In Search to Repeat “Berlin Patient” HIV Cure, Questions About How It Worked

A new study analyzes nuances in a cohort of six people who also received stem cell transplants for blood cancers.

October 17, 2018 By Benjamin Ryan

Researchers are ever seeking to better understand the mechanisms by which “the Berlin Patient,” Timothy Ray Brown, was cured of HIV and how others may achieve the thus-far-singular feat by similar means, MedPage Today reports.

Brown received a pair of stem cell transplants to treat his leukemia from a donor who harboreda so-called CCR5 delta-32 genetic mutation that made his immune cells resistant to the virus.

While this genetic oddity might have been instrumental to Brown’s cure, researchers in a new paper published in Annals of Internal Medicine note that four other major factors might have contributed to the success in Brown’s cure attempt, including: 1) specifics about the regimen used to condition his body for his stem cell transplants; 2) characteristics of his immune system that favored the activation of CD4 cells and the reactivation of HIV that was resting in a latent state in reservoir cells; 3) his immune system’s greater effectiveness at blocking virus spread by the donor’s cells, compared with the capacity of antiretrovirals to do so; and 4) the body’s reaction to the stem cell transplant, in particular what is known as graft-versus-host disease, a dramatic inflammatory response that might have killed off HIV-infected cells.

The paper’s authors conducted a small observational study in which they analyzed six people with HIV who also received what is known as an allogenic hematopoietic stem cell transplant (allo-HSCT) for blood cancer and about whom there was at least two years of posttransplant follow-up. The donors all lacked the CCR5 delta-32 mutation.

All six participants achieved full remission from their blood disease, stayed on antiretroviral treatment during follow-up and no longer had a suppressed immune system. Five of them had no measurable HIV reservoir in their lymph nodes, the portion of the small intestine known as the ileum, bone marrow or cerebrospinal fluid, according to tests that were 10 to 100 times more sensitive than those previous similar studies have used.

These five individuals saw their stem cell graft fully integrate within a year (known as achieving full donor chimerism), meaning their entire immune system was that of their donor's by that point. Four of them developed graft-versus-host disease.

Extensive study of one of these five people indicated the person's virus became undetectable according to the supersensitive tests just as the individual achieved full donor chimerism and also developed graft-versus-host disease.

The one individual who maintained a detectable HIV reservoir did not develop graft-versus-host disease.

The study authors found that a smaller decline in HIV reservoir cells in the study subjects was associated with receiving cord blood stem cells as well as a treatment known as a transplant-conditioning treatment called antithymocyte globulin (ATG). Consequently, the investigators concluded that greater suppression of the immune system from the ATG treatment as well as the greater immaturity of cord blood stem cells (compared with stem cells drawn from more mature sources, such as an adult's bone marrow) might have diminished the likelihood of graft-versus-host disease attacking the HIV reservoir following the stem cell transplant.

To read the MedPage Today article, click here.

To read the study abstract, click here.
