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New finding affecting immune reconstitution related to B cells

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Researchers from the Children's Center for Cancer and Blood Diseases at Children's Hospital Los Angeles examined the mechanisms of B cell immune reconstitution in pediatric patients who had undergone bone marrow transplantation and discovered a disruption in the maturation of B cells - critical to the immune system - preventing the production of antibodies that fight infection. The results of the study were published in the journal *Biology of Blood and Marrow Transplantation* on May 12.

"In order to be fully functional, B cells must go through different stages of maturation. We found that in pediatric patients after transplant, the B cell formation reaches a certain point, but then stops and is unable to progress to complete maturation and remains unable to fight infection, we further dissected the factors that affect various B cell maturation stages" said the lead author Hisham Abdel-Azim, MD, MS, of the Division of Hematology, Oncology and Blood and Marrow Transplantation at CHLA. The research team is the first to provide a conceptual model for B cell development and to determine the exact point at which disruption of B cell maturation occurs leading to impaired immune reconstitution.

Bone marrow transplantation (BMT) is the only potentially curative therapy for a wide range of malignant diseases such as leukemia and non-malignant diseases including aplastic anemia, thalassemia and sickle cell disease. Part of the preparation for BMT may involve total body irradiation or immune therapy, wiping out the patient's immune system, making them vulnerable to serious infection. If the immune system does

not fully recover, the patient can get very sick and catch fatal infections.

Rebuilding the immune system following transplantation is critical because it is a key factor in helping patients fight infection. Previous studies investigating immune reconstitution following transplantation have focused primarily on T cells. "We found that even with full T cell recovery, children after BMT have impaired antibody immune reconstitution," added Abdel-Azim.

Rather than looking at patient response over the course of only 6 months or one year, the research team evaluated patients for 10 years after transplant. The study demonstrated a problem in the B cell immune reconstitution in children involving a disruption in the maturation of a specific type of B cell called IgM memory B cell—which is independent of T cell recovery and leads directly leads to an impairment of antibody immune reconstitution post-transplant.

"We now know that we need to monitor those patients closely and specifically look into B cell reconstitution so that we can tailor prophylaxis after transplant and the immunization schedule depending on their response," said Abdel-Azim.

More information: Hisham Abdel-Azim et al, Humoral Immune Reconstitution Kinetics Following Allogeneic Hematopoietic Stem Cell Transplantation in Children: a Maturation Block of IgM Memory B Cells May Lead to Impaired Antibody Immune Reconstitution, *Biology of Blood and Marrow Transplantation* (2017). DOI: 10.1016/j.bbmt.2017.05.005

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