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Bortezomib-based treatment of acute antibody-mediated rejection: a case report

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ABSTRACT. Antibody-mediated rejection (AMR) is an important factor affecting survival after renal transplantation. A highly selective proteasome inhibitor, bortezomib, clears activated plasma cells from the body and has important therapeutic effect on AMR. We investigated the effects of bortezomib on AMR in a patient after a second renal transplant. Biopsy confirmed the diagnosis of mixed cellular rejection and AMR. Bortezomib was administered on day 1 (1.3 mg/m^2), day 4 (1.0 mg/m^2), and day 8 (1.0 mg/m^2). On the same days, 250 mg methylprednisolone was administered once, and cyclosporine dose (5 mg·kg^{-1}·day^{-1}) was reduced by 50%. Oral mycophenolate mofetil and steroid were withdrawn on day 1 of bortezomib treatment. Intermittent double-filtration plasmapheresis was also performed. We monitored parameters, including T lymphocyte subsets, CD139 and CD19 expression, panel reactive antibody (PRA), and serum creatinine concentration. At follow-up 6 months after bortezomib treatment, we observed: 1) serum creatinine stabilized at 130 µM from a peak level of 337 µM; 2) PRA decreased from a maximum of 66.7 to 0%; 3) blood plasma cell percentage rebounded after significantly decreasing following

the first dose of bortezomib; 4) in renal allograft biopsy, immunohistochemical staining for C4d shifted from strongly positive to negative, and cellular rejection shifted from type IIA to borderline; and 5) adverse effects such as platelet suppression, hypotension, and grade 3 peripheral neuropathy emerged. Bortezomib effectively treated antibody-mediated renal transplantation rejection in this case study, but clinical trials with large sample sizes are still needed to explore clinical safety and tolerability.

Key words: Bortezomib; Antibody-mediated rejection; Renal transplantation

