

## Mai 05/08: Antinucleolar antibodies

Using indirect immunofluorescence (IIF) on HEp-2 cells in some cases a nucleolar pattern arises. The antibodies which cause a nucleolar pattern react with different antigens such as anti-Scl-70, PM-Scl, fibrillar and often unidentified ones. The pattern may occur in patients with scleroderma and scleroderma overlap syndromes. Additional associations include other rheumatological and connective tissue diseases, infections and malignancies. The clinical relevance of antinucleolar antibodies (ANoA) is still unknown and was the topic of the following study:

Khan S, Alvi A, Holding S, Kemp ML, Raine D, Doré PC, Sewell WAC  
**The clinical significance of antinucleolar antibodies**  
*J Clin Pathol (2008) 61:283 - 286*

A total of 104 consecutive ANoA positive sera were identified out of 7842 samples submitted to the laboratory for "ANA testing". Titers  $\geq 1$  in 40 were considered positive and classified into homogeneous (55%), clumpy (14%) and speckled (31%) antinucleolar subtypes. Subsequent testing showed only two patients with additional antibodies against ENA (weak Ro and U1RNP). These patients had clinical diagnoses of breast cancer and non-small cell carcinoma of the lung, respectively.

Systemic sclerosis was evident in only 2 (1.8%) ANoA positive patients. None of these 2 patients had anti-Scl-70 antibodies. Various rheumatological disorders identified in 33 of 104 patients (32%) were polymyalgia rheumatica, polymyositis/dermatomyositis, rheumatoid arthritis, crystal arthropathy, systemic lupus erythematosus and others. None of the disorders had any association with a specific ANoA pattern or titer. Interestingly, the clinical features more commonly seen with ANoA were hypertension (48/104), malignancy (22/104), disordered liver function (22/104) and anaemia (22/104) rather than systemic sclerosis.

The authors did a further retrospective survey to characterise the HEp-2 patterns on 17 patients who were subsequently confirmed to have Scl-70 antibodies on immunoblot. This showed that there were mixtures of various patterns on IIF; none had a predominance of a nucleolar pattern.

Excluding the 33 patients with rheumatological manifestations and the 22 patients with malignancy, 49 patients (47%) with ANoA had no definite clinical characteristics identified.

The authors conclude that the presence and subtype of antinucleolar antibodies has a low specificity for systemic sclerosis. Reporting the subtype of antinucleolar patterns on routine screening results is not recommended.

Several comparative studies about ANA Screening by IIF versus ELISA have been done in the last years. Always, some samples are positive in the one and negative in the other method. While IIF has a weakness to find anti-Ro and anti-DNA positive samples, ELISA does only find a low percentage of sera with nucleolar patterns. However, this study confirms the finding of comparative studies that most ANoA positive samples do not correspond with connective tissue diseases.

