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Democracy Dies in Darkness

Longtime HIV patient is effectively cured after stem cell transplant

The man is among a handful who have gone into remission after the procedure, but it is not an option for most people with the virus

By Mark Johnson
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A 66-year-old man with HIV is in long-term remission after receiving a transplant of blood stem cells containing a rare mutation, raising the prospect that doctors may someday be able to use gene editing to re-create the mutation and cure patients of the virus that causes AIDS, a medical team announced Wednesday.

For now, the crucial virus-defeating mutation is rare, leaving the treatment unavailable to the vast majority of the 38 million patients living with HIV, including over 1.2 million in the United States. Bone marrow transplants also carry significant risk and have been used only on HIV patients who have developed cancer.

The patient, who had lived more than half his life with the virus, is among a handful of people who went into remission after receiving stem cells from a donor with the rare mutation, said doctors from City of Hope, a cancer and research center in Duarte, Calif., who treated him.

“This is one step in the long road to cure,” said William Haseltine, a former Harvard Medical School professor, who founded the university’s cancer and HIV/AIDS research departments. Haseltine, now chairman and president of the nonprofit think tank Access Health International, was not involved in the City of Hope case.

While the announcement at the 24th International AIDS Conference in Montreal does not have immediate implications for most people living with HIV, it continues the long, slow progression of treatment that began with federal approval of the drug AZT in 1987, advanced a decade later with the use of protease inhibitors to reduce the virus in the body, and went further in 2012, with the approval of PrEP, which protects healthy people from becoming infected.

As a result of those developments, an HIV patient diagnosed at around age 20 today can receive antiretroviral therapy and live another 54 years, according to a 2017 study in the journal AIDS.

“When I was diagnosed with HIV in 1988, like many others, I thought it was a death sentence,” said the City of Hope patient, who asked not to be identified, in a statement shared by the hospital. “I never thought I would live to see the day that I no longer have HIV.”

The man received the transplant in early 2019 but continued taking antiretroviral therapy until he had been vaccinated against covid-19. He has been in remission for almost a year and a half.

“He’s doing great,” said Jana T. Dickter, an associate clinical professor in the division of infectious diseases at City of Hope, who presented the data at the conference. “He’s in remission for HIV.”

Dickter said the patient is being treated for painful ulcers in his mouth caused by the donor’s stem cells attacking his tissue.

The patient received the transplant from an unrelated donor in 2019, after being diagnosed with acute myelogenous leukemia. His doctor at City of Hope chose donor stem cells that had a genetic mutation found in about 1 in 100 people of northern European descent.

Those having the mutation, known as CCR5-delta 32, cannot be infected by HIV because it slams shut the doorway used by the virus to enter and attack the immune system. That doorway is the cell receptor CCR5, which the virus uses to enter white blood cells that form an important part of the body’s defense against disease.

The City of Hope patient is among a small, select group of HIV patients to go into remission after receiving such a transplant.

“This is probably the fifth case in which this type of transplant appeared to cure someone. This approach clearly works. It’s curative and we know the mechanism,” said Steven Deeks, a professor of medicine at the University of California at San Francisco, who cared for the first such patient, Timothy Ray Brown. In 2007, Brown was cured by a medical team in Berlin using a transplant from someone who had the same mutation.

Following the transplant, Brown no longer had a detectable level of HIV in his blood. He was known as “the Berlin patient” until he released his name in 2010 and moved to San Francisco.

“I will not stop until HIV is cured,” Brown vowed in a 2015 essay in the journal AIDS Research and Human Retroviruses. Brown died in September 2020 of leukemia unrelated to his HIV. He was 54.

Similar successes followed in patients in London, New York and Düsseldorf, Germany.

“It is yet another case that resembles Timothy Brown from years ago,” said David D. Ho, one of the world’s leading AIDS researchers and director of the Aaron Diamond AIDS Research Center at Columbia University. “There are several others as well, each using approaches that are not feasible for most infected patients.”

The other patients also received bone marrow transplants, a relatively risky procedure that involves wiping out the patient’s immune system with chemotherapy drugs. Chemotherapy destroys remaining cancer cells, makes room in the marrow for the donor cells and reduces the likelihood that they will come under attack from the immune system. The transplanted blood stem cells are then injected into the bloodstream and make their way to the marrow, where — ideally — they begin producing new, healthy blood cells.

Although the survival rate for bone marrow transplant recipients has risen significantly, 30 percent of the patients die within a year of the procedure.

“I think it’s highly feasible to identify appropriate donors — in particular when more people register as bone marrow donors, with more representation of different racial and ethnic backgrounds,” said Eileen Scully, associate professor of medicine at Johns Hopkins University School of Medicine. “That will enable this type of approach to be used for more people.”

But she added that “bone marrow transplantation is a significant medical procedure that carries its own risks.”

Doctors at City of Hope said they prepared the HIV patient for the transplant by giving him a lower-intensity regimen of chemotherapy developed by the cancer center and used with older patients.

HIV patients in wealthy countries like the United States, where antiretrovirals are widely available, live longer, but they also run a higher risk of developing certain cancers such as leukemia. In addition, they have a higher risk of developing heart disease, diabetes and even some brain conditions.

Dickter said that when the City of Hope patient was diagnosed with acute myelogenous leukemia in 2019, his doctors searched for a bone marrow match that contained the HIV-resistant mutation.

The nonprofit National Marrow Donor Program now routinely screens donors to learn whether they have the CCR5-delta 32 mutation, said Joseph Alvarnas, a City of Hope hematologist-oncologist and a co-author of the abstract.

The possibility of someday being able to effectively cure much larger numbers of people by using gene-editing techniques to generate the mutation may be a decade off, Deeks said.

Deeks said he is working with a San Francisco-based company called Excision BioTherapeutics to develop the first-in-human trials that would involve editing the genes of patients with HIV. Studies have shown some success in editing genes inside mice and monkeys infected with HIV.

Deeks said that it is not hard in the lab to use a gene-editing tool to knock out the receptor that allows HIV to invade the immune system. Carrying out that task inside the body of a human patient is where the work gets complex.

“That’s the challenge — to do that effectively and safely,” Deeks said. “And that’s a whole can of worms.”

Haseltine said that researchers must figure out how to reach enough of the right cells inside the body. At the same time, they must ensure the treatment does not cause unwanted effects to other genes.

“The message to people living with HIV is that this is a signal of hope,” said Scully, of Johns Hopkins. “It is feasible. It has been replicated again. It’s also a signal that the scientific community is really engaged with trying to solve this puzzle.”