Results: Plasma levels of Clusterin were significantly decreased in active LN patients when compared to healthy controls (p<0.05). Plasma Clusterin levels were negatively correlated with CRP, SLEDAI, and 24 hours proteinuria (p<0.01, p<0.05, and p<0.05). In sixteen patients with lupus nephritis, we found that the expression of Clusterin in glomeruli was significantly enhanced in severe LN when compared to mild LN (figure 1, p<0.05).

Conclusions: Decreased Clusterin could involve in the pathogenesis of LN, and the role of renal Clusterin need to be further explored. These findings suggested that Clusterin would be a therapeutic target for lupus nephritis in the future.

Disclosure of Interest: None declared


Background: Renal involvement in ANCA-associated vasculitis (AAV) and systemic lupus erythematosus (SLE) manifests as autoimmune-mediated glomerulonephritis (AIGN). In AAV, crescentic lesions and a pauci-immune immunofluorescence is typically seen while in SLE endo- and extracapillary proliferative lesions and a full-house immunofluorescence is seen. Although these are clinically divergent autoimmune diseases, neutrophil extracellular traps (NETs) are postulated to be involved in their pathogenesis. NETs are immunogenic, extracellular DNA structures harbouring relevant ANCA- and nuclear auto-antigens. However, it is still unclear how and if NETs can act as a common pathway for both AAV and SLE.

Objectives: To increase our understanding of the potential pathogenic role of NETs in AAV and SLE, the aim of this study was to compare the characteristics of ex vivo AAV- and SLE-induced NET formation.

Methods: Ex vivo NET formation was quantified by our highly-sensitive NET quantification assay using 3D-confocal microscopy for 82 AAV, 56 SLE patients and 10 healthy controls (HC). Live cell imaging was used to study the morphology and kinetics. Qualitative characteristics of NETs were investigated by immunofluorescence microscopy that detected co-localisation of NET-markers, including citrullinated histon-3 (CitH3) and high mobility group box-1 (HMGB1). Also, the presence of IgG, IgM or IgA autoantibodies on AAV- and SLE-induced NETs was studied. Autoantibodies as trigger of NET formation were investigated by depleting serum from IgG and NET inhibition assays were performed using peptidylarginine deiminase-4 (PAD4) and NADPH inhibitors.

Results: Quantifying ex vivo NET formation demonstrated excessive NET formation for both AAV and SLE as compared to HC. AAV-induced NET formation (median [Q1 – Q3]: 20.7 [9.6–74.1]) was significantly higher compared to SLE-induced NET formation (5.6 [2.3–14.3]; p<0.0001). Secondly, live cell imaging revealed lytic NET formation in AAV peaking after 2–4 hours while in SLE non-lytic NET formation with neutrophil clustering occurred within minutes. Thirdly, the presence of CitH3 was significantly higher on AAV-induced NETs, whereas SLE-induced NETs contained significantly more HMGB1. AAV-NETs were triggered independent of IgG, in contrast to IgG dependence of SLE-NETs. Intriguingly, immunofluorescence staining of immunoglobulins revealed a pauci-immune expression on AAV-NETs compared to a full-house expression of IgG, IgM and IgA on SLE-NETs. Both PAD4 and NADPH were involved in AAV- but not in SLE-induced NET formation. To further corroborate on these differences, we found that SLE-NETs were enriched for oxidised mitochondrial DNA as demonstrated by TOM20 and MitoSOX.

Conclusions: This study demonstrates that excessive NET formation in AAV is intrinsically different to NET formation in SLE. AAV-NETs are characterised by a suicidal lytic PAD4- and NADPH-dependent expulsion of citrullinated NETs, whereas SLE-NETs are characterised by rapidly-induced clusters with HMGB1, enriched for mitochondrial DNA and enhanced immune complex formation altogether supporting a pro-inflammatory role of NETs in the pathophysiology of SLE, including immune-complex mediated, full-house lupus nephritis.

Disclosure of Interest: None declared


EXCESSIVE FORMATION OF NEUTROPHEL EXTRACELLULAR TRAPS HAVE A DIFFERENT ROLE IN THE PATHOGENESIS OF ANCA-ASSOCIATED VASCULTIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

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