ANTI-C1q ANTIBODIES BUT NOT ANTI-DOUBLE STRANDED DNA ANTIBODIES ARE USEFUL BIOMARKER OF RENAL FLARE IN PEDIATRIC LUPUS NEPHRITIS.

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ABSTRACT

BACKGROUND: Several biomarkers have been used for assessment of lupus nephritis (LN) patients. One of these biomarkers is anti- C1q antibodies (Abs) which are thought to be specific for renal flare. **OBJECTIVE:** To study the value of serum anti-C1q Abs in diagnosis and prediction of renal flare in pSLE in comparison to serum anti-double stranded DNA (anti-ds DNA) Abs and complement-3 (C3). **METHODS:** This was a prospective study that included 40 pSLE patients with regular follow up every 3 months for 15 months. During each visit, clinical evaluation and routine laboratory markers for SLE patients in addition to serum anti-C1q Abs was measured using enzyme linked immunosorbent assay were done. Also, SLE disease activity index (SLEDAI) and the British Isles Lupus Assessment Group (BILAG)-2004 renal score were measured. Renal biopsy was done for 38 patients. **RESULTS:** Anti-C1q Abs titre was positive in 79% of the patients. Anti-C1q Abs had a significant positive correlation with 24 hours urinary proteins and BILAG-renal score ($p < 0.05$), while neither C3 nor anti-dsDNA correlated significantly with any of them ($p > 0.05$). An initial anti-C1q Abs titre of 11 U/ml was significantly able to differentiate LN class III and IV from LN class II ($p = 0.02$), while a titre of 16 U/ml can significantly differentiate between active LN from inactive LN ($p = 0.02$). Both C3 and anti-dsDNA Abs were non-significant tools ($p > 0.05$). **CONCLUSION:** Anti-C1q Abs is a useful biomarker of LN and differentiate active from inactive nephritis. However, its absence could not exclude LN.

BACKGROUND

Renal disease is present in up to 80% of patients with pediatric systemic lupus erythematosus (pSLE). In approximately 90% of these patients, the nephritis is manifested within the first year after diagnosis of SLE. Anti-C1q Abs are present in 30– 60% of SLE patients and their clinical interest originates from their strong association to active renal disease. The high prevalence of anti-C1q Abs in SLE patients might have important consequences for the clinical management as well as for the understanding of pathogenic mechanisms in SLE. Very high titres of anti-C1q Abs strongly increase the likelihood of the presence of severe LN.

OBJECTIVES

To study the value of serum anti-C1q Abs in diagnosis and prediction of renal flare in pSLE in comparison to serum anti-double stranded DNA (anti-ds DNA) Abs and complement-3 (C3).

METHODS

This was a prospective study that included 40 pSLE patients with regular follow up every 3 months for 15 months. During each visit, clinical evaluation and routine laboratory markers (Complete blood count, ESR, serum creatinine, urea, complete urine analysis, 24 hours urinary proteins and creatinine clearance) for SLE patients in addition to the immunological markers where anti-ds DNA and serum anti-C1q Abs were measured using enzyme linked immunosorbent assay. Complement-3 was measured as well using turbidimetery. SLE disease activity index (SLEDAI) and the British Isles Lupus Assessment Group (BILAG)-2004 renal score were measured. Renal biopsy was done for 38 patients.

RESULTS

Anti-C1q Abs titre was positive in 79% of the patients. The frequency of positive anti-C1q Ab, anti-dsDNA Ab and consumed C3 was comparable among histo-pathological classes of LN ($p > 0.05$) (Figure 1). Anti-C1q Abs had a significant positive correlation with 24 hours urinary proteins and BILAG-renal score ($p < 0.05$), while neither C3 nor anti-dsDNA correlated significantly with any of them ($p > 0.05$) (table 1). An initial anti-C1q Abs titre of 11 U/ml was significantly able to differentiate LN class III and IV from LN class II ($p = 0.02$) (figure 2). Anti-C1q Abs was significantly higher among patients with LN class III and IV versus those with LN class II (table 2). A titre of 16 U/ml can significantly differentiate between active LN from inactive LN ($p = 0.02$) (figure 3). Both C3 and anti-dsDNA Abs were non-significant tools ($p > 0.05$).

Table 1. Correlation of the measured serological markers with the clinical and laboratory parameters in the studied patients.

Variable	Serum anti-C1q	Serum anti-dsDNA	Serum C3
Age (years)	r = 0.095 p = 0.563	r = -0.108 p = 0.511	r = 0.094 p = 0.57
Duration of LN (years)	r = -0.263 p = 0.106	r = -0.276 p = 0.089	**r = 0.393** **p = 0.013***
ESR mm/hr	**r = 0.541** **p = 0.008***	r = -0.046 p = 0.470	r = -0.197 p = 0.229
SLEDAI score	**r = 0.474** **p = 0.002***	r = 0.2 p = 0.223	**r = -0.400** **p = 0.012***
24 hour urinary proteins (gm/dl)	r = **0.32** p = **0.048***	r = -0.183 p = 0.265	r = -0.085 p = 0.608
Corrected creatinine clearance (ml/min/1.73m^2)	r = -0.1 p = 0.534	r = 0.185 p = 0.260	r = 0.039 p = 0.814
BILAG score	r = 0.37 p = **0. 021***	r = 0.122 p = 0.459	r = -0.165 p = 0.315

Table 2. Comparison of the studied serological markers between patients with LN class III and IV and those with LN class II.

	Patients with LN class III-IV N= 26	Patients with LN class II N= 12	Z	p
Anti-C1q Abs (U/ml)				
Median	22	8.5	-2.29	0.02*
Range	4-100	3-50		
Anti-ds DNA Abs (IU/ml)				
Median	288	140	-1.18	0.24
Range	49-1614	102-812		
C3 (mg/dl)				
Median	75	97.5	0.92	0.35
Range	20-245	30-260		

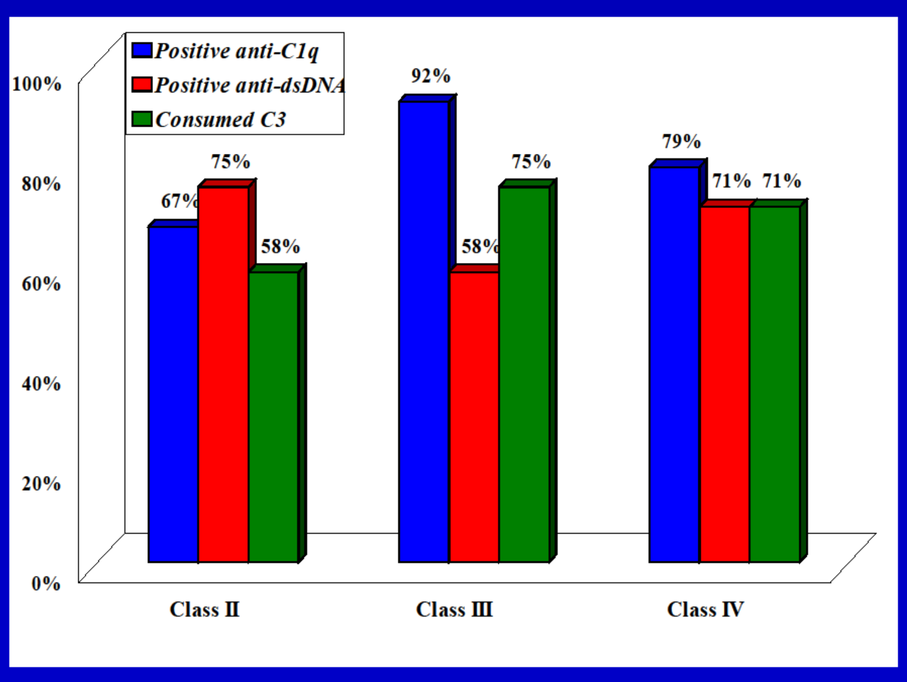

Figure 1: The frequency of positive anti-C1q Ab, anti-dsDNA Ab and consumed C3 among different histopathological classes of LN. The frequency of positive anti-C1q Ab, anti-dsDNA Ab and consumed C3 was comparable among histopathological classes of LN ($p > 0.05$)

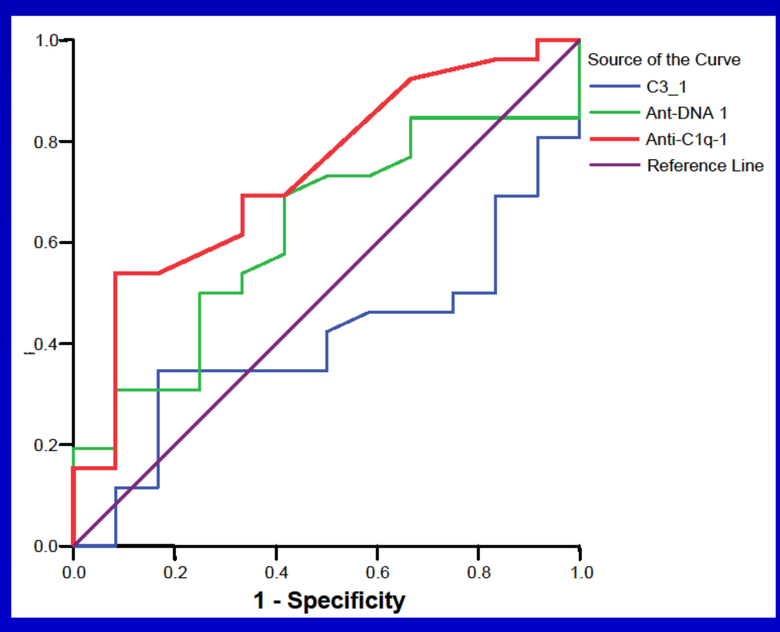

Figure 2: Receiver-operating characteristic (ROC) curve comparing serum levels of C3, anti-dsDNA Abs, anti-C1q Abs in their ability to differentiate LN class III and IV from LN class II. For anti-C1q, AUC was found to be 0.73, while it was 0.62 for anti-dsDNA and 0.41 for C3. Anti-C1q Abs titre of 11 U/ml was able significantly to differentiate LN class III and IV from LN class II with sensitivity 69 % and specificity 67% ($p = 0.02$).

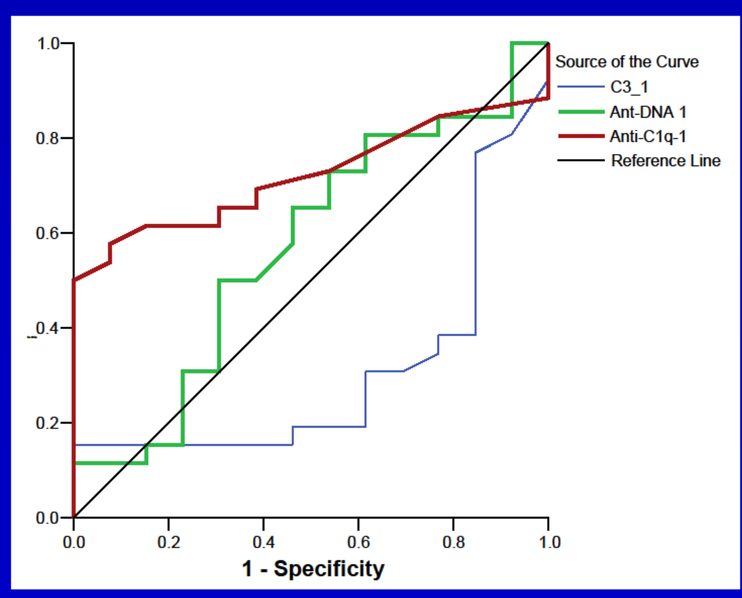

Figure 3: Receiver-operating characteristic (ROC) curve comparing serum levels of C3, anti-dsDNA Abs, anti-C1q Abs in their ability to differentiate active (BILAG A, B, C) LN from inactive (BILAG D, E) LN. For anti-C1q, AUC was found to be 0.72, while it was 0.57 for anti-dsDNA and 0.31 for C3. Anti-C1q Abs titre of 16 U/ml was able significantly to differentiate active LN from inactive LN with sensitivity of 62 % and specificity of 85 % ($p = 0.02$).

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CONCLUSIONS

Anti-C1q Abs is a useful biomarker of LN and differentiate active from inactive nephritis. However, its absence could not exclude LN.

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