TITLE

BORTEZOMIB IN THE TREATMENT OF RESISTANT ACUTE ANTIBODY- MEDIATED REJECTION: A SINGLE CENTRE EXPERIENCE

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OBJECTIVES

Acute antibody-mediated rejection (AMR) represents a rare complication after kidney transplantation that often leads to renal allograft loss. Previously reported therapeutic superiority of combination of plasmapheresis (PP) and intravenous immunoglobulin (IVIG) may however fail in some resistant cases. Thus, the aim of this study was to analyze the efficacy and safety of bortezomib based treatment of resistant AMR in kidney transplant recipients.

METHODS

Resistant AMR was defined as a persisting deterioration or non-function of renal allograft in patients with histological verification of AMR, positive C4d+ staining and detection of donor specific antibodies (DSA) receiving standard antirejection treatment with PP + IVIG. Novel therapeutic approach to resistant acute AMR protocol was based on administration of bortezomib [1 cycle of 4 doses of bortezomib (1.3 mg/m2)], plasmapheresis and a dose of Rituximab (375mg/m2). Patients were followed for 3-12 months.

RESULTS

7 patients received bortezomib based protocol to cure resistant AMR. Their peak PRA was 47.57 ± 36.69%, mean HLA mismatch in HLA- A 1.57 ± 0.53, HLA-B 1.57 ± 0.53, HLA- DR 1 ± 0, and median dialysis vintage was 53. 2 months, patients underwent 1st kidney transplantation, while 4 patients retransplantation (2nd Tx n=2, 4th Tx n=3). Immunosuppressive protocol consisted of induction with antithymocyte globulin (n=6) or basiliximab (n=1). Diagnosis of resistant acute AMR was made on 15.th POD (9- 450 days).

Based on therapeutic effect, three patients received 1 cycle, while four patients received 2 cycles of therapy. The side- effects observed were urinary tract infection (n= 2), colitis (n= 2), polyneuropathia (n= 2), hepatotopathia (n= 3) and fluid retention (n=5).

After bortezomib based regimen, the DSA decreased in both HLA class I (MFI before treatment 9614 ± 9531 vs. MFI after treatment 1393 ± 1760, $p < 0.05$) and class II (12822 ± 6264 MFI, 6200 ± 6099 MFI, respectively, $p = 0.03$). A trend towards the improvement of renal function was observed during the follow-up (S-Cr 304.86 ± 201.15 µmol/l before treatment vs. S-Cr 195 ± 8.68 µmol/l after treatment, $p = 0.21$, eGFR-MDRD 0.42± 0.30 ml/s vs. 0.58± 0.25 ml/s, respectively, $p = 0.21$).

CONCLUSIONS

Combination of bortezomib, plasmapheresis and rituximab seems to be the effective approach to cure resistant acute antibody mediated rejection.