

The Scourge of Antibody Mediated Rejection in Renal Transplantation

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Editorial

The past decade has been witness to significant successes in effective strategies to prevent and treat cell-mediated rejection after renal transplantation, both in adults and in children, such that acute rejection rates have declined considerably [1]. This however, has not translated into improved long-term graft survival due to a variety of factors. One of these is the increasing recognition of antibodies as a major player in contributing to graft injury. Antibody mediated rejection is much harder to treat, especially if its diagnosis and recognition are delayed, and not infrequently leads to allograft loss; moreover, conventional therapies remain quite invasive and are associated with significant toxicity [2]. Many newer strategies are under investigation to address this need, including eculizumab and bortezomib, to name a few. Similar to other centers, in our own small experience, the use of bortezomib has been somewhat effective in reducing donor specific antibodies, and reversing rejection, albeit with greater success in the setting of early antibody mediated rejection [3]. Until now, randomized control trials using this potentially exciting agent, have been lacking. A recent study, the BORTEJECT Trial [4], is one study that moves us one step towards bridging this gap. Results from this study, a randomized trial of bortezomib in late (after 6 months) antibody mediated rejection were disappointing, in that the use of this agent was not associated with improvements in GFR, the slope of decline of the GFR, or in graft survival. Toxicities, were, however, encountered in the treatment arm. Data, on the use of eculizumab for treating antibody mediated rejection are even more limited. In 2016, a case report in a 61-year-old renal transplant recipient first highlighted the possible role for this agent in refractory rejection [5]; following failure of standard therapy, 5 doses of eculizumab were administered and resulted in dramatic improvement in renal function such that the patient became dialysis free. Its role, however, remains controversial, not only with respect to its efficacy [6], but also because of its potential toxicities and expense. While limited in scope because of the small patient numbers, anecdotal nature of these reports and the limited choices investigators had in one of the

studies in adjusting immunosuppression, these data do highlight the need for more robust and controlled trials for newer agents that are being considered for introduction into the armamentarium that transplant providers can use to try to improve long-term graft function and survival. A recent meta-analysis and systematic review reinforced the lack of clarity with respect to the role of bortezomib and eculizumab in the treatment of antibody mediated rejection [7]. The time is ripe for collaborative studies to help improve the quality of life for transplant recipients.

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