FR-PO1923

Impact of a Functional Polymorphism of Vascular Endothelial Growth Factor (VEGF) Gene on Primary Glomerulonephritis Christos Bantis, Peter J. Heering, Nicoletta-Maria Kouri, Maria Stangou, Christina Schwandt, Nicola Kuhr, Lars C. Rump, Katrin Ivens. *Department of Nephrology, Heinrich-Heine University, Düsseldorf, Germany.*

Background: Vascular endothelial growth factor (VEGF)regulates endothelial cell proliferation and participates in interstitial remodelling. In the kidney, VEGF is mainly expressed by podocytes. We evaluated the influence of C-2578A polymorphism, located in the promoter of the VEGF gene, on primary glomerulonephritis.

Methods: We studied 284 patients with biopsy proven primary glomerulonephritis (IgA nephropathy: n=143, focal segmental glomerulosclerosis: n=82, membranous glomerulonephritis: n=59) followed up for 7.0 ± 5.7 years. According to the slope of reciprocal serum creatinine (≥or< -0.1 dl * mg-1 * year-1) group A (slow progressors, n=192) and group B (fast progressors, n=92) were defined. One hundred volunteers were analysed as controls. The biopsies of 156 patients were analysed by the same pathologist. VEGF polymorphism was determined by PCR. VEGF serum levels were determined by ELISA in 105 patients with chronic kidney disease.

Results: VEGF serum levels correlated to the C-2578A genotype: CC/CA: 396 ± 251, AA: 558 ± 425 pg/ml (p=0.018). The genotype frequencies were similar in patients and controls (ns). The initial renal function correlated to the degree of glomerular sclerosis (r=0.520, p<0.001), tubulointerstitial fibrosis (r=0.557, p<0.001) and arteriosclerosis (r=0.469, p<0.001). The percentage of sclerosed glomeruli was higher in group B (44.0 ± 31.1% vs 32.9 ± 28.7% in group A, p=0.051) as was the degree of tubulointerstitial fibrosis (34.1 ± 26.3% vs 24.7 ± 20.2% in group A, p=0.043). There was no significant difference regarding the histological parameters between patients with different genotypes (ns). VEGF gene polymorphism influenced the progression as shown by the genotype distribution in group A (CC/CA: 70.3%, AA: 29.7%) compared to group B (CC/CA: 81.5%, AA: 18.5%, p=0.05). There was also a significant difference in the actual rate of progression (CC/CA genotypes: -0.160 ± 0.417, AA: -0.085 ± 0.132 dl*mg-1 *year-1; p=0.021).

Conclusions: The functional VEGF C-2578A polymorphism is a progression marker in primary glomerulonephritis.

FR-PO1924

Acute Manifestation and 1-Year Follow-Up of a Big Cohort of Patients with Atypical Hemolytic Uremic Syndrome (aHUS) Magdalena Riedl,[1] Johannes Hofer,[1] Alejandra Rosales,[1] Reinhard Würzner,[1] Therese C. Jungraithmayr.[1,2] *[1]Pediatrics, Medical University, Innsbruck, Austria; [2]Gemeinschaft für Pädiatrische Nephrologie (GPN).*

Background: The atypical HUS is a form of thrombotic microangiopathy. Dysfunction of complement proteins are associated with the pathogenesis of the disease. Long-term prognosis is poor.

Methods: Since 2002 the HUSnet Registry investigates the role of complement in aHUS and collects clinical data on long-term outcome. Here we present data of 116 aHUS patients at diagnosis and the 1 year follow-up of 72 patients.

Results: During acute phase the hemoglobin value dropped to 6.03±1.4 mg/dl, the platelet count to 51.3±43.8x109 and mean creatinine was elevated to 4.8±3.5mg/dl. Oliguria/anuria was seen in 59% (mean duration: 13±15 days) of patients. Dialysis was performed in 66% (mean duration: 26±44 days) of patients, of which 30% required chronic dialysis. Arterial hypertension was seen in 79%. Other organ involvement was reported as follows: GI (44%), CNS (28%), cardiac (12%) and pancreas (8%). Treatment of first episode included plasma infusions (PI, 42%) and plasma exchange (PE, 50%). PT was initiated in patients with a higher rate of CNS involvement (p<0.05, X^2) and a tendency towards an increased need for dialysis (p=0.057, X^2).HUS recurrences were reported in 68% (mean 2.6±2.2) of the patients. The first recurrence occurred in median after 4.5 months (range 1-26 months).

One year after diagnosis arterial hypertension was seen in 65%, dialysis in 33% and chronic renal insufficiency in 13% of patients. 51% of the patients had a normal renal function. Two patients died within the first year, due to cardiopulmonary insufficiency. CNS sequel was reported in 1 patient. Patients treated with plasma therapy (PT) showed comparable outcomes to patients without PT after 1 year as measured by the incidence of hypertension, kidney function, CNS sequel and recurrences.

Conclusions: In the acute phase aHUS presents as a multisystem disorder, but in the long term impaired renal function is the main concern. PT is considered as first line treatment, it was especially used in severe cases. Outcome after 1 year was comparable between patients with vs without PT.

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Transcianocobalamin C Deficiency: A Common Cause of Neonatal Thrombotic Mycroangiopathy Gianluigi Ardissino,[1] Francesca Tel,[1] Sara Testa,[1] Fabio Paglialonga,[1] Cristina Felice Civitillo,[1] Francesca Menni,[2] Marta Cerutti,[2] Gabriella Chiarelli,[2] Lorenza Pugni,[3] Fabio Mosca,[3] Alice Monzani.[1] *[1]Pediatric Nephrology Unit, Fondazione Ca'Granda Osp. Maggiore Policlinico, Milano, Italy; [2]Dept. of Pediatrics, Fondazione Ca' Granda Osp. Maggiore Policlinico, Milano, Italy; [3]Neonatal Intensive Care Unit, Fondazione Ca' Granda Osp. Maggiore Policlinico, Milano, Italy.*

Background: Thrombotic mycroangiopathy (TMA) in neonates is extremely rare but when it occurs, transcianocobalamin C deficiency should be suspected.

Methods: We reported 4 cases admitted in our hospital over the past five months.

Results: In all cases symptoms started very early in life with feeding difficulties, failure to thrive and severe hypotonia. In one case left ventricular dilatation had been detected antenatally.

Hereafter, we report the main clinical characteristics of patients at onset.

Patients' characteristics

	SP	MP	DC	MD
Age (days)	21	30	21	19
Weight (Kg)	2.79	3.38	3.30	3.49
PLT (10^3/mm^3)	142	76	120	32
Hb (g/dl)	6.5	7.3	7.8	9.0
LDH (IU/l)	768	911	1101	818
Haptoglobin (mg/dl)	<20	<20	<20	<20
Homocysteine (µmol/l)	17	36	28	>50
sCr (mg/dl)	0.7	0.4	0.6	0.3
uPr/uCr	2.0	10.3	3.8	n.a.
uHb	++++	++	++	+++

uPr/uCr: urinary protein over creatinine ratio - n.a.: not available

The finding of hypomethioninemia, homocystinuria and methylmalonic aciduria led to the diagnosis of methylmalonic acidemia with homocystinuria. Intravenous hydroxocobalamin, oral betain and folic acid were immediately started. During the course of the disease, the first 3 patients developed AKI stage F pRIFLE criteria). Remission of TMA and the recovery of kidney failure took place within next 10 days. Presently, at a mean age of 6 months, all four children are alive and well.

Conclusions: The described "cluster" of TMA due to transcianocobalamin C deficiency, points out that this disease might be a lot more common than diagnosed. Whenever neonatal TMA is detected homocysteinemia should be determined and the disease ruled out. We expect that this report will contribute to an increased awareness regarding this disease among pediatric nephrologists.

FR-PO1926

Mass Spectrometry as a Novel Method for Detection of Podocyturia in Preeclampsia Iasmina Craici,[1] Steven Wagner,[1] Stephen T. Turner,[1] Joseph P. Grande,[2] Vesna D. Garovic.[1] *[1]Nephrology and Hypertension, Mayo Clinic, Rochester, MN; [2]Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN.*

Background: Increasing evidence suggests that podocyturia may serve as both a reliable diagnostic tool for preeclampsia and as a marker of active disease in proteinuric renal diseases. Reservations exist regarding both the research and clinical utilities of the current method to detect podocyturia, mainly due to its technical complexity, time commitment, and the level of expertise required for interpretation of the results.

Methods: The aim of this study was to develop a new technique for the identification of urinary podocytes based on the detection of podocyte specific tryptic peptides by liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS), which will provide an operator-independent and highly reproducible method. Urine samples collected within 24 hours prior to delivery were centrifuged. One half of the sediment was cultured for 24-hours and then stained with podocin antibody followed by a FITC-labeled secondary antibody to identify viable podocytes. The second half of the pellet was solubilized, digested and analyzed by LC-MS/MS using an internal standard.

Results: We have recruited 12 patients with preeclampsia and 6 patients with HELLP. The diagnosis of preeclampsia was confirmed by the presence of hypertension (>140/90 mm Hg) and proteinuria >0.3 g/24 hour. The diagnosis of HELLP was confirmed based on the accepted clinical criteria of Hemolysis, Elevated Liver enzymes, and Low Platelet count. The presence of podocytes was confirmed in all patients by the podocyte culture method. With the LC-MS/MS technology, we documented the presence of a podocin-specific tryptic peptide in all samples.

Conclusions: LC-MS/MS technology may facilitate the use of podocyturia, as confirmed by the presence of podocyte-specific proteins in the urine, both as a diagnostic test and as a research tool in studying renal injury in human disease and animal models of preeclampsia. In addition, if validated in preeclamptic patients, this technology may be used in future studies to assess both disease activity and response to treatment in a variety of proteinuric renal diseases.