Behavior of Complement Levels and Risk of Organ Involvement in SLE Patients

Ignacio Javier Gandino[1], Marina Scolnik[1], Emmanuel Bertiller[1], Valeria Scaglioni[2] and Enrique R. Soriano[3], [1]Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, Instituto Universitario Hospital Italiano de Buenos Aires, and Fundacion PM Catoggio, Buenos Aires, Argentina, [2]Rheumatology, Hospital Italiano, Buenos Aires, Argentina, [3]Internal Medicine, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

Background/Purpose: the complement system plays a major role in autoimmune diseases, and in particular in systemic lupus erythematosus (SLE). Complement deficiencies are a genetic risk factor for SLE. Also a reduction in complement levels has been associated with an increase in SLE activity, with certain organ involvement (ie glomerulonephritis) and as a predictor of a SLE flare. Our objective was to analyze clinical course of SLE patients with permanent low complement levels, and compare them with those with fluctuant levels or persistently normal levels.

Methods: complement determinations (C3 and C4 levels) were analyzed in patients with SLE (fulfilling ACR or SLICC criteria) seen at a University hospital between 2000 and 2013. Patients were grouped in those with permanent C3 and/or C4 low values (low complement group) those with C3 and C4 constant normal values (normal complement group), and those with fluctuant values (periods of normal and periods of low values, during follow up: fluctuant group). Mortality, clinical characteristics, organ involvement and antibodies were analyzed and compared between groups.

Results: Two hundred and seventy SLE patients were included (242 females, 89.6%), mean age at diagnosis was 34.2 years (SD 15.8). Patients were divided according to complement levels during follow up in 3 groups: persistent low complement levels (n=79), normal complement levels (n=116), and fluctuant levels (n=75). Demographics, clinical and serological characteristics are shown in table 1. Mortality was similar between the three groups (5%, 4% and 7%, respectively). Lupus glomerulonephritis was more frequent in patients with fluctuant levels of complement (both proliferative and membranous glomerulonephritis). Patients with normal complement had less frequency of hematological involvement and antiDNA antibodies. On multivariable analysis persistent low complement levels were neither associated with mortality nor with

organ damage as measured by SLICC (SLICC>0). Only increased age was associated with mortality, and increased age and neurologic involvement with SLICC >0.

Conclusion: Different behavior of complement levels in SLE patients was not associated with differences in outcomes (mortality and organ damage). Although there were some differences in organ involvement (higher prevalence of glomerulonephritis in fluctuant levels group, and hematological involvement and anti DNA antibodies in low and fluctuant levels groups), do not appear to represent clear different sub-groups of patients.

Table 1. SLE patients grouped by behavior of complement levels during follow up.

	Normal complement (n=116)	Persistent Low complement (n=79)	Fluctuant complement (n=75)	P value
Females, n (%)	107 (92.2)	70 (88.6)	65 (86.7)	0.439
Age at diagnosis, average, years (SD)	36.4 (16.5)	32.4 (14.7)	32.7 (15.8)	0.1397
Follow-up, median, years (IQR)	6.4 (8.2)	6.1 (7.6)	9.2 (5.6)	0.345
Fulfilling ACR criteria, n (%)	76 (65.5)#	64 (81)*	66 (88)&	0.001 * and & vs #
Fulfilling SLICC criteria, n (%)	96 (82.7)#	73 (92.4)	74 (98.7)&	0.001 & vs #
Cutaneous Lupus, n (%)	76 (65.5)	50 (63.3)	44 (58.7)	0.773
Oral ulcers, n (%)	24 (20.7)	19 (24.1)	20 (26.7)	0.624
Serositis, n (%)	37 (31.9)	15 (18.9)	17 (22.7)	0.102
Artritis, n (%)	59 (50.9)	47 (59.5)	35 (46.7)	0.261
Neurologic, n (%)	15 (12.9)	7 (8.9)	7 (9.3)	0.598

Renal, n (%)	57 (49)#	44 (56)*	56 (75)&	0.002 & vs # and *
Leukopenia or lymphopenia, n (%)	35 **(30.2)#**	39 (49.4)*	34 (45.3)&	0.007 * vs # and 0.033 & vs #
Thrombocytopenia	20 **(17.2)#**	28 (35.4)*	25 (33.3)&	0.026 * and & vs #
ANA positive, n (%)	109 (94)	77 (97.5)	68 (90.7)	0.202
DNA positive, n (%)	52 (44.8)#	54**(68.3)***	57 **(76)&**	<0.001 * and & vs #
Sm positive, n (%)	12 (10.3)	10 (12.7)	8 (10.7)	0.882
Lupus anticoagulant positive, n (%)	14 (12.1)	16 (20.2)	11 (14.7)	0.254
Anticardiolipins positive, n (%)	17 (14.7)	20 (25.3)	13 (17.3)	0.405
SLICC at the end of follow up, mean (SD)	0.98 (1.4)	1 (1.4)	1.33 (1.7)	0.2345