Another Man Appears Cured of HIV After Stem Cell Transplant

While the risky procedure is not suitable for most people living with HIV, it offers clues for more feasible approaches.

July 27, 2022 By Liz Highleyman

A 66-year-old Southern California man appears to be cured of HIV after undergoing a stem cell transplant to treat leukemia, Jana Dickter, MD, of City of Hope Cancer Center reported during a media briefing today at the 24th International AIDS Conference in Montreal.

The City of Hope Patient received a stem cell transplant for cancer treatment using cells from a donor with a rare genetic mutation, called CCR5-delta32, that blocks HIV from entering T-cells. He has remained free of HIV for more than 17 months after stopping antiretroviral therapy.

The man is older than the handful of other people previously cured after stem cell transplants, he has been living with HIV longer and he received less harsh conditioning chemotherapy, suggesting that this approach may be feasible for a wider subset of people with both HIV and cancer.

“The City of Hope patient’s case, if the right donor can be identified, may open up the opportunity for more older patients living with HIV and blood cancers to receive a stem cell transplant and go into remission for both diseases,” Dickter said in a press release.

Nonetheless, the risky transplant procedure will not be an option for most people with HIV, who can live long and healthy lives if they stay on effective antiretroviral treatment. But these findings provide clues that could help researchers develop more widely applicable approaches for long-term HIV remission.

“These cases are still interesting, still inspiring and illuminate the search for a cure,” International AIDS Society president-elect Sharon Lewin, MD, of the Peter Doherty Institute for Infection and Immunity in Melbourne, told reporters during an advance media briefing last week.

Stem Cell Cures to Date

So far, only a handful of people have been cured of HIV after stem cell transplants. The first, Timothy Ray Brown (known as the Berlin Patient) received two transplants to treat leukemia in 2006. His doctor, Gero Hütter, MD, came up with the idea to use cells from a donor with the CCR5-delta32 mutation, speculating that it might cure both cancer and HIV.

Brown stopped antiretroviral treatment at the time of his first transplant, but his viral load did not rebound. Researchers extensively tested his blood, gut and other tissues, finding no evidence of functional HIV anywhere in his body. At the time of his death in September 2020, due to a recurrence of leukemia, he had been free of HIV for more than 13 years.

The second man, Adam Castillejo, known as the London Patient (featured in POZ's June 2022 issue), underwent a stem cell transplant to treat lymphoma, receiving cells from a donor with the same mutation. A year and a half after the transplant, with no evidence of viable HIV, he stopped antiretroviral therapy in September 2017. He has now been HIV-free for more than four years.

At this year's Conference on Retroviruses and Opportunistic Infections in February, researchers described a middle-aged woman with leukemia who received a combination of umbilical cord blood cells with the CCR5-delta32 mutation and partially matched adult stem cells from a relative. The mutation is present in only around 1% of people of northern European descent and is even rarer in other populations. Being of mixed race, the woman's chances of finding an adult donor who was both a genetic match and carried the mutation were slim, so her doctors tried a hybrid approach. She stopped antiretroviral therapy three years after the transplant, and her viral load remains undetectable a year and a half later.

Some experts also include another individual, dubbed the Dusseldorf Patient, who has not experienced HIV rebound for more than three years after stopping antiretroviral therapy post-transplant. But less is known about this case—which has not yet been published—and it has not received widespread media attention.

The City of Hope Patient

The City of Hope patient was diagnosed with HIV in 1988. In fact, his CD4 count declined so much (below 200) that he was diagnosed with AIDS. He started combination antiretroviral therapy when it became available in the mid-1990s.

In early 2019, at age 63, he received a stem cell transplant from an unrelated donor with the CCR5-delta32 mutation to treat acute myelogenous leukemia, the same cancer Brown had.

Prior to his transplant, Brown, then age 40, underwent intensive chemotherapy and whole-body radiation (known as conditioning therapy) to kill off his cancerous immune cells, allowing the donor stem cells to rebuild a new HIV-resistant immune system. But the donor immune cells attacked his body, resulting in near-fatal graft-versus-host disease.

Such a harsh conditioning regimen was not considered suitable for the City of Hope Patient, so he received reduced-intensity chemotherapy designed for older and less fit patients, Dickter said. Although the chemo did not kill off all his existing immune cells, the HIV-resistant donor cells appear to be doing their job nonetheless.

The man continued his antiretroviral therapy for two years after the transplant. With an undetectable viral load, he and his doctors decided to try a carefully monitored treatment

interruption.

More than three years after the transplant, and over 17 months after stopping antiretrovirals, he has no evidence of HIV RNA rebound and no detectable HIV DNA. What's more, he has no detectable HIV-specific cellular immune responses and his HIV antibody level has declined. His leukemia also remains in remission. (Further details will be presented at AIDS 2022 on August 1.)

"We were thrilled to let him know that his HIV is in remission and he no longer needs to take antiretroviral therapy that he had been on for over 30 years," Dickter said.

"When I was diagnosed with HIV in 1988, like many others, I thought it was a death sentence," said the man, who wishes to remain anonymous. "I never thought I would live to see the day that I no longer have HIV."

Clues to a Cure

Researchers are still trying to figure out why these people appear to be cured after stem cell transplants while other attempts have failed. Using stem cells from donors with the CCR5-delta-32 mutation appears to be a key to success. Researchers previously reported that two HIV-positive men who received stem cell transplants from donors without the mutation had delayed viral rebound after stopping antiretrovirals, but ultimately their HIV came back.

Some experts have suggested Brown's severe graft-versus-host reaction might have helped eliminate HIV. But Castillejo, who was 35 at the time of his transplant, received less aggressive chemotherapy and had milder graft-versus-host disease. The New York Patient did not develop graft-versus-host disease, which is less common with cord blood. The City of Hope Patient also appears to be cured despite receiving milder chemotherapy.

Even if the mystery is solved, stem cell transplants are too risky for people who do not need them to treat life-threatening cancer. What's more, the procedure is medically intensive and costly, and it would not be scalable to treat the millions of people living with HIV worldwide.

But the new case adds more evidence that could lead to feasible cure approaches. One potential strategy uses gene therapy to snip out the genes that encode CCR5 receptors, leaving immune cells resistant to HIV.

"These cures are no longer anecdotal—we now have a real case series," Steven Deeks of the University of California at San Francisco, told POZ. "That this approach is curative is no longer really questioned. The key is to come up with a safer, more affordable and more scalable approach. I am hopeful that with emerging gene editing technologies we will one day leverage these cures for something that could have a global impact."

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