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Ischemia and Reperfusion Injury Activates Rejection-Related Immune Factors

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Introduction: Ischemia/reperfusion injury (I/RI) is the major cause of acute renal failure and delayed graft function (DGF) unavoidable in renal transplantation. Enormous studies on ischemia damage playing a roll in activating graft rejection factors, such as T cells or macrophages, are being reported. Present study was performed to determine whether ischemia time would play an important roll in activating rejection related factors or not in rat models of I/RI.

Materials and Methods: Uninephrectomized male SD rats were submitted to 30, 45, and 60 minutes of warm renal ischemia and control animals underwent sham operation (unilateral nephrectomy). Renal function and survival rates were evaluated on day 0, 1, 2, 3, 5, and 7. Immunohistochemistry staining of CD4, CD8, dendritic cells (DCs), natural killer (NK) cells, macrophages, and B cells were measured on day 1 and 7 after renal IRI.

Results: Serum creatinine levels rose the highest on day2 following 45 or 60 minutes and on day 1 following 30 minutes of unilateral IR injury compared to sham animals. The survival rates began decreasing past day 1 and none of the animals survived after day 3 following 60 minutes of IRI. Histologic analysis of ischemic kidneys revealed a significantloss of tubular architecture and infiltration of inflammatory cells. More severe IRI induced more infiltration of inflammatory cells. Macrophages, DCs, and NK cells showed increase from day 1 whereas T cells and B cells were increased on day 7, after serum creatinine level has returned to its normal range.

Conclusions: The kidney infiltrates mainly of antigen presenting cells (DCs, NK cells or macrophages) 24 hours post- IRI, which is at the time of acute tubular necrosis. During the regeneration phase, T cells and B cells were most prominent. These changes of infiltrating cells resulting from each IRImodel shows that ischemic time plays a roll in activating rejection related immune factors and have consequences on progression of renal disease in transplanted and native kidneys.

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