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Clinical characteristics and outcomes of PTLD after kidney transplant: a single center experience

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Background and Aims: Post-Transplant Lymphoproliferative Disorder (PTLD) is a serious and potentially fatal complication of immunosuppression in kidney transplantation. Given the rarity of this entity, a high index of suspicion is necessary. We aimed to review the incidence, clinical presentation, histological subtypes, treatment, patient and graft survival of PTLD in kidney transplant patients in our unit.

Methods: Observational retrospective study, including adults diagnosed with PTLD between 1998 and 2023 in a Kidney Transplantation Center.

Results: Of 1390 kidney transplant recipients, 4 (0.3%) developed PTLD with a mean age of 52 ± 12.5 years. All cases were late-onset, occurring one year after transplantation with a median time from transplantation to diagnosis of 16.7 ± 7.3 years (range: 5-22 years). Of these, none had EBV donor/recipient mismatch. Two patients had prior rejection episodes (one patient, acute T cell-mediated rejection and the other patient, acute T cell-mediated rejection and active antibody mediated rejection). Clinical presentation was variable. Non-specific constitutional symptoms such as fever, fatigue and night sweats were present in all patients. Organ-specific symptoms were also present: lumbar pain in one patient with bone involvement, and *delirium* and lethargy in two patients with central nervous system involvement. Laboratory analyses revealed an increase in serum LDH in all patients. The primary sites of involvement were central nervous system (50%), lymph nodes (25%) and bone (25%). At PTLD diagnosis, immunosuppression included: tacrolimus (100%), mycophenolate mofetil (75%), low-dose of steroids (50%) and everolimus (25%). Regarding histologic classification, 75% were monomorphic and 25% polymorphic. In the monomorphic group, all patients had Diffuse Large B Cell Lymphoma (CD20 positive). In the polymorphic group, the patient had a Mixed Cellularity Classic Hodgkin Lymphoma (CD20 negative). Immunosuppression therapy was reduced in all patients with discontinuation of mycophenolate mofetil and tacrolimus. In the patient who was taking everolimus, the dose was increased due to the potential clinical antitumor effects of mTOR inhibition. Additional therapies included, rituximab in monotherapy or in combination with chemotherapy (R-CHOP) in the monomorphic group. Palliative measures were selected for one patient of this group due to advanced disease. The patient with Mixed Cellularity Classic Hodgkin Lymphoma (CD20 negative) did chemotherapy with ABVD. None of the patients underwent surgery or radiation therapy. Two patients needed dialysis. Three patients died in the first four weeks after PTLD diagnosis, all due to infectious complications. Patient survival was 25% one year after diagnosis.

Conclusions: Although the incidence of PTLD was low following kidney transplantation, its impact was significant in kidney graft and overall patient survival. Given the poor prognosis, new therapies combining high efficacy and low toxicity are an urgent unmet medical need in this field.