Introduction.—High-mobility group box 1 (HMGB1) is a nuclear protein that acts as an alarm when released by necrotic or activated cells. High serum HMGB1 levels have been associated with active nephritis as well as with granulomatous manifestations in patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). This study aims to evaluate HMGB1 levels, CD4+ T-cells and effector memory T-cells (CD4+ TEM) in urine from patients with AAV and active nephritis.

Methods.—Twenty-four AAV patients with active nephritis and ten healthy controls (HC) were evaluated. Diagnosis of GPA or microscopic polyangiitis (MPA) was based on the European Medicines Agency algorithm whereas patients with isolated renal involvement, ANCA positivity and/or biopsy-proven pauci-immune necrotizing glomerulonephritis were classified as renal limited vasculitis (RLV). Urinary levels of HMGB1 were measured by Western blot while CD4+ T-cells and CD4+ TEM cells (CD4+ CD45 + RO + CCR7−) in urine were analyzed by flow cytometry.

Results.—Median urinary intensity of HMGB1 was higher in AAV patients than in HC (5.15 [IQR: 3.52–9.25] vs. 2.58 [1.88–4.24]; P = 0.006) whereas no difference was found among different AAV subsets regarding median urinary intensity of HMGB1 [GPA: 4.1 (2.6–16.4) vs. MPA: 5.1 (4.4–5.6) vs. RLV: 5.7 (1.4–13.6); P = 0.951] and HMGB1/creatinine ratio [GPA: 0.93 (0.29–3.91) vs. MPA: 1.29 (0.90–1.89) vs. RLV: 0.54 (0.14–1.28); P = 0.186]. Urine levels of HMGB1 were positively correlated with CD4+ T-cell counts in urine (rho: 0.407; P = 0.034) whereas there was a tendency for a positive correlation with CD4+ TEM cells and CD4+ TEM cells (CD4+ CD45 + RO + CCR7−) in urine were analyzed by flow cytometry.

Conclusion.—Urinary HMGB1 levels are increased in AAV patients with active nephritis when compared to HC and are associated with CD4+ T-cells in urine. These findings suggest that urine HMGB1 is a biomarker for active nephritis when compared to HC and are associated with CD4+ T-cells in urine. These findings suggest that urine HMGB1 is a biomarker for active nephritis.

Further readings


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P194

Functionally effect regulatory B cells in patients with active ANCA vasculitis


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Introduction.—Immunopathogenesis of ANCA disease is B cell dependent; yet, how B cell subsets contribute is unknown. CD19 + CD24hiCD38hi B cells play a role in immunological tolerance by suppression of TH1 cells via IL-10 secretion. We hypothesize that a decrease in functional, IL-10 producing B cells is a component of B cell dysregulation that accompanies active ANCA disease.

Methods.—We examined 140 ANCA patients samples and 19 healthy controls by flow cytometry. To determine the competency of B cell subsets to produce IL-10 in patients with ANCA disease, PBMCs were stimulated with CD40 ligand and CpG DNA and processed for intracellular staining of IL-10.

Results.—Patients with ANCA disease had similar percentages of Bregs as healthy individuals: 14% vs 10%; P = 0.2. In sub-group analysis, active MPO ANCA patients had significantly less Bregs than those in remission (14.3 vs 7; P = 0.01). In contrast, regardless of Breg percentage, B cells from patients with active disease produced significantly less IL-10 than patients in remission (15%); P = 0.0096. Patients in remission are similar to healthy individuals with regard to IL-10 producing B cells (26%) and 26% (P = 0.9), respectively.

Discussion.—ANCA patients and healthy individuals had similar percentages of Bregs; yet, active ANCA patient B cells produced less IL-10. These data suggest that Bregs are present in patients with active ANCA disease but functionally impaired.

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