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UI Health validates cure for sickle cell in adults

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Physicians at the University of Illinois Hospital & Health Sciences System have cured 12 adult patients of sickle cell disease using a unique procedure for stem cell transplantation from healthy, tissue-matched siblings.

The transplants were the first to be performed outside of the National Institutes of Health campus in Maryland, where the procedure was developed. Physicians there have treated 30 patients, with an 87 percent success rate. The results of the phase I/II clinical trial at UI Health, in which 92 percent of treated patients were cured, are published online in the journal *Biology of Blood & Marrow Transplantation*.

The new technique eliminates the need for chemotherapy to prepare the patient to receive the transplanted cells and offers the prospect of cure for tens of thousands of adults suffering from sickle cell disease.

About 90 percent of the approximately 450 patients who have received stem cell transplants for sickle cell disease have been children. Chemotherapy has been considered too risky for adult patients, who are often more weakened than children by the disease.

"Adults with sickle cell disease are now living on average until about age 50 with blood transfusions and drugs to help with pain crises, but their quality of life can be very low," says Dr. Damiano Rondelli, chief of hematology/oncology and director of the blood and marrow transplant program at UI Health, and corresponding author on the paper.

"Now, with this chemotherapy-free transplant, we are curing adults with sickle cell disease, and we see that their quality of life improves vastly within just one month of the transplant," said Rondelli, who is also the Michael Reese Professor of Hematology in the UIC College of Medicine. "They are able to go back to school, go back to work, and can experience life without pain."

Sickle cell disease is inherited. It primarily affects people of African descent, including about one in every 500 African Americans born in the U.S. The defect causes the oxygen-carrying red blood cells to be crescent shaped, like a sickle. The misshapen cells deliver less oxygen to the body's tissues, causing severe pain and eventually stroke or organ damage.

Doctors have known for some time that bone marrow transplantation from a healthy donor can cure sickle cell disease. But few adults were transplanted because high-dose chemotherapy was needed to kill off the patients' own blood-forming cells—and their entire immune system, to prevent rejection of the transplanted cells, leaving patients open to infection.

In the new procedure, patients receive immunosuppressive drugs just before the transplant, along with a very low dose of total body irradiation—a treatment much less harsh and with fewer potentially serious side effects than chemotherapy.

Next, donor cells from a healthy and tissue-matched sibling are transfused into the patient. Stem cells from the donor produce healthy new blood cells in the patient, eventually in sufficient quantity to eliminate symptoms. In many cases, sickle cells can no longer be detected. Patients must continue to take immunosuppressant drugs for at least a year.

In the reported trial, the researchers transplanted 13 patients, 17 to 40 years of age, with a stem cell preparation from the blood of a tissue-matched sibling. Healthy sibling donor-candidates and patients were tested for human leukocyte antigen, a set of markers found on cells in the body. Ten of these HLA markers must match between the donor and the recipient for the transplant to have the best chance of evading rejection.

In a further advance of the NIH procedure, physicians at UI Health successfully transplanted two patients with cells from siblings who matched for HLA but had a different blood type.

In all 13 patients, the transplanted cells successfully took up residence in the marrow and produced healthy red blood cells. One patient who failed to follow the post-transplant therapy regimen reverted to the original sickle cell condition.

None of the patients experienced graft-versus-host disease, a condition where immune cells originating from the donor attack the recipient's body.

One year after transplantation, the 12 successfully transplanted patients had normal hemoglobin concentrations in their blood and better cardiopulmonary function. They reported less pain and improved health and vitality.

Four of the patients were able to stop post-transplantation immunotherapy without transplant rejection or other complications.

"Adults with sickle cell disease can be cured without chemotherapy - the main barrier that has stood in the way for them for so long," Rondelli said. "Our data provide more support that this therapy is safe and effective and prevents patients from living shortened lives, condemned

to pain and progressive complications."

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