Using antibody in treatment of 'bubble boy disease' shows early promise

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Researchers at the School of Medicine said they are encouraged by early results from a clinical trial in which participants are being given an antibody-based treatment rather than chemotherapy or radiation to prepare them for a blood stem cell transplant.

The trial is the first time that the approach has been tested in humans. The researchers noted that these are preliminary results from the first two participants in the trial. Judith Shizuru, MD, Ph.D., professor of medicine, discussed the trial Feb. 27 at the annual meeting of Stanford's Center for Definitive and Curative Medicine.

The phase-1 trial involves participants who have a condition known as severe combined immunodeficiency. SCID, also known as "bubble boy disease," is a genetic disorder that disturbs the normal development of immune cells, leaving people with the condition vulnerable to infections that most people ward off easily.

SCID patients can be given infusions of stem and progenitor blood-forming cells to boost their immune response, but that effect can wear off over time if significant numbers of the healthy stem cells can't replace the diseased stem cells. The only cure for SCID involves a blood stem cell transplant, in which the patient's defective stem cells are wiped out with chemotherapy or radiation so that large numbers of normal blood stem cells from a donor can take their place.

The problem with chemotherapy or radiation is that they can be very damaging. "Physicians often choose not to give chemotherapy or radiation to young children with SCID because there are lifelong effects: neurological impairment, growth delays, infertility, risk of cancer, etc.," Shizuru said.

Administering an antibody

The current trial is testing a different method of removing the defective stem cells. Shizuru and her colleagues—including Rajni Agarwal, MD, associate professor of pediatrics; and Maria Grazia Roncarolo, MD, Ph.D., professor of medicine and of pediatrics and co-director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine—are giving the participants an antibody to CD117, a cell surface marker found on blood and immune stem cells.

The potential therapy is based on work originating in the laboratory of Irving Weissman, MD, director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine. Assistant professor of pediatrics Agnieska Czechowicz, MD, Ph.D., while still a graduate student in Weissman's lab, showed that an antibody could be used to block, in mice, a critical stem cell factor from binding to the receptor CD117. This binding had been previously shown in the Weissman lab to be required to keep blood stem cells alive. The use of the antibody could thereby eliminate most blood stem cells, clearing the way for donor stem cells to take up residence in the bone marrow.

Early data from the clinical trial show that the antibody's activity in humans is similar to what was observed in mouse studies. Specifically, the antibody appears to be effective in the depletion of genetically defective stem cells.

Nine and six months after the treatment, respectively, the two participants have shown evidence that the donor stem cells have taken root and are producing immune cells, Shizuru said.

Given these results, the researchers plan to continue their clinical trial and include infants with the disease, since infancy is a time when the negative effects of chemotherapy or radiation can be particularly acute.

The first cases also suggest that the antibody-based conditioning may be useful in combating

other diseases, including cancer, Shizuru said.

Autoimmune diseases like Type 1 diabetes, multiple sclerosis and lupus may be curable through blood stem cell transplantation, but are not currently treated this way because the dangers of chemotherapy or radiation usually outweigh the benefits.

Provided by Stanford University Medical Center