

Increased complement C5a expression in IgA immune complexes from children with inflammatory renal disease

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Background: Glomerular immunoglobulin deposition is a common finding in inflammatory renal diseases, including immunoglobulin A (IgA) related nephritis and lupus nephritis (LN)^{1,2}. Previous biological studies within the literature have demonstrated that IgA and immunoglobulin G (IgG) alone are unable to induce a direct pathogenic response in renal mesangial cells^{2,3} leading to the hypothesis that complement components bound to the immune complex may be the source of this damage. This study aimed to explore the extent of active complement component binding to IgA immune complexes isolated from patients with inflammatory renal disease.

Methods: This study used the ThermoScientific CaptureSelect system with Pierce spin columns to isolate IgA immune complexes from 200µL plasma from a small pilot cohort of patients with immunoglobulin A vasculitis nephritis (IgAVN), LN and age- and sex-matched healthy controls (n=6/group). The immune complexes were then analysed for their expression of complement components C3a and C5a using western blotting after normalisation to IgA concentration. Data are expressed as median [range] and are analysed using Kruskal-Wallis with Dunn's multiple comparisons test.

Results: There were no significant differences between age or gender between groups (Table 1). There was no significant difference in the total protein concentration obtained from 200µL of plasma between any of the groups (data not shown). When normalised to the concentration of IgA with the immune complexes there was no difference in the expression of complement C3a within the immune complexes between the groups (Figure 1A). There was, however, a significantly increased expression of complement C5a in the immune complexes isolated from patients with LN (0.004 [0.003-0.009]; p=0.006) compared to healthy controls (0.002 [0.0008-0.003]) (Figure 1B). When normalised to the concentration of IgG within the immune complexes there were no significant differences between any of the groups for either complement C3a or complement C5a (Figures 1C-D).

Discussion: These pilot data suggest a potential increased expression of complement C5a in IgA immune complexes isolated from children with LN compared to healthy controls. Building on these data with further laboratory studies may provide evidence of the potential usefulness of targeting the complement system in these renal inflammatory diseases.