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P431 -Seronegativity in biopsy-proven lupus nephritis: 4 cases observed in white Caucasian men

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Introduction: Systemic lupus erythematosus (SLE) is a chronic immune-mediated condition. It is most commonly seen in females, particularly those of African or Asian origin. Renal involvement in SLE is seen in 50-70% cases¹ and is associated with significant morbidity and mortality. ANA-negative SLE has been recognised since 1979². However the incidence of seronegative patients – in particular white Caucasian men - with biopsy-proven lupus is unclear. We present 4 case reports with a review of the relevant literature.

Methods: For the literature review a MEDLINE search was performed, using terms such as ‘lupus nephritis’, ‘nephropathy’, ‘seronegative’ and ‘antibody-negative’. Cases were selected if the patient had biopsy findings consistent with lupus nephritis, were seronegative for anti-nuclear antibody (ANA), anti-double-stranded DNA antibody (anti-dsDNA), anti-smith antibody (anti-SM), anti-phospholipid antibody (APA) and had normal complement levels.

Results: 17 articles with 64 cases (n=64) of proposed seronegative lupus nephritis were identified. The data were published between 1983 and 2018. All patients showed seronegativity at initial presentation however 45.3% (n=29) of patients developed positive serology at follow up. The age range of patients was between 5 months to 70 years. 31 patients were female, 12 were male and in 21 cases the gender was not reported. The ethnicity was reported in only 9.4% (n=6) of cases. Excluding the absent demographic data, there were no reported cases in white Caucasian men. We present 4 cases of white Caucasian men who presented with deranged renal function and either nephritic (n=1) or nephrotic (n=3) syndrome. They were found to be negative for all SLE-associated autoantibodies and had normal complement levels. Immunofluorescence microscopy demonstrated “full house” positivity for C3, C1q, IgA, IgM, and IgG in all patient samples (n=4). Their biopsy findings on light microscopy are detailed in table 1. All patients have had repeat serological testing and have all shown persistent seronegativity.

Discussion: As evidenced by our brief literature review and another recent literature review³ there is a growing number of cases with reported seronegativity in lupus nephritis. The mechanism remains unknown. One theory speculates that antibodies such as ANA become trapped in circulating immune complexes⁴. Alternatively, the reported results may be secondary to technical failure⁴ or conversely the biopsy findings may have been wrongly diagnosed, and perhaps other conditions should be considered^{5,6}.

Conclusion: In summary, we present 4 cases of an increasingly recognised phenomenon in a novel demographic group. Renal disease in SLE is associated with significant morbidity and mortality. Therefore the recognition of this pathology is vital, yet may be challenging in patients that present with seronegativity.