MODERN MARKERS OF RHEUMATIC AND AUTOIMMUNE DISEASES

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Autoimmune diseases (AID) are not just one pathology but a class of health disorders characterized by the loss of tolerance to one's own antigens. The exact mechanisms of their origin are unclear, but many internal and external factors act as triggers. Autoantibodies damage organs and systems by targeting autoantigens-substances from the body's own cells recognized as foreign by the immune system [1,2,3].

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Antinuclear antibodies (ANA) are a heterogeneous group of autoantibodies that react with various nuclear components. The "gold standard" for ANA testing in serum is indirect immunofluorescence (IIF) using cryostat sections of mouse or rat liver, or HEp-2 cells as a substrate. Using standardized HEp-2 cells is preferable as it significantly increases sensitivity and accurately describes different types of nuclear fluorescence. ANA testing results are reported with the maximum detection titer and the intensity and type of immunofluorescence, which reflect the presence of various types of ANAs that are somewhat specific to certain autoimmune diseases [4,5,6].

Other screening methods for ANAs, such as enzyme-linked immunosorbent assay (ELISA) and new solid-phase analysis techniques, increase the rates of false-negative and false-positive results and cannot replace IIF testing. Patients with positive ANA results should undergo confirmatory tests for specific ANAs using methods like ELISA, immunoblotting, and double immunodiffusion [7,8,9].

Certain types of ANAs (e.g., anticentromere antibodies, PCNA, antibodies to the

mitotic apparatus-NUMA) can only be detected by IIF on HEp-2 cells, eliminating the need for further confirmatory testing. Normal ANA titers are < 1:40 when using cryostat sections of the liver or kidneys of laboratory animals. ANAs are valuable markers for assessing the prognosis and monitoring juvenile chronic arthritis with associated uveitis and secondary Raynaud's phenomenon in systemic diseases. Positive ANA results have no proven diagnostic or prognostic significance in conditions like rheumatoid arthritis, multiple sclerosis, thyroid diseases, infections, idiopathic thrombocytopenic purpura, and fibromyalgia. The recommended frequency for ANA testing is every 6 months to 1 year [10,11,12].

Antibodies to deoxyribonucleic acid (DNA) are divided into two main types: antibodies that react with double-stranded (native) DNA (dsDNA) and those that react with single-stranded (denatured) DNA (ssDNA). dsDNA antibodies are serological markers for systemic lupus erythematosus (SLE). dsDNA antibodies are more specific for diagnosing SLE than ssDNA antibodies, which may be present in sera of patients with other diseases and lack significant diagnostic value [13].

Standard methods for detecting dsDNA antibodies include ELISA, IIF using Crithidia luciliae, and radioimmunoassay (RIA). The primary screening test for dsDNA antibodies is ELISA, which can detect both low- and high-avidity antibodies, leading to lower specificity compared to other methods. High rates of false positives in ELISA can arise from contamination of dsDNA with ssDNA and spontaneous denaturation. ELISA detects IgG and IgM antibodies to dsDNA, with IgG antibodies having the most clinical significance. Confirmatory tests for positive dsDNA antibody results should include IIF and the Farr test, which have lower sensitivity but higher specificity for diagnosing SLE [14,15,16].

Normal levels of dsDNA antibodies using ELISA are < 10-20 IU/ml, using IIF with Crithidia luciliae are < 1:10, and the Farr method is < 7 IU/ml. Detection of histone antibodies can be useful for diagnosing drug-induced lupus. Histone antibodies are most commonly found in drug-induced lupus caused by procainamide and hydralazine but can also appear in patients taking these drugs without symptoms (44%) and in patients with SLE (50-80%) [17,18].

Positive results for Sm antibodies are a specific serological marker and diagnostic criterion for SLE but have no value in assessing disease activity or subtype characteristics.

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