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LETTER TO THE EDITORS

False-positive CDC x-match after Rituximab

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Dear Sirs,

Rituximab is nowadays frequently used in the pretransplant period especially in sensitized patients with preformed HLA antibodies or in ABO incompatible live donor transplantation [1,2]. However, rituximab itself exerts a cytolytic effect on B-cells that may cause a positive result in a complement-dependent cytotoxicity B-cell cross-match (CDC) in the absence of preformed HLA antibodies (false positive). Additionally, as a humanized antibody, it may also interfere with commonly used flow cytometric cross-matches (FCXM) by binding of the secondary anti-human immunoglobulin antibodies directed against the Fc receptor returning a positive cross-match result [3]. Rituximab can remain in the serum for several months after application [4]. Gatault *et al.* recently reported an association between rituximab concentration in the serum and a positive result in the B-cell cross-match (CDC) in two kidney transplant recipients [5]. In one of these cases, transplantation was not performed based on a positive B-cell cross-match result with a historic serum despite zero HLA mismatch and a negative B and T-cell cross-match with the current serum. A negative cytotoxicity or flow cytometric cross-match is generally considered a conditio sine qua non for kidney transplantation.

We report the case of a successful kidney transplantation in a 46-year-old woman with a positive B-cell CDC following treatment with rituximab. The patient was treated with rituximab according to our local desensitization protocol for a planned ABO incompatible live donor kidney transplantation 14 days prior to the scheduled transplantation. However, on day 4, the patient received an offer for a deceased donor kidney graft with zero mismatch at the HLA-A, HLA-B, and HLA-DR loci. A recently performed solid phase assay (luminex technology) was available and did not show any preformed HLA antibodies (negative virtual cross-matching), and the patient was transplanted subsequently without awaiting the results of the actual cross-match to reduce ischemia time. Only after transplantation, the result of the CDC was available and returned a positive B-cell cross-match result. Being the first transplant, plausible sensitization events included two prior pregnancies. The father of the children had been evaluated as a potential donor, and cross-matching did not show any reactivity. Other factors that were discussed included a mismatch in minor histocompatibility antigens (mHA), especially H-Y antigens in a female recipient of a male donor organ, but no specific testing was available and data on clinical relevance of mHA mismatch in acute antibody-mediated rejection are still scarce [6,7]. Finally, testing with a historic serum that was obtained prior to rituximab therapy did not show a positive result in both CDC and FCXM. In the follow-up, no episode of hyperacute or acute rejection was observed and the patient has a good graft function 3 months after transplantation. A per protocol biopsy at 3 months showed no histological findings suggestive of an antibody-mediated rejection. The positive CDC result was therefore interpreted as false positive caused by rituximab-induced B-cell lysis.

With the increasing number of highly sensitized patients requiring desensitization prior to transplantation, more patients will be treated with rituximab in the pretransplant period. The timing of rituximab treatment and the presence of preformed DSAs have to be taken into consideration when interpreting a positive B-cell cross-match result in such patients.

Roman Reindl-Schwaighofer[1] and Rainer Oberbauer[1,2]
1 Department of Nephrology, KH Elisabethinen, Linz, Austria
2 Department of Nephrology, Medical University of Vienna, Vienna, Austria
e-mail: rainer.oberbauer@meduniwien.ac.at

Conflicts of interest

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