and indirect immunofluorescent staining was performed with anti-neutrophil elastase (NE) (neutrophil), CD68 (MØ), CD3 (T cell), synaptopodin (podocyte), cytokeratin (tubular epithelial cell), and claudin1 (CL1). CL1 is one of the tight junction proteins that are specifically expressed on epithelial cells of Bowman's capsule. The relationship between the positive cell number for various markers and the crescent formation rate (<30%: low, >30%: high) or global sclerosis rate (<10%: low, >10%: high) was evaluated.

Results: The numbers of CL1+ and NE+ cells were significantly increased in those patients with high crescent formation (p=0.04 and 0.001, respectively). However, no significant differences in CL1+ or NE+ cells were found in relation to the global sclerosis rate. We also evaluated the data from the state of crescents (cellular, fibro-cellular, fibrous, or no crescent). The numbers of CL1+ and NE+ cells were significantly increased in the patients with cellular crescent but was unchanged in those with fibro-cellular or fibrous crescents. The number of CD68+ cells was significantly increased in patients with cellular and fibro-cellular crescents but was unchanged in those with fibrous crescents. No other markers showed any significant difference in relation to crescent formation rate, glomerular sclerosis rate or state of crescents.

Conclusions: These data suggest that the immunostaining for CL1, NE and CD68 of urinary sediment is useful for the evaluation of glomerulonephritis, which may help for the decision of steroid and immunosuppressants.

SA-PO2340

Histopathological Classification of Primary Renal Vasculitis: What's New?

Ana Pinho,[1] Ana Cabrita,[1] Anabela Malho,[1] André Fragoso,[1] Sandra Sampaio,[1] Elsa Morgado,[1] Ana Paula Silva,[1] Isabel Pinto,[1] Idalecio Bernardo,[1] Pedro Neves,[1] Helena Carreira.[2] *[1]Nephrology Department, Faro Hospital, Faro, Portugal; [2]Public Health Institute of Oporto Universtity, Oporto.*

Background: Current histopathological classifications for renal vasculitis are not consensual. A new classification for ANCA-associated glomerulonephritis based on chronic damage extension has been recently described (focal, crescentic, mixed and sclerotic). Our aim was to determine the predictive value for renal outcome according to chronic and active glomeruli damage extension observed on kidney biopsy samples from patients with primary vasculitis.

Methods: We performed a 25 years retrospective study of 66 patients (56% female) with clinical vasculitis (45 had Systemic Lupus Erythematosus and 21 had ANCA-associated glomerulonephritis). Demographic and laboratory data were recorded at the time of biopsy. Biopsy samples were classified as active (≥33% glomeruli combining cellular proliferation, leukocyte infiltration or fibrinoid necrosis-G1); sclerotic (≥33% sclerotic glomeruli-G2); mixed (≥33% combining crescentic and sclerotic glomeruli- G3); crescentic (≥33% glomeruli with cellular crescents-G4) and as focal (≥66% not affected glomeruli-G5). Survival analysis was used to assess differences in renal outcomes according to pathologic groups.

Results: The median of observed glomeruli was 10(49.3% of samples). At 5 years follow-up, the actuarial renal survival was 64.8% in G1, 55.6% in G2, 66.7% in G3, 36.4% in G4 and 93.5% in G5. The Cox regression revealed that hemoglobin (Hazard Ratio(HR)=0.70;p=0.004) and serum creatinine levels (HR=1.22; p=0.046) had a statistically significant effect on renal survival. Compared to G5, the HR for G1 was 5.3 fold higher (p=0.012) and the overall G2, G3 and G4 HR was 4.5 fold higher (p=0.006) .The type of vasculitis had no influence in this Cox model.

Conclusions: Extension damage in excess of one third on renal histologic analysis, in patients with primary vasculitis, emerged as an independent risk factor for progression to renal failure.

SA-PO2341

Misdiagnosed Cases of C3 Glomerulopathy among Children with Post Infectious Glomerulonephritis

Badria M. AlGhaithi,[1] Paul S. Thorner,[2,3] Christoph Licht.[1,3] *[1]Nephrology, The Hospital for Sick Children; [2]Pathology, The Hospital for Sick Children; [3]U of Toronto.*

Background: C3 glomerulopathy (C3G) is a disease entity that has been recently introduced. C3G has been linked to dysregulation of the alternative complement pathway, and is characterized by isolated C3 glomerular deposits in the absence of immunoglobulins (Ig). There are a number of diseases that together with C3G form a phenotypic spectrum including dense deposit disease (DDD), atypical hemolytic uremic syndrome, and more recently, CFHR5 nephropathy. Clinically, C3G varies from mild degrees of hematuria, proteinuria, and renal impairment to end stage renal disease. We postulate that cases of C3G have been misrepresented in the past, possibly as post infectious glomerulonephritis (PIGN).

Methods: Based on this rationale, 33 patients who clinically presented with PIGN at our center from 1985 to 2010 having undergone renal biopsy were retrospectively reviewed for possible re-classification. Clinical characteristics including renal function, complements, urine profile and blood pressure data was captured from first presentation to last available follow up, which ranged from one month to 10 years.

Results: Serum C3 was low for all patients at first presentation. From re-review of the original renal biopsies, 25 patients (76%) were confirmed as PIGN based on the presence of subepithelial hump-like deposits and C3 depositions with or without Ig. Four patients (12%) were categorized as 'possible C3G' based on the absence of subepithelial humps in the presence of C3 but with Ig, while two (6%) had 'probable C3G' based on the presence of C3 only without subepithelial humps. Two patients (6%) demonstrated intermediate features suggesting both DDD and C3G. Five cases in the 'probable' and 'possible' C3G categories had a mild disease course initially resembling PIGN, however due to persistent low C3 and mild proteinuria, a renal biopsy was performed. Of these, 67% (4/6) continued to have proteinuria at last follow-up.

Conclusions: These results support our hypothesis that cases of C3G may have been categorized in the past as PIGN. Genetic testing for complement pathway abnormalities is warranted to further support this hypothesis.

SA-PO2342

Eculizumab as Life Saving Treatment in Complement Mediated MPGN

Seetha Radhakrishnan, Fred G. Pluthero, Christoph Licht. *Division of Nephrology, The Hospital for Sick Children, Toronto, ON, Canada.*

Background: Membranoproliferative glomerulonephritis (MPGN) is a rare glomerulopathy with risk of progression to ESRD and post transplant recurrence. Pathogenetically, there is increasing evidence for dysregulation of the alternative complement pathway (AP). Eculizumab is a monoclonal C5 antibody that prevents terminal complement pathway activation. We present a treatment resistant case of MPGN where eculizumab served as an organ and life sustaining measure.

Methods: A 16 year old healthy female presented with nephrotic range proteinuria, peripheral edema and anemia (LDH and haptoglobin normal; occasional schistocytes). Renal biopsy showed mesangial interposition, wire loops, subendothelial and mesangial deposits and full house IF. In light of negative ANA and dsDNA a diagnosis of MPGN I was made and treatment with steroids and MMF commenced.

At 8 weeks, work up for fever and pancytopenia revealed group A strep, pseudomonas bacteremia, and CMV viremia, which was treated. Bone marrow showed signs of possible macrophage activation syndrome. MMF was held, steroid pulses and IVIG x3 were provided. Patient had persistent thrombocytopenia and anemia, increasing creatinine, and anuria eventually requiring hemodialysis (HD). Complement analysis revealed strong AP activation (undetectable C3; high C5b-9; low CH50; positive C3NeF). While no complement mutation was found, CFHR1/3 was absent on western blot. CFH antibodies were not detected.

Results: To regain complement control, plasma therapy (infusion x5 followed by pheresis x7) was commenced. While there was subtle treatment response (improvement in creatinine and C3) anuria persisted and clinical status deteriorated with respiratory compromise, GI bleeding and seizures. With eculizumab (900 mg/wk x4), treatment response was dramatic: following 1st dose neurologic complications ceased, urine output normalized and HD was discontinued. Thrombocytopenia and anemia recovered after 2nd dose.

Conclusions: Recovery of this patient from life threatening conditions in response to eculizumab strongly suggests (i) a role for AP dysregulation in MPGN pathogenesis and (ii) future AP controlling treatment strategies for MPGN – a remarkable breakthrough for this condition.

SA-PO2343

Platelets Serve as Source of Complement Factor H (CFH) Activity in a Modified Fluid-Phase Alternative Complement Pathway Cofactor Activity Assay

Jiawei Zhao, Fred G. Pluthero, Antony Jeganathan, Christoph Licht. *Division of Nephrology, The Hospital for Sick Children, Toronto, ON, Canada.*

Background: We have recently shown that that the alternative complement pathway regulator complement factor H (CFH) is present in a non-granular compartment in human blood platelets and that platelets are capable of taking up and releasing CFH (Licht et al, Blood 2009). The physiological role of platelet CFH remains to be determined, given the high concentrations of this protein (up to 600 μg/ml) normally present in plasma.

Methods: In order to assess the potential physiological relevance of platelet CFH, washed normal platelets were used as the sole source of CFH in a modified fluid-phase alternative complement pathway cofactor activity assay. This assay allows for testing the potential of a protein to serve as cofactor to complement factor I (CFI) in cleaving C3b, the active form of complement C3, by observing the appearance of C3b cleavage products.

Results: Varying platelet concentrations ranging from 600 to 30/nL were incubated with 2 μg/mL C3b and 6 μg/mL CFI at 37°C for 60 min, and supernatants assayed via immunoblotting for the presence of C3b cleavage products. CFH cofactor activity was observed to increase with platelet concentration, while platelets remained in a resting state. A time course analysis with a platelet concentration of 300/nL (within the normal range of blood platelet concentration) gave results similar to those observed with plasma and purified CFH.

Conclusions: These results show that like endothelial cells, platelets can serve as a cellular source of CFH cofactor activity *in vitro*. This provides support for the emerging hypothesis that in addition to their established roles in the blood coagulation, inflammatory and immune systems, platelets may actively participate in the regulation of the complement system, particularly the constitutively-active alternative pathway that is involved in several complement-related diseases.