is a grueling procedure which carries significant risks, so will only be suitable for very severe patients who have run out of other options," Dr Atkins comments. "Most myasthenia gravis patients can be controlled on drug therapy, and this is not appropriate for them. Because the immune system is eliminated with very-high-dose chemotherapy during stem cell therapy, this brings about many toxic side effects and carries a small risk of death, so patients really do have to be having regular myasthenia crises and be refractory to all other therapies before considering this. But for some of these patients it is a promising option."

The seven patients reported in the current paper had a mean age of 44 years. They all had persistent severe or life-threatening myasthenia gravis-related symptoms despite continued use of intensive immunosuppressive therapies.

Autologous hematopoietic stem cell grafts were mobilized with cyclophosphamide and granulocyte colony-stimulating factor, collected by peripheral blood leukapheresis, and purified away from contaminating lymphocytes using CD34 immunomagnetic selection. Patients were treated with intensive conditioning chemotherapy regimens to destroy the autoreactive immune system, followed by graft reinfusion for blood and immune reconstitution.

All patients achieved durable complete stable remission with no residual myasthenia gravis symptoms and freedom from any ongoing therapy.

**Side Effects**

In terms of side effects, three patients experienced transient viral reactivations, and one developed a secondary autoimmune disease after stem cell therapy, but all of these resolved or stabilized with treatment. There were no treatment- or myasthenia-related deaths.

The researchers note that the side effects in their patients so far have been manageable, but in other populations undergoing stem cell transplants the conditioning regimen and the associated immunosuppression have led to opportunistic infections and cardiac, renal, or other organ toxic effects. Late complications may involve endocrine dysfunction, including gonadal failure, infertility, and thyroid dysfunction. Immune dysregulation can lead to viral reactivations, secondary malignant tumors, and secondary autoimmune disease.

In addition, although there was no transplant-related mortality in the current cohort, large registry data have shown mortality rates of 6% to 8% for recipients of autologous hematopoietic stem cell transplants for autoimmune diseases, but this can be reduced to 1% to 5% with improved supportive care, patient selection, and increasing center-specific experience, the authors state.

They conclude that: "The role of autologous hematopoietic stem cell transplants for myasthenia gravis warrants further exploration with prospective testing."

Dr Atkins told Medscape Medical News that his group is continuing to explore other autoimmune diseases for which such therapy may be effective. "It won't work for all autoimmune conditions — for example it doesn't seem to work well in inflammatory bowel disease. There seems to an interplay of genetics and environmental triggers at play in these conditions which determine how well this treatment works.

"We are also looking for ways to make the treatment better tolerated, with more supportive care measures," he added.

**Many Questions Remain**

In an [accompanying editorial](http://archneur.jamanetwork.com/article.aspx?articleid=2506776), Daniel B. Drachman, MD, Johns Hopkins School of Medicine, Baltimore, Maryland, says the apparent success of the treatment raises many questions.

"Were these patients truly refractory? Have they been cured? What are the risks of autologous hematopoietic stem cell transplant? Which patients meet the criteria for treatment?" he writes.

He stresses that autologous hematopoietic stem cell transplant is an invasive procedure and should be performed only in a facility with the infrastructure and personnel capable of caring for immunologically compromised patients and skilled in the treatment of myasthenia gravis.

Dr Drachman concludes that the current report represents proof of the principle that autologous hematopoietic stem cell transplant can be used to treat severe myasthenia gravis. However, its application will require careful evaluation of the severity of the condition, the level of response to the most appropriate modern immunologic treatment, and the risks and benefits of the procedure.

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