Detecting and treating dnDSA early preserves allograft function

February 5 2018

Development of de novo donor-specific antibodies (dnDSA) is known to cause graft failure. Therefore, a protocol aimed at prospective monitoring and treating dnDSA—before it can cause graft damage—was developed for kidney transplant recipients at Children National Health System. This helped to decrease dnDSA in 76 percent of pediatric patients and prevented graft failure in the first few years, indicates a longitudinal cohort study published online Jan. 22, 2018, in *Pediatric Transplantation*. However, the benefit of preserving function of transplanted kidneys came at a price: Heightened hospitalization rates for infection.

An estimated 20 percent to 30 percent of children develop dnDSA and many of these patients go on to develop allograft failure after three to six years, write the study authors.

Clinical signs of graft failure due to antibodies appear too late to safeguard long-term graft survival. According to the study authors, developing earlier methods to detect dnDSA offers the opportunity to intervene before irreversible graft injury occurs.

"Children's National Health System instituted a routine protocol that standardizes monitoring and treatment of dnDSA," says Asha Moudgil, M.D., FASN, associate chief of the Division of Nephrology at Children's National and the study's senior author. "We followed this protocol as we monitored and treated all children younger than 19 who received a kidney transplant at Children's National from Jan. 1, 2008, to Dec. 31,

2013."

After transplant, these children were monitored for development of dnDSA at six months and then yearly. Upon detection of DSA, these children underwent kidney biopsy to assess for acute rejection. Additionally, monitoring was intensified to every two months.

Sixty-seven of the 72 children who received kidney transplants during that six-year period were included in this retrospective analysis. Their mean age was 14.1 years old. Acute cellular rejection was treated according to a prespecified protocol.

- The team treated de novo DSA with high-dose intravenous immunoglobulin (IVIG) if antibody titers were low and added two doses of rituximab to that treatment regimen if antibody titers were high.
- If either C1q binding of immunodominant DSA was present or C4d+ were seen on biopsy, six sessions of plasma exchange were added to the above protocol.
- Kids who were resistant to such treatment approaches received additional four doses of IVIG monthly.

Nearly 39 percent of the children developed dnDSA within a median of 1.36 years. Ten of these 26 children had increased creatinine, 12 had new onset proteinuria and six had newly diagnosed hypertension at the time the dnDSA was detected. The multivariate analysis found that coefficient of variance of tacrolimus, which measures adherence to immunosuppressive drugs, was the only statistically significant predictor for developing dnDSA.

DSA-positive patients had higher rate of admissions (1.23 hospital admissions for infectious- or immunosuppressive-related side effects per patient, compared with 0.59 hospital admissions for the DSA-negative

patients), which the study team attributes to aggressive treatment of dnDSA.

"Our patients did not have a statistically significant increase in graft loss or dysfunction, suggesting that early and targeted treatment of dnDSA may benefit patients," Dr. Moudgil adds. "There was a higher risk of treatment-related complications, however, and this risk must be balanced against the short-term benefit of prolonging allograft function."

More information: Olga Charnaya et al, Results of early treatment for de novo donor-specific antibodies in pediatric kidney transplant recipients in a cross-sectional and longitudinal cohort, *Pediatric Transplantation* (2018). DOI: 10.1111/petr.13108

Provided by Children's National Medical Center