Mosaic Pattern of Progenitor Cell Marker CD133 Expression to Identify Podocyte Proliferation Supports Collapsing Variant of Focal Segmental Glomerulosclerosis (FSGS)

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POS-166
THE EFFECTS OF PLASMA EXCHANGE IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS: AN UPDATED SYSTEMATIC REVIEW AND META-ANALYSIS
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Introduction: The effects of plasma exchange on important outcomes in ANCA associated vasculitis are uncertain. We performed a systematic review and meta-analysis of randomized controlled trials to understand the effects of plasma exchange in ANCA associated vasculitis.

Methods: We updated a prior systematic review by searching Medline, EMBASE, and CENTRAL to July 2020. Randomized controlled trials investigating 12 month and longer effects of plasma exchange in patients with antineutrophil cytoplasm antibody associated vasculitis or pauci-immune rapidly progressive glomerulonephritis were eligible. Reviewers independently screened studies, extracted data and assessed the risk of bias. Meta-analyses were conducted using random effects models to calculate risk ratios and 95% confidence intervals. Quality of evidence was summarized in accordance with GRADE methods. Outcomes were assessed at 12 months and longer-term follow-up and included all-cause mortality, end-stage kidney disease, serious infections, relapses of disease, serious adverse events, and health related quality of life.

Results: Nine trials including 1060 participants met eligibility criteria. Data from 7 trials including 999 participants demonstrated with high certainty that plasma exchange reduced the risk of end-stage kidney disease at 12 months (relative risk 0.58, 95% confidence interval 0.38 to 0.89, moderate certainty) with no evidence of subgroup effects. Plasma exchange increased the risk of serious infections at 12 months (relative risk 1.27, 95% confidence interval 1.03 to 1.56, moderate certainty). Plasma exchange did not have important effects on all-cause mortality or other outcomes at 12 months or longer follow-up.

Conclusions: Plasma exchange reduces the 12-month risk of end-stage kidney disease but increases the risk of serious infections.

No conflict of interest

POS-167
PREDICTING THE 1-YEAR RISK OF KIDNEY FAILURE IN ANCA ASSOCIATED VASCULITIS
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Introduction: Being able to predict whether ANCA associated vasculitis will cause kidney failure may inform healthcare providers’ management decisions. We developed a simple risk calculator to estimate the risk of kidney failure requiring dialysis or transplantation in ANCA associated vasculitis.

Methods: We used the combined data from 7 multi-national randomized controlled trials conducted by the European Vasculitis Study Group that included 786 patients. The primary outcome was kidney failure by 1-year post-enrollment. Candidate predictors included age, sex, ANCA type and kidney function (as determined by either serum creatinine or estimated glomerular filtration rate). Models were fit sequentially by reducing the parameters that did not improve model fit. Models were internally validated using bootstrapping. Alternative models were compared using discrimination and calibration statistics and decision curve analysis.

Results: 54 kidney failure outcomes occurred in 786 included participants. Serum creatinine, fit with a cubic spline, and need for dialysis at baseline resulted in the simplest, most parsimonious model with an excellent C-statistic of 0.919 and Brier score of 0.0500. Using estimated glomerular filtration rate instead of creatinine, sex and need for dialysis at baseline as covariates resulted in a C-statistic of 0.847 and Brier score of 0.0693. Simpler models using only serum creatinine as multiple categories or dichotomized as ≤300 or >300 μmol/L performed similarly to the more complicated models for patients at <11% risk of kidney failure at one year but less well for higher risk patients.

Conclusions: A single serum creatinine is a useful estimator of the risk of kidney failure at one year in patients with ANCA associated vasculitis. Even simple categorization of serum creatinine can reliably identify patients at low, moderate and high risk of kidney failure.

No conflict of interest

POS-168
MOSAIC PATTERN OF PROGENITOR CELL MARKER CD133 EXPRESSION TO IDENTIFY PODOCYTE PROLIFERATION SUPPORTS COLLAPSING VARIANT OF FOCAL SEGMENTAL GLomerulosclerosis (FSGS)
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Introduction: Previous studies using immunofluorescent methods indicate that both the cellular crescents in crescentic glomerulonephritis and the podocyte proliferation in collapsing FSGS may both originate from parietal epithelial cells, which serve as CD133 positive progenitor cells. We have previously confirmed positive CD133 staining in the cellular crescents of crescentic glomerulonephritis. However, the role of CD133 expression in highlighting the proliferative podocytes in collapsing FSGS has not been adapted to the renal pathology practice.

Methods: We have identified 19 collapsing FSGS from our archive over past 10 years (out of 3942 renal biopsies, 0.5%). The collapsing FSGS cases were either HIV positive (1/19, 6%) or negative (16/19, 84%). All patients were of African American descent with prominent renal failure and nephrotic proteinuria. We used immunohistochemical methods to stain the following specimens with CD133: 19 biopsies of collapsing FSGS, 24 biopsy controls from other renal diseases, and 10 negative controls from other nephrectomy specimen. The glomerular and tubular expression of CD133 between the three groups was evaluated by light microscopy.

Results: Both negative controls and biopsy controls revealed positive CD133 in parietal epithelial cells without staining in the podocytes (Below, Figure 1A [normal], and 1B [FSGS, not otherwise specified] by CD133 staining). Negative controls did not stain for CD133 in proximal tubules while biopsy controls showed focal to diffuse CD133 staining in proximal tubules. The striking finding was that all collapsing FSGS showed positive CD133 staining in the clusters of proliferative podocytes (ranging from 4.3% to 81% of all glomeruli in all cases), which displayed a mosaic pattern intermingled with collapsed glomerular capillary loops (Figure 1B and 1C [collapsing FSGS] by CD133 staining; proliferative podocytes indicated by arrows). In addition, proximal tubules of the collapsing group all showed diffuse and strong CD133 staining (Figure 1C [collapsing FSGS] by CD133 staining; proliferative podocytes indicated by arrows). Corresponding to high serum creatinine levels in the patients with collapsing FSGS.

Conclusions: Our data indicate that the combination of distinctive mosaic CD133 staining pattern of proliferative podocyte with intermingled capillary tufts and diffuse proximal tubular expression of CD133 can support a diagnosis of collapsing FSGS. In addition, our finding using the immunohistochemical staining of CD133 in proliferative podocytes of collapsing FSGS further supports the view that both...
the cellular crescents from crescentic glomerulonephritis and the proliferative podocytes are derived from the same progenitor source: peritubular epithelial cells.

No conflict of interest

POS-169
LEVAMISOLE IS A PROMISING ALTERNATE IMMUNOSUPPRESSIVE THERAPY IN FREQUENT RELAPSING AND STEROID DEPENDENT CHILDHOOD NEPHROTIC SYNDROME

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Introduction: Frequent Relapsing Nephrotic Syndrome (FRNS) and Steroid Dependent Nephrotic Syndrome (SDNS) are often difficult to manage in terms of need of prolonged steroid use, recurrent relapses, frequent infection and hospital admission. Similarly, alternate immunosuppressive therapies have themselves risk of bone marrow suppression and organ toxicities. Levamisole is an anthelmintic with less immunomodulatory action which can be effective in managing FRNS and SDNS.

Methods: This is a retrospective chart review of data from Feb 2018 to Jan 2020 of children with nephrotic syndrome who received levamisole and whose initiation on levamisole was begun before August 2019. The response of levamisole on course of Nephrotic Syndrome and side effect profile among FRNS and SDNS was observed.

Results: 45 cases were put on levamisole during the study period, of which 9 cases were SDNS and remaining were FRNS. The mean age of FRNS was 6±2 yrs., among FRNS cases remission for at least 6 months was achieved among 61.1%, while 22.2% had In-Frequent Relapsing course. On the other hand, switch over to other immunosuppressive therapy was required in just 16.6% of the cases. The mean age of SDNS was 4.5±2 yrs., 22.2% among SDNS had sustained remission for at least 6 months and 55.5% had in frequent relapsing course and 22.2% needed switch over to other immunosuppressive therapy. 1 case of FRNS was admitted with pneumonia while 2 cases of SDNS needed admission (1 with pneumonia and 1 with peritonitis). No cases had bone marrow suppression, 2 cases with SDNS had skin manifestation in the form of Tinea cruris and molluscum contagiosum.

Conclusions: Levamisole is one of the cheap and effective alternate immunosuppressive agents which can be used in FRNS and SDNS, with better advantage in FRNS and also has minimum side effect profile.

No conflict of interest

POS-170
TB OR NOT TO BE, THAT IS THE QUESTION

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Introduction: Although the incidence of Tuberculosis (TB) worldwide is decreasing, the risk of pulmonary and disseminated disease remains high in recipients of solid organ transplants. The presentation of TB may not always overt and should be considered in all transplantation patients.

Methods: A case report of a patient presenting to a tertiary renal transplantation centre.

Results: We present a case report of a 71-year-old man who underwent a kidney transplant due to end stage renal failure secondary to diabetic nephropathy. The induction agent was Basiliximab on day zero and day four and he was immunosuppressed with MMF, Tacrolimus and Prednisolone. Seven months after transplantation he presented with vague symptoms of abdominal pain, fevers and leukopenia. On admission his LFTs were deranged and an MRCP showed a diffuse cholangiopathy of infective origin which was stented with ERCP. The patient did not respond to antibiotics and continued to spike temperatures with dwindling transplant function. A CT Chest Abdo Pelvis was suggestive for an infective cholangiopathy. The patient was treated with quadruple tuberculosis therapy and made a good recovery, including transplant kidney function. Throughout admission the patient did not culture TB in sputum or blood.

Conclusions: Tuberculosis should be considered in all transplant kidney recipients presenting with vague or unclear symptomatology despite successive negative TB cultures.

No conflict of interest