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CLINICAL NEPHROLOGY, PRIMARY AND SECONDARY GLOMERULONEPHRITIS - 1

SP134 GUT - KIDNEY AXIS IN THE PATHOGENESIS OF IGA NEPHROPATHY

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Introduction and Aims: IgA nephropathy (IgAN) is the most common primary glomerulonephritis worldwide. It is characterized by deposition of deglycosylated IgA1 and IgG antibodies in the glomeruli and its pathogenesis is only partially defined. Intestinal microbiota could be involved in IgAN, as suggested by the observation that B-cell activation factor (BAFF) transgenic mice had high levels of aberrantly glycosylated serum polymeric IgA, the presence of commensal flora and the circulation of corresponding specific IgA antibodies being essential for the development of IgA deposits (*J Clin Invest. 2011; 121:3991-4002*). BAFF is an important regulator of B cell maturation, survival and function. The aim of the study was to analyze the role played by gut-kidney axis in the pathogenesis of IgAN.
Methods: 16 healthy controls (HC) and 32 IgAN patients (16 non progressors - NP and 16 progressors - P) were included in the study. Serum creatinine, estimated Glomerular Filtration Rate, 24h-proteinuria and histological lesions following Oxford Classification (MEST score) were analyzed. Gut microbiota, urinary and fecal metabolome of all subjects were characterized by 16S sequencing, Biochrom 30 series amino acid analyzer and gas-chromatography mass spectrometry/solid-phase microextraction (GC-MS/SPME).Galactose-deficient IgA1 (Gd-IgA1) were measured by helix aspersa agglutinin binding assay. BAFF serum levels were quantified by ELISA.
Results: Some traits of the gut microbiota and urinary and fecal metabolome profiles significantly differed between P, NP and HC. Gd-IgA1 and BAFF were significantly higher in IgAN patients, particularly in P, compared to HC (Gd-IgA1: $p < 0.01$ P vs HC; $p < 0.05$ NP vs HC; BAFF: $p < 0.01$ P vs HC). IgAN patients with histological grade at diagnosis M1, E1, S1 and T1 had significantly higher levels of serum BAFF than HC. Moreover, serum BAFF levels were positively correlated with 24h-proteinuria ($r = 0.47$, $p = 0.0069$) and with the levels of fecal phenolic metabolites ($r = 0.61$, $p = 0.0003$).
Conclusions: Gut-kidney axis might play an important role in the pathogenesis of IgAN.