Autoantibodies Against C1q: View on Association Between Systemic Lupus Erythematosus Disease Manifestation and C1q - autoantibodies

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Introduction

Activation of the complement system is the first step in the prevention of damage by immune complexes. Systemic lupus erythematosus is the prototype of immune complex diseases. The classical pathway of the complement system is considered to be the most important pathway in immune complex clearance. This pathway may be activated by IgM- and IgG-containing immune complexes after binding to C1q (1).

In 1984 autoantibodies to C1q (C1qAb) were reported to be present in serum of patients with systemic lupus erythematosus (SLE) (2). The recognition that C1q may serve as a non-organ-specific autoantigen has attracted a growing number of investigators (3).

Patients and Methods

We studied 42 patients (38 female and 4 male, aged 19-64) with systemic lupus erythematosus. Twenty eight of them (66,66%) have proven with renal biopsy lupus nephritis (2 patients hat WHO class II lesions, 4 – WHO class III, 18 – WHO class IV, 4 – WHO class V), 14 of patients (33,33%) have evidence for lupus pneumonitis and 11 (29,19%) – for central nervous system involvement (Tabl.1). All patients were tested for both basic and subclass ELISAs for C1qAb using modification of the methods of J.J. Wisnieski and S.M. Jones (4). Whole C1q was purified from human plasma by the method of A.J. Tenner, P.H. Lesarve and N.R. Cooper (5).

Table 1. Basic clinico-laboratory parameters in study patients

№ / sex / age (years)	C1qAb	Anti-dsDNA	ANA	Lupus nephritis/WHO class/ proteinuria (g/24 h±SD)	**Pneumonitis**	**Central nervous system involvement**
1. / f / 28	+			+ WHO class IV (6,8±2,4)	+	
2. / f / 19	+	+	+	+ WHO class IV (8,7±3,1)	+	+
3. / f / 36					+	
4. / f / 25	+		+	+ WHO class V (5,4±0,5)		+
5. / f / 34						
6. / m / 33				+ WHO class II (2,1±0,9)	+	+
7. / f / 41						
8. / f / 27	+	+	+	+ WHO class IV (7,2±3,4)		
9. / f / 34	+					+
10. / f / 50				+ WHO class IV (3,5±1,4)		
11. / f / 44			+	+ WHO class IV (4,1±1,5)		+
12. / f / 26	+	+		+ WHO class IV (4,4±2,3)		
13. / f / 30	+			+ WHO class V (7,1±1,2)	+	+
14. / f / 64			+	+ WHO class IV (2,5±0,9)	+	
15. / f / 24	+	+	+	+ WHO class IV (3,4±1,7)		
16. / f / 38					+	+
17. / f / 40				+ WHO class IV (1,2±0,7)		
18. / f / 47		+	+	+ WHO class IV (2,4±0,8)	+	+
19. / f / 29	+			+ WHO class IV (4,2±1,3)	+	
20. / f / 22	+	+	+			
21. / f / 34	+			+ WHO class IIIB (3,8±1,7)		

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22. / f / 31	+					
23. / f / 28	+	+		+ WHO class IV (5,3±2,0)	+	
24. / f / 42						
25. / m / 36	+	+	+	+ WHO class IIIB (4,8±1,4)		
26. / f / 32	+					+
27. / f / 25	+					
28. / f / 31		+	+	+ WHO class IV (3,1±1,7)	+	
29. / f / 36					+	+
30. / f / 27			+			
31. / f / 23	+					
32. / m / 24		+	+	+ WHO class V (4,0±1,1)	+	
33. / f / 34				+ WHO class IIIA (2,3±0,8)	+	
34. / f / 41	+			+ WHO class IV (4,2±2,3)		+
35. / f / 28		+	+	+ WHO class IV (3,0±0,6)		
36. / f / 23						
37. / m / 31		+	+	+ WHO class IV (2,4±0,3)		
38. / f / 36				+ WHO class V (1,7±0,3)		
39. / f / 25				+ WHO class IV (1,7±0,5)		
40. / f / 34				+ WHO class IIIB (2,1±0,4)		
41. / f / 27		+	+	+ WHO class IV (5,2±2,6)		
42. / f / 20				+ WHO class II (0,9±0,3)		

Abbreviation are: ANA-antinuclear antibodies, C1qAb- autoantibodies to C1q, Anti-dsDNA - Anti dsDNA antibodies, f - female, m – male

Results

Raised C1qAb titres were found in 18 of patients (42,86%). Among all patients with C1qAb 12 had renal manifestation of SLE (83,33% of them had focal or diffuse proliferative glomerulonephritis), 6 -central nervous system involvement and 5 – lupus pneumonitis. Patients with raised C1qAb titres were younger, 7 of them were positive for antibodies to dsDNA. The magnitude of proteinuria was positively associated with the presence of C1qAb.

In 7 of our patient (№№ 6, 11, 16, 18, 28, 32, 33) was established selective complete C1q deficiency, in two of them (№№ 18, 28) there were clinical data for presence of systemic lupus erythematosus in the family.

Available sera testing positive for IgG C1qAb were analyzed for C1qAb IgG subclass distribution. Six patients (33,33%) had IgG2 C1qAb only, 3 patients (16,67%) – IgG1C1qAb only, and 9 (50%) had both IgG1 and IgG2C1qAb. Therefore, IgG2C1qAb was present in 83,33% of patients. The subsets of sera from patients with IgG1 or IgG2C1qAb were assayed for total serum IgG1 and IgG2 levels by radial immunodiffusion. The mean total serum IgG1 was 7,9±4,5 mg/ml, the mean total serum IgG2 was 2,6±1,4 mg/ml. The mean ratio of G1/G2 (3,4±2,1) was similar to that reported in the literature for disease free individuals (6). The percentage of IgG2C1q relative to total IgG2 was significantly greater than percentage of IgG1C1qAb relative to total IgG1 (0,03±0,06% vs. 0,01±0,02% respectively, $P<0,005$, t-test). Thus, in our patient population the IgG2 component of the autoantibody response to C1q is disproportionately enriched relative to the overall IgG subclasses distribution, as no alteration in IgG subclass distribution was noted. The C1qAb in our population were predominantly of IgG2 and IgG1 subclasses. This distribution is consistent with that found by JJ Wisnieski and SM Jones in a study characterizing C1qAb in patients with SLE and hypocomplementemic urticarial vasculitis (4), but contrasts with the IgG3 and IgG2 predominance reported by IEM Coremans et al. in patients with SLE (7). The mechanisms mediating autoantibody pathogenicity remain unclear. It has been proposed that C1qAb may act systemically by up-regulating activation of classical complement pathway (8). Alternatively, C1qAb may act locally within the renal glomerulus to enhance tissue injury initiated by immune complex deposition. The association of C1qAb with proliferative lupus nephritis is now well established (2), but significance of C1qAb for lupus pneumonitis and cerebrovasculitis is target to future investigations.

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