Analysis of Cases Positive for Antinuclear Antibodies by Indirect Immunofluorescence but Negative on Bioplex 2200

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Antinuclear antibodies (ANA) are associated with several systemic rheumatic diseases. However, they may be present in nonrheumatic conditions. Screening for ANA is routinely performed by indirect immunofluorescence (IIF) on HEp-2 cells. There are several multiplex systems available to detect antibodies to specific nuclear antigens. Our laboratory uses the BioPlex 2200 (Bio-Rad, Benicia, CA) to detect antibodies to 13 specific nuclear antigens of known clinical importance (dsDNA, chromatin, ribosomal protein, SSA-52, SSA-60, SSB, Sm, Sm RNP, RNP-A, RNP-68, Scl-70, Jo-1, and centromere B). Our study evaluated the clinical scenario of patients whose ANA screen was positive by IIF at a titer >160 with no antibodies detected to the 13 nuclear antigens on the BioPlex 2200. A retrospective search for such cases was done in our laboratory over a 3-month period, and an in-depth analysis of their clinical data was performed. A total of 30 such cases were identified, none of which had systemic lupus erythematosus. The ANA titers ranged from 1:160–1:1,280. The mean age of the patients was 50 years (range 7-84 years). Eight (26.7%) of the 30 cases had degenerative joint disease, four had malignancy (breast cancer with paraneoplastic dermatomyositis, metastatic melanoma with inflammatory bowel disease, thyroid cancer with osteoarthritis and thyroid cancer with rheumatoid arthritis), three were categorized as undifferentiated connective tissue disease, two had fibromyalgia, two had rheumatoid arthritis and one each had primary biliary cirrhosis, polymyalgia rheumatic, polyarthralgia with chronic fatigue syndrome, chronic kidney disease, subdural hemorrhage with peripheral neuropathy, usual interstitial pneumonia, otitis media, acne, bipolar disorder with type 2 diabetes, and fatigue with multiple fractures. Three cases had no identifiable clinical disease. In conclusion, high-titer ANA by IIF may be indicative of inflammatory disease, which emphasizes the importance of continuing to perform ANA by IIF in addition to specific antibody characterization.