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Original article

Anti-C1q antibodies and systemic lupus erythematosus in the Tunisian population

Anticorps anti-C1q et lupus érythémateux systémique dans la population tunisienne

B. Trad [a], H. Ben Hassine [b], M. Khalifa [c], N. Idriss [b], F. Slama [b], F. Bahri [c], C. Laouani kechrid [d], J. Boukadida [a], R. Sghiri [a,*]

[a] *Laboratory of Microbiology-Immunology, Farhat Hached Hospital, Ibn Al Jazzar street, 4000 Sousse, Tunisia*
[b] *Laboratory of Immunology, Research Unit UR 807, Faculty of Medicine of Sousse, Sousse, Tunisia*
[c] *Department of Internal Medicine and Infectious Diseases, Farhat Hached Hospital, Sousse, Tunisia*
[d] *Department of Internal Medicine, Sahloul Hospital, Sousse, Tunisia*

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ABSTRACT

Objectives. – The presence of a wide variety of autoantibodies is a characteristic feature of systemic lupus erythematosus (SLE). Although non-specific, anti-complement C1q (anti-C1q) were shown to correlate with the occurrence of active nephritis. The present study aimed to investigate the prevalence of anti-C1q in Tunisian SLE patients and their association with clinical manifestations, especially renal involvement.
Patients and methods. – IgG anti-C1q antibodies were assessed by Elisa in 98 SLE patients, 55 patients with rheumatoid arthritis (RA) and 65 healthy individuals (HI).
Results. – Anti-C1q were found in 53 (54.1%) patients with SLE, three (5%) patients with RA and six (9.3%) HI. Among the 65 patients with renal involvement, anti-C1q were present in 35 (53.8%) patients. There was no significant association between anti-C1q and renal or extrarenal manifestations. In addition, there was no correlation between anti-C1q titer and SLEDAI index. Anti-C1q were significantly associated with anti-nucleosome ($P = 0.001$), anti-Sm ($P = 0.01$) and a low C4 level ($P = 0.046$). Concomitant presence of anti-C1q and anti-dsDNA antibodies was not associated with renal manifestations.
Conclusion. – Our study shows that prevalence of anti-C1q was comparable with that previously reported in Caucasian populations. These antibodies were associated with a low C4 level. However, there was no association between anti-C1q and renal involvement or severity of nephritis.

Mots clés :
Anticorps anti-C1q
Lupus érythémateux systémique
Néphrite
Index SLEDAI
Biopsie rénale

RÉSUMÉ

Objectifs. – Le lupus érythémateux systémique (LES) est caractérisé par la présence d'un grand nombre d'autoanticorps. Plusieurs auteurs ont montré que les anticorps anti-C1q (anti-C1q) sont associés à la présence de néphrite active. Le but de notre étude était de déterminer la prévalence des anti-C1q dans une population de patients tunisiens et de voir si ces autoanticorps sont associés à certaines manifestations, en particulier rénales.
Patients et méthodes. – Les anti-C1q ont été recherchés par Elisa chez 98 patients atteints de SLE, 55 patients atteints de polyarthrite rhumatoïde (PR) et chez 60 individus sains (IS).
Résultats. – Les anti-C1q étaient présents chez 53 patients (54,1 %) atteints de SLE, trois patients (5 %) atteints de PR et six IS (9,3 %). Parmi les 65 patients lupiques ayant une atteinte rénale, les anti-C1q étaient présent chez 35 patients (53,8 %). Nous n'avons pas trouvé d'association significative entre les anti-C1q et l'atteinte rénale ou les autres manifestations extrarénales. Il n'y avait pas non plus de corrélation entre le titre des anti-C1q et l'index SLEDAI. Les anti-C1q étaient significativement associés aux anticorps anti-nucléosome ($p = 0{,}001$), anti-Sm ($p = 0{,}01$) et à un C4 bas ($p = 0{,}046$). La présence concomitante d'anti-C1q et d'anti-DNA double brin n'était pas associée aux manifestations rénales.

* Corresponding author.
E-mail address: sghiririm@yahoo.com (R. Sghiri).

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Conclusion. – Notre étude montre que la prévalence des anti-C1q est comparable à celle rapportée dans les populations caucasiennes. Les anti-C1q étaient associés à un C4 bas. Comme d'autres auteurs, nous n'avons pas trouvé d'association entre ces anticorps et l'atteinte rénale.

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic, relapsing and remitting disease affecting different organs such as skin, joints, central nervous system and kidney. The disease is characterised by several immunologic disorders including B cell hyperstimulation, production of autoantibodies and circulating immune complexes [1]. Autoantibodies recognise a heterogeneous group of antigens, mainly nuclear or cell surface antigens. However, soluble antigens such as complement components are also targeted [2]. The classical pathway of complement is activated by the binding of C1q to complexed immunoglobulins or C-reactive protein and it was demonstrated that antibodies against C1q are present during SLE [3,4]. The presence of anti-C1q antibodies is correlated with reduced C1q levels and associated with more severe illness and nephritis in patients with SLE [5,6].

It was assumed that defective clearance of dead and dying cells could elicit autoimmunity and induce the production of autoantibodies against apoptotic cell debris [7]. C1q, as the first molecule of the classical complement pathway, plays an important role in the clearance of immune complexes and apoptotic cell debris [8,9]. Anti-C1q antibodies, by binding C1q molecule, might alter the physiological role of C1q and interfere with the proper uptake of immune complexes and apoptotic debris.

The aim of the present study was to investigate the prevalence of anti-C1q antibodies in Tunisian SLE patients and to see if there is any association between anti-C1q antibodies and clinical or biological manifestations especially renal involvement.

2. Patients and methods

2.1. Patients

In this retrospective study, 98 unselected SLE patients meeting at least four of the 11 American College of Rheumatology criteria for the classification of SLE [10] were recruited from the internal medicine departments of Farhat Hached and Sahloul hospitals in Sousse, Tunisia.

Proteinuria was defined as 500 mg/24 hours or higher, renal dysfunction as increase in creatinine, proteinuria or hematuria. Active nephritis was defined as persistence of proteinuria or by the presence of cellular casts in urine and proliferative nephritis as class III and IV according to the ISN/RPS criteria [11].

The hospital ethics committees approved the present study and all participants gave their consent.

2.2. Methods

IgG anti-C1q antibodies were assessed by enzyme linked immunosorbent assay (Elisa) (Orgentec®, Hambourg, Germany) using human purified C1q according to the manufacturer's instructions. The cut-off value for defining a positive test result was determined by the manufacturers as 20 U/mL.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS 9.0, 1999). Correlation study was performed by calculating Pearson's correlation coefficient. Chi^2 test and Fisher's exact test were used for testing the significance of association of anti-C1q antibodies with clinical and biological features of the disease. Significance was assumed at $P < 0.05$.

3. Results

3.1. Patients' characteristics

Among SLE patients, 11 (11.2%) were male and 87 (88.8%) female with a median age of 33.8 years (range 2–73 years). Among them, 11 (11.2%) were children ($\leq$ 15 years) and ten patients (10.2%) were older than 60 years.

Sixty-five (66.3%) patients have renal involvement (Table 1). Among them, 59 (60.2%) have active nephritis and only 22 have conclusive renal biopsy. Among these, 13 (59.1%) had class IV nephritis, seven (31.9%) class III, one (4.5%) class II nephritis and one (4.5%) class V nephritis and 20 (90.9%) a proliferative nephritis (class III and/or class IV nephritis).

3.2. Anti-C1q antibodies prevalence and association with immunological markers

Anti-C1q antibodies were present in 53 (54.1%) SLE patients. Mean anti-C1q antibodies titre was 42.2 IU/mL (ranges: 20–370 UI/mL).

Anti-C1q antibodies were present in 7/11 (63.6%) children, 42/77 (54.5%) adults and 4/10 (40%) elderly. Mean anti-C1q antibodies titre was 43.5 IU/mL in children, 44.6 IU/mL in adults and 21.4 IU/mL in elderly patients. There was no significant association between presence of anti-C1q antibodies and age and anti-C1q antibodies titre was not correlated with age. Anti-C1q antibodies were significantly associated with anti-nucleosome ($P = 0.001$), anti-Sm ($P = 0.01$) and a low C4 level ($P = 0.046$) but not with anti-dsDNA.

3.3. Anti-C1q antibodies and clinical manifestations

There was no correlation between anti-C1q antibodies titre and disease activity estimated by SLEDAI index (Pearson correlation coefficient = 1.171, $P = 0.093$).

Anti-C1q antibodies were present in 35 (53.8%) patients among the 65 patients with renal involvement and in 18 (54.5%) patients without renal manifestations. They were present in 31/59 (52.5%) patients with active nephritis and in 12/20 (60%) patients with proliferative nephritis. Thirty-one (58.4%) positive anti-C1q patients out of 53 have active nephritis and 28 (47.4%) anti-C1q negative patients out of 59 have active nephritis.

There was no significant association between anti-C1q antibodies and renal or extrarenal manifestations. Particularly, anti-C1q were associated neither with active nor with proliferative nephritis. In addition, there was no significant difference between mean anti-C1q in patients with and without renal manifestation (44.8 IU/mL versus 37.1 IU/mL, $P = 0.46$).

Concomitant presence of anti-C1q and anti-dsDNA antibodies was not associated with renal manifestations.

4. Discussion

In the present study, anti-C1q antibodies were present in 54.1% patients. This prevalence is comparable with that previously reported which varied between 35 and 50% [12,13]. Anti-C1q occur in SLE but also in other autoimmune diseases and in healthy individuals. Siegert et al. have shown that anti-C1q are present in 3 to 4% of healthy individuals in the fifth decade of life and up to 18% in healthy individuals in the eight decade [14]. As rheumatoid factor (RF) and antinuclear antibodies (ANA), their frequency increase with age and reach 15% in patients after 40 years. However, unlike RF and ANA, titres of anti-C1q are comparable both in healthy individuals and sick patients [15]. In our SLE patients, anti-C1q were more frequent in children. However,