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LETTER TO THE EDITORS

Rituximab and memory antibody levels after desensitization

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The recent article by Rogers *et al.* [1] yields a valuable insight into antibody levels after desensitization and subsequent renal transplantation. The authors employed a desensitization protocol incorporating a single dose of rituximab, and a course of plasmapheresis with administration of intravenous immunoglobulin. Levels of antibody to tetanus and pneumococcus were reduced over the first 6 months post-transplant, but this finding was not attributable to the desensitization regimen described, since matched, unsensitized, contemporaneous transplant recipients from the same unit exhibited similar levels. Instead, it seems that the maintenance immunosuppression received by all transplant patients was responsible for this reduction.

The implication that rituximab has no discernable effect on these circulating antimicrobial antibody levels accords with the results of a study of rituximab therapy in lupus patients [2]. Indeed the value of anti-CD20 antibody in desensitization protocols is not without controversy [3]. It has been shown that rituximab does not affect splenic plasma cells or memory B-cells when used as pretransplant therapy [4]. In the study of Rogers *et al.* it is quite conceivable that the persistent reduction in donor-specific HLA-antibody levels after transplantation was attributable to the combination of maintenance immunosuppression, and absorption of donor-specific antibodies onto the allograft. A similar post-transplant suppression or elimination of detectable donor-specific antibody has been observed by the Johns Hopkins group, which has removed rituximab from its desensitization protocol [5].

A high rate of early infectious complications was reported in the desensitization group of Rogers *et al.* Logically, this must be attributable either to plasmapheresis, rituximab administration, or the combination of both. A randomized trial in immunosuppressed patients with lupus nephritis did not find an excess risk of infection with the addition of plasmapheresis [6]. A small study examining the effect on rejection rates of adding plasmapheresis to high-dose intravenous immunoglobulin in sensitized transplant patients found no resultant increase in infections [7].

With regard to rituximab, the study of Grim *et al.*, [8] compared the rate of infectious complications between groups of antibody-incompatible transplant patients who received and did not receive rituximab as induction therapy. There was a trend (48% vs. 11%) towards an increased rate of infections in the rituximab group, but this retrospective study was underpowered and did not reach significance. Kamar *et al.* found an increased risk of infection-related death in patients treated post-transplant with rituximab for a variety of indications [9]. A recent review concluded that despite a shortage of information, existing data suggested that the use of rituximab in the renal transplant population carried an increased risk of infection [10]. Another recent review of rituximab-associated infections noted a growing series of case reports recounting infectious complications of anti-CD20 in solid organ transplant recipients [11].

The excess of infections reported in the desensitized patients of Rogers *et al.* is most likely therefore to be attributable to the use of rituximab. Given that anti-CD20 use is questionable in terms of HLA antibody reduction, avoidance of rituximab might mitigate the infection risk at no cost to transplant outcomes.

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Conflicts of Interest

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