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# Antichromatin Antibodies – A Useful Marker for Lupus Nephropathy

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**Introduction**

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease whose etiology and pathogenesis are incompletely understood. It may affect any organ of the body and display a broad spectrum of clinical and immunological manifestations. The presence of certain autoantibodies is one of the factors associated with some symptoms of the disease and aids in the classification of patients with SLE into specific subsets. One of the most severe events in the course of SLE is the development of glomerulonephritis, and much effort has been spent to find a useful and early marker of this complication. Anti-dsDNA antibodies are often associated with lupus nephritis, and the presence of anti-dsDNA is hallmark of SLE [1, 2]. In recent years there are data that anti-chromatin autoantibodies are correlated even better with lupus nephritis than anti-dsDNA. In recent years there are data that anti-ribosomal P - autoantibodies are correlated even better with neuropsychiatric lupus and lupus nephritis than anti-dsDNA [3].

Chromatin is the native histone-DNA complex found in the nucleus of eukaryotic cells, and it is organized into a repeating series of nucleosomes. Evidence has accumulated that anti-chromatin-chromatin immune complexes can bind to the glomerular basement membrane in vivo [4,5]. Chromatin is an antigen for T and B cells from patients with SLE [6-9].

In this study we investigated the prevalence of both anti-dsDNA and anti-chromatin antibodies in a large series of patients with SLE in order to assess their clinical significance and, particularity, their value as a marker of lupus nephropathy. To determine the specificity of these antibodies for systemic lupus erythematosus (SLE), patients with other connective tissue diseases were tested for anti-chromatin antibodies.

**Patients and methods**

We studied 81 patients (42 of them with lupus nephropathy; 9 male, 72 female) with SLE (all fulfilled four or more of the 1982 American College of Rheumatology-ACR- revised criteria for the classification of SLE) [10], 22 patients with Sjogren's syndrome (classified according to the European criteria) [11], 14 patients - with systemic sclerosis (classified according to the ACR criteria) [12] and 18 healthy blood donors from the blood bank of Medical Institute – MIA. 42 patients with SLE had clinical evidence of lupus nephropathy. Renal biopsies disclosed type V lesions in 11 patients, type IV – in 24, type III – in 2, type II - in 4, type I-in 1 patient (Table 1).

**Table 1.** Distribution of patients with lupus nephritis

| Class | Classification of Lupus Nephritis | № of patients |
|---|---|---|
| I | Minimal mesangial lupus nephritis | 1 |
| **II** | Mesangial proliferative lupus nephritis | 4 |
| **III** | Focal lupus nephritis | 2 |
| **IV** | Diffuse segmental (IV-S) or global (IV-G) lupus nephritis | 24 |
| **V** | Membranous lupus nephritis | 11 |
| **VI** | Advanced sclerosing lupus nephritis | 0 |

Anti-chromatin antibodies of the IgG isotype were measured by a commercial semiquantitative enzyme linked immunosorbent assay (ELISA, INOVA Diagnostics, San Diego, USA) according to the manufacturer's instructions. ELISA method for determination of anti-ribosomal antibodies were used [13]. Disease activity was assessed by the European Consensus Lupus Activity Measurement (ECLAM).

**Results**

Positive levels (> 20 U) of antichromatin antibodies were detected in 58 patients (71,6%) with SLE (37 of them with lupus nephropathy). In contrast, they were found in only 2 (9,09%) patients with primary Sjogren's syndrome, in 1 patient (7,14%) with systemic sclerosis and in 0 (0%) healthy blood donors (Table 2).

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**Table 2.** Prevalence of anti-chromatin antibodies in patients and healthy blood donors

| Group | Patients | Anti-chromatin antibodies № (%) |
|---|---|---|
| **Systemic Lupus Erythematosus** | 81 | 58 (71,6%) |
| **Primary Sjogren's syndrome** | 22 | 2 (9,09%) |
| **Systemic sclerosis** | 14 | 1 (7,14%) |
| **Healthy blood donors** | 18 | 0 (0%) |

Patients with antichromatin antibodies had a 1,63-fold higher prevalence of lupus nephropathy, than those without these antibodies (88,09% vs. 53,84%). The mean level of anti-chromatin antibodies in patients with lupus nephropathy was 64 U± 12 U and in patients without nephropathy 44 U±10 U. No differences in the prevalence of the other clinical manifestations were found among patients with and without antichromatin antibodies.

25 patients with lupus nephropathy (LNP) had positive levels of both anti-dsDNA and anti-chromatin antibodies, but 12 patients had anti-chromatin antibodies without anti-dsDNA antibodies, while nobody had not anti-dsDNA without antichromatin antibodies. 32 patients with LNP had positive levels of both anti-ribosomal P-antibodies and anti-chromatin antibodies, but 10 patients had anti-chromatin without anti-ribosomal P-antibodies (Table 3).

**Table 3.** Autoantibody Profile in Patients with Lupus Nephropathy

| №, Sex, Age | Class LGN | Serology | Anti-chromatin antibody |
|---|---|---|---|
| ***01. F., 19*** | **IV G** | ds, Ro, RNP, anti-P, ANA | + |
| ***02. F., 21*** | IV G | ds, anti-P, ANA | + |
| ***03. F., 24*** | V | anti-P, ANA | + |
| ***04. F., 20*** | IV G | Ro, La, RNP, anti-P, ANA | + |
| ***05. F., 18*** | IV G | Ro, Sm, RNP, anti-P, ANA | + |
| ***06. M.,20*** | V | ds, anti-P, ANA | + |
| ***07. F., 19*** | V | ds, La, RNP, anti-P, ANA | + |
| ***08. F., 32*** | IV G | RNP, anti-P, ANA | + |
| ***09. F., 26*** | V | ds, Ro, anti-P, ANA | + |
| ***10. F., 27*** | IV G | ds, anti-P, ANA | + |
| ***11. M.,23*** | IV G | ds, anti-P, ANA | + |
| ***12. F., 22*** | IV G | ds, anti-P, ANA | + |
| ***13. F., 19*** | IV G | ds, La, RNP, anti-P, ANA | + |
| ***14. F., 33*** | V | anti-P | + |
| ***15. F., 22*** | V | ds, Ro, La, Sm, RNP, ANA, anti-P | + |
| ***16. F., 30*** | IV G | anti-P, ANA | + |
| ***17. F., 27*** | IV G | ds, Ro, anti-P, ANA | + |
| ***18. M., 24*** | IV G | ds, anti-P, ANA | + |
| ***19. F., 28*** | II | ds, anti-P, ANA | + |
| ***20. F., 25*** | III | ds, La, RNP, anti-P, ANA | + |
| ***21. F., 30*** | V | RNP, anti-P, ANA | + |
| ***22. F., 22*** | IV G | anti-P, ANA | + |
| ***23. F., 20*** | II | ds, Ro, anti-P, ANA | + |
| ***24. F., 19*** | IV G | ds, Ro, Sm, anti-P, ANA | + |
| ***25. F., 34*** | IV G | ds, La, anti-P, ANA | + |
| ***26. F., 29*** | IV G | anti-P, ANA | + |
| ***27. F., 28*** | V | Ro, RNP, anti-P, ANA | + |
| ***28. M., 21*** | V | ds, RNP, anti-P, ANA | + |
| ***29. F., 27*** | II | ds, La, RNP, anti-P, ANA | + |
| ***30. F., 21*** | IV G | ds, La, anti-P, ANA | + |
| ***31. F., 20*** | IV G | ds, RNP, anti-P, ANA | + |
| ***32. F., 30*** | IV G | ds, Ro, anti-P, ANA | + |
| ***33. M., 27*** | IV G | **ds, ANA** | + |
| ***34. F., 24*** | V | **Ro, RNP, ANA** | + |
| ***35. F., 29*** | IV G | ds, La, ANA | + |

| №, Sex, Age | Class LGN | Serology | Anti-chromatin antibody |
|---|---|---|---|
| ***36. F., 28*** | IV G | Ro, ANA | + |
| ***37. F., 29*** | I | ds, ANA | + |
| ***38. M.,21*** | **IV G** | **La, ANA** | - |
| ***39. F.,26*** | II | Ro, RNP, ANA | - |
| ***40. F.,30*** | III | RNP, ANA | - |
| ***41. F.,29*** | IV G | Sm, Ro, La, ANA | - |
| ***42. F.,26*** | V | RNP, ANA | - |

**Discussion**

Most studies have found that anti-chromatin antibodies are quite sensitive and specific for SLE [1,4,6,7], but a few have found a high prevalence in other diseases [4,14]. Our results agree with the group of studies showing both high sensitivity and specificity. Also in agreement with these studies, anti-chromatin showed a higher prevalence than anti-dsDNA in patients with SLE. In our study using ELISA to measure anti-dsDNA and anti-chromatin antibodies no samples were positive for anti-dsDNA and negative for anti-chromatin antibodies, suggesting that anti-dsDNA antibodies were a subset of anti-chromatin antibodies.

The measurement of antichromatin antibodies appears to be a useful addition to the laboratory tests that can help in the diagnosis and treatment of SLE. These antibodies are both sensitive and specific for SLE and are a useful marker for an increased risk of lupus nephritis.

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