FP221 B CELL AND MONOCYTE PHENOTYPING IN IGA NEPHROPATHY: A QUICK ASSET TO INVESTIGATE THE IMMUNE STATUS IN PATIENTS WITH IGA NEPHROPATHY

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INTRODUCTION: IgA nephropathy (IgAN) is a leading cause of end stage renal disease and it is the most common glomerulonephritis worldwide. Naive and adaptive immune cells play a major role in the development and progression of disease, therefore unraveling a correlation between changes in the immune status of the patient and clinical outcomes is of great value. In this study, we aimed to investigate B cell and monocyte phenotype, comparing the IgAN patients with disease controls (patients with polycystic kidney disease) and healthy individuals.

METHODS: IgAN patients (n = 13) were recruited from the Department of Nephrology at Danderyd University Hospital, Karolinska Institutet, Stockholm, Sweden. Patients (men 46%) with a median age of 45 years (IQR 38-60), had a median estimated glomerular filtration rate (eGFR) of 57 ml/min x1.73m2 (IQR 42-84) and median urine albumin-to-creatinine ratio (UACR) of 74 mg/mmol (IQR 18-116). Disease controls with polycystic kidney disease (n=13) were matched for kidney function, gender- and age (±10 years). Healthy controls ($n = 13$) were gender- and age-matched (±5 years) with patients. CD3+ cells were isolated from freshly separated peripheral blood mononuclear cells by positive selection using a magnetic cell sorting system. CD3+ and CD3- cells were then divided and stained for different subsets of B cells and analyzed by flowcytometry. Cytokines were analyzed by ELISA.

RESULTS: We report a significant decrease in the proportion of CD19+ CD27+ IgD+ cells (pre-switched B), CD19+ CD27+ CD38+ cells (plasmablasts) but an increase in CD19- CD27hi CD38 hi (transitioned plasma cells) in the peripheral circulation of IgAN patients comparing to healthy individuals. Comparing IgAN to disease controls no significant difference could be found in levels of CD19+ CD27+ IgD+ cells (pre-switched B) and CD19+ CD27+ CD38+ cells (plasmablasts) and CD19- CD27hi CD38 hi. Disease controls showed an increase in CD19- CD27hi CD38 hi (transitioned plasma cells) comparing to healthy individuals. The proportion of CD14+ CD16++ cells (non-classical monocytes) was significantly higher in IgAN patients comparing to healthy individuals and disease controls. These data were related to chemistry laboratory data and relevant cytokine profiles.

CONCLUSIONS: Immunoglobulin (Ig)A immune complex deposition in the kidneys leads to glomerular and tubulointerstitial injury, fibrosis and renal failure. The antibody production is mainly induced by displaced mucosal B-cells to the systemic sites. The decrease in the number of circulatory pre-switched B cells and plasmablasts, but an increase of transitioned plasma cells in our study suggests a possible trafficking of various subsets of B cells in IgAN patients. This might increase our understanding in how B-cell maturation reflects the immune status in patients with IgAN. Increase in the proportion of inflammatory monocytes may play a role in the high inflammatory state and possible crosstalk between different sectors of the immune system through cytokines in the patients. Our study could not detect a significant difference in B cell subsets between IgAN patients and patients with polycystic kidney disease, which might be indicative of the importance of kidney function decline. Further analyses are warranted to investigate if these cell profiles are differently presented in different stages of the disease and may have a correlation to the progression of IgAN.