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Impact of Splenectomy on Kidney Repair and B Cell Response in Ischemic Acute kidney Injury

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Objectives : Lymphocytes regulate kidney repair and chronic kidney disease (CKD) transition in acute kidney injury (AKI). Although the spleen is likely to be involved in kidney immune responses after AKI considering the role in immune regulation, its specific role in post-AKI repair remains unknown. We hypothesized that splenectomy may affect repair/fibrosis in AKI by altering spleen-derived kidney immune responses.
Methods : Severe AKI was induced with 45-min unilateral ischemia-reperfusion injury (IRI) surgery in C57BL/6 mice, after which mice were divided into two groups: IRI alone and IRI with concurrent splenectomy (IRI+SPX). Kidneys were collected during late recovery phase after AKI. Kidney sections were stained with H&E, Masson's trichrome, and CD45 immunohistochemistry. Kidney lymphocytes were studied with flow cytometry. Cytokine/chemokine expression was measured from kidney protein extracts.
Results : Post-AKI kidneys of IRI+SPX group exhibited greater tubular damage (IRI vs. IRI+SPX, 38.0±3.7% vs. 68.0±8.0%, P=0.032) and fibrosis (12.0±2.0% vs. 20.0±0.0%, P=0.047) compared to IRI group. Post-AKI kidneys of IRI+SPX group showed more pronounced leukocyte infiltration compared to IRI group ($CD45^+$ cells among total nucleated cells, 4.2±0.5% vs. 8.1±0.7%, P<0.001). While T cell profiles were comparable between groups, splenectomy led to significant changes in B cell composition. Activated B cells (9.7±1.2% vs. 19.3±2.6%, P=0.008), $MHCII^+$ B cells (7.0±1.2% vs. 13.6 ± 1.5%, P=0.008), and memory B cells (8.6±0.4 vs. 15.9±0.8%, P=0.008) were significantly higher in post-AKI kidney of IRI+SPX group. Expression of pro-inflammatory and fibrotic cytokines including IL-17 (2.1±0.2 vs. 2.9±0.2pg/mg, P=0.024), MCP-1 (170.8±15.1 vs. 226.7±17.2pg/mg, P=0.040), and TGF-β (1122±55.5 vs. 1436±60.2pg/mg, P=0.016) were also upregulated in IRI+SPX group.
Conclusions : Splenectomy aggravated tubular injury and fibrosis after AKI and significantly affected renal immune responses, especially B cell activation. Our findings suggest that kidney–spleen axis may play a reparative role in AKI, which could be a potential therapeutic target to mitigate AKI-to-CKD transition.