Tuesday, 8 September 2015, 17.00–19.00, Hall 2
OFP-12 Oral Free Paper Session Nephropathology

OFP-12-001
Recombinant human erythropoietin treatment in a rat model of nephrectomy
S. Ribeiro*, H. Vala, P. Garrido, J. Fernandes, E. Costa, L. Belo, F. Reis, A. Santos Silva
*IUCIBIO, REQUIMTE, Laboratory of Biochemistry, University of Porto, Portugal

Objective: We aimed to evaluate the impact of rHuEPO on anemia, renal function and structure in chronic renal failure (CRF), using a rat model of nephrectomy.
Method: Male Wistar rats, 12 weeks old, were divided in 3 groups: CRF (induced by a two-stage 5/6 nephrectomy); rHuEPO-CRF (treated with 100 IU/kg/week during 3 weeks) and Sham (surgery without mass reduction). Hematological and biochemical studies were performed. Kidney tissue sections were stained with Periodic acid-Schiff for histological studies. Statistical analysis were performed using the Mann-Whitney test.
Results: At the end of protocol, CRF group presented anemia ($p < 0.05$) and reduced glomerular filtration rate (GFR), whereas rHuEPO-CRF group showed an improvement in hematological parameters ($p < 0.05$) and a slight improvement in GFR. The histopathological analysis of kidney tissue showed that CRF group presented global glomerulosclerosis, tubular necrosis, IFTA and arteriolosclerosis. Due to surgery, we also found some inflammatory cell infiltration. The rHuEPO-CRF group presented mesangial expansion and a reduction in tubulointerstitial and vascular lesions, as compared to CRF rats.
Conclusion: The introduction of rHuEPO corrects the anemia associated with renal failure and improved the degree of renal lesions, slowing the progress of renal failure.

OFP-12-002
Role of macrophage differentiation in the pathogenesis of Lupus nephritis
K. Amann*, G. Olmes, F. Ferrazzi, C. Daniel, M. Büttner-Herold
*Universität Erlangen-Nürnberg, Institut für Nephropathologie, Germany

Objective: The role of macrophages in particular their differentiation (e.g. M1 or M2) in lupus nephritis is unknown. We investigated if macrophage differentiation is associated with stage of lupus nephritis and clinical parameters.
Method: 69 renal biopsies with lupus nephritis (ISN/RPS classes II-V) were assessed for M1(iNOS/CD68), M2a(CD206/CD68) and M2c(CD163/CD68). Blood pressure, proteinuria and serum urea were correlated using Spearman-test. Cluster analysis was used to define Lupus nephritis subtypes by macrophage activation markers.
Results: The mean number of CD68+macrophages was related to ISN/RPS class with the highest macrophage infiltration in diffuse proliferative class IV and the lowest number in class V. In all ISN/RPS classes more CD163+/CD68+ M2c-like than CD206+/CD68+ M2a-like cells were seen. We predominantly detected M2-macrophages independent of ISN/RPS classification. The majority of M2a- and M2c-macrophages were localized in the tubulointerstitium. Using data for macrophage activation markers, 3 different clusters were described. Interestingly, some beeing dominated by one ISN/RPS-class; e.g. >75 % of patients from cluster 1 were allocated to ISN/RPS class IV. Serum creatinine correlated positively with the number of CD68+ ($r = 0.411$; $p < 0.002$) and CD206+/CD68+ M2a-like macrophages in the tubulointerstitium ($r = 0.441$; $p = 0.001$). The number of tubular CD163+/CD68+ M2c-like cells was related to serum urea ($r = 0.611$;$p = 0.001$). Mean number of CD206+/CD68+macrophages was sig. higher in hypertensive compared to normotensive patients ($p < 0.007$).
Conclusion: M2-type macrophages are key players in lupus nephritis and macrophage subpopulations seem to be involved in the development of disease progressing hypertension.

OFP-12-003
Effect of chronic therapy with chaethomellic acid A on renal fibrosis in 5/6 nephrectomized rats: A preliminary study
A. Nogueira*, H. Vala, C. Nobrega, C. A. Pires, B. Colaço, P. A. Oliveira, M. J. Pires
*CITAB, Dept. of Therapeutic and Diagn. Tech., Bragança, Portugal

Objective: The high prevalence of chronic kidney disease underscores the failure to provide therapies to effectively halt, prevent, and/or reverse renal fibrosis. Thus, the aim of this study was to evaluate the effect of chronic treatment with chaethomellic acid A (CA) on renal fibrosis associated to 5/6 nephrectomy.
Method: Male Wistar rats were subjected to 5/6 nephrectomy (RMR) or sham-operated (SO). One week after surgery, rats were placed in four experimental groups: RMR: rats without treatment ($n = 13$); RMR+CA: rats treated with CA ($n = 13$); SO: rats without treatment ($n = 13$); SO+AC: rats treated with CA ($n = 13$). CA was intraperitoneally administered in a dose of 0.23 μg/Kg three times a week for 6 months. Renal samples were scored for the following lesions: glomerulosclerosis, interstitial fibrosis, arteriolosclerosis and interstitial inflammation.
Results: Animals from the SO and SO+AC groups presented no kidney histological changes. Glomerulosclerosis, interstitial fibrosis and arteriolosclerosis scores were significantly lower ($p < 0.001$) in RMR+AC group when compared with RMR group. There were no significantly differences in interstitial inflammation score between RMR+AC and RMR groups.
Conclusion: This preliminary data suggests that pharmacological inhibition of Ras (small GTPase proteins) activation may be a future strategy in the prevention of renal fibrosis.

OFP-12-004
Polyvinylpyrrolidone storage disease in opioid addicted patients
H. Grønseth*, F. J. Leh, T. Bjånes, C. Ohldieck, E. Svarstad, S. M. Leh
*Haukeland University Hospital, Dept. of Pathology, Bergen, Norway

Objective: Opioid addicted patients may inject oral substitution drugs such as methadone or buprenorphine. Some of these drugs contain high molecular polyvinylpyrrolidone (PVP) as an excipient, which is not excreted from the body when given intravenously. PVP deposition is diagnosed histologically by characteristic macrophages with bluish, vacuolated cytoplasm in various tissues. We present a biopsy series from opioid addicted patients showing renal insufficiency as a main clinical sign of PVP deposition disease.
Method: Biopsies ($n = 28$) and one autopsy with characteristic PVP deposition were collected between 2009 and 2013, from 13 opioid addicted patients (mean age 38 years, 12 males, 1 female).
Results: Renal biopsies ($n = 8$) showed interstitial PVP storing macrophages accompanied by various degrees of tubular atrophy and signs of glomerular hypoperfusion. Other main biopsy sites showing the characteristic macrophages were bone/bone marrow ($n = 11$) and the gastrointestinal tract ($n = 5$). Main clinical signs were reduced kidney function (mean serum creatinine 219 micromol/L) and anemia (mean hemoglobin 9.9 g/dL). Abdominal discomfort and fractures were found sporadically. Two patients died. One autopsy confirmed PVP deposition as underlying cause of death.