Editorial

Anticentromere (ACA)-positive Sjögren's syndrome: a disease entity?

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Paul Ehrlich, at the beginning of the twentieth century, suggested that the presence of autoimmunity can be deleterious for the organism (1). Ehrlich was asked: how he can explain the fact that animals produce antibodies against their own sperm but they remain healthy? He answered that "these are not autotoxins within our meaning since they did not produce disease" (1). The genius of Ehrlich had at that time proposed two important major classes of autoantibodies: the ones which can be deleterious and incompatible with the well-being and the others the "non-toxic", *i.e.* which do not produce disease. The discovery of lupus erythematosus cell phenomenon (2) and subsequently the antibodies to nuclear antigens (ANA) (3, 4), as well as the extraction of anti-dsDNA antibodies from kidneys of patients with lupus nephritis, heralded the notion that some autoantibodies can be pathogenetic and can explain some pathogenetic aspects of autoimmune diseases (5).

The lack of appropriate animal models for many autoimmune diseases, as well as the genetic complexity of their predisposition, did not allow, for most of the autoantibodies, to prove a cause and effect relationship with disease picture or pattern, nor did it exclude such a strict relationship. Instead the idea of the "serological association" emerged from observational and controlled clinical studies; it was based on a statistically significant prevalence of a certain autoantibody within a patient group with a particular clinical characteristic as compared to patients lacking this characteristic. In this context, anticentromere antibodies (ACA) were shown initially to be associated with limited systemic sclerosis (lSSc) (6).

Subsequently, a number of reports described ACA-positive Sjögren's syndrome (SS) as a clinical entity characterised by combined features of SS and lSSc such as puffy hands, telangiectasia, sclerodactyly, gastroesophageal reflux and limited lung fibrosis, (7, 8, 9). Baldini C *et al*. in this issue of the Journal (10), explore the association of ACA with a particular disease entity characterised by criteria as SS and at the same time by the Le Roy criteria as early SSc. There were 41 patients of whom 26 derived from a database of 209 ACA-positive SSc and 15 from a database of 209 SS patients, respectively fulfilling classification criteria of both disorders. Baldini *et al*. showed that these patients express significantly less often sclerodactyly, digital ulcers and active capillaroscopy patterns and more often sicca manifestations (100%), parotid gland enlargement, articular involvement, leucocytopenia, hypergammaglobulinaemia, as well as anti-Ro, anti-La antibodies and rheumatoid factor (RF), as compared with the SSc patients. Furthermore, 61% of the ACA-positive SSc/SS overlap patients fulfilled the ARA criteria for SSc implying that the remaining 39% could be defined as ACA-positive SS patients; in addition ACA-positive SSc/SS overlap patients developed lymphoma significantly more often that the remaining SSc patients. These data are in line with other findings already cited in the paper which, taken together, support the notion that ACA-positive SS has a clinical phenotype intermediate between SS and SSc. One could deduce that the disease evolves over time and the prevalence of various findings changes with time in a way that all these patients will finally evolve to SSc. Bournia *et al*., however, using Kaplan-Meier analysis showed that the probability of being free of SSc-related features such as telangiectasias, digital

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ulcers and esophageal involvement remains high among ACA-positive SS patients, at least, for a follow-up of nearly 80 months, suggesting that they show little tendency to evolve to SSc.

Regardless of what terminology is used to describe these patients, either, "ACA-positive SSc/SS overlap", or "ACA-positive SS", the beauty of this finding is that the presence of ACA goes in parallel with some SSc-related features, even among patients fulfilling classification criteria for SS. This implies either that the antibody governs some clinical features regardless of the disease setting, or alternatively, an underlying cause possibly related to the genome or genome-environment interaction, predisposes to both, the presence of antibody and the development of a particular disease pattern.

References

1. SILVERSTEIN AM: Autoimmunity versus horror autotoxicus: the struggle for recognition. *Nature Immunology* 2001; 2: 279-81.
2. HARGRAVES MM, RICHMOND H, MORTON R: Presentation of two bone marrow dements; the "tart" cell and the "LE" cell. *Proc Staff Meet Mayo Clin* 1948; 23: 25-8.
3. HOLMAN HR, KUNKEL HG: Affinity between the lupus erythematosus serum factor and cell nuclei and nucleoprotein. *Science* 1957; 126: 162-63.
4. KRISHNAN C, KAPLAN MH: Immunopathologic studies of systemic lupus erythematosus II. Antinuclear reaction of γ-globulin eluted from homogenates and isolated glomeruli of kidneys from patients with lupus nephritis. *J Clin Invest* 1967; 46: 569-79.
5. TAN EM, SCHUR PH, CARR RI, KUNKEL HG: Deoxyribonucleic acid (DNA) and antibodies to DNA in the serum of patients with systemic lupus erythematosus. *J Clin Invest* 1966; 45: 1732-40.
6. STEEN VD, ZIEGLER GL, RODNAN GP, MEDSGER TA JR.: Clinical and laboratory associations of anticentromere antibody in patients with progressive systemic sclerosis. *Arthritis Rheum* 1984; 27: 125-31.
7. VLACHOYIANNOPOULOS PG, DROSOS AA, WIIK A, MOUTSOPOULOS HM: Patients with anticentromere antibodies, clinical features, diagnoses and evolution. *Br J Rheumatol* 1993; 32: 297-301.
8. SALLIOT C, GOTTENBERG JE, BENGUFFA D, DESMOULINS F, MICHELI-RICHARD C, MARIETTE X: Anticentromere antibodies identify patients with Sjögren's syndrome and autoimmune-overlap syndrome. *J Rheumatol* 2007; 34: 2253-8.
9. BOURNIA V-KK, DIAMANTI KD, VLACHOYIANNOPOULOS PG, MOUTSOPOULOS HM: Anticentromere antibody positive Sjögren's syndrome: a retrospective descriptive analysis. *Arthritis Res Ther* 2010; 12:R47.
10. BALDINI C, MOSCA M, DELLA ROSSA A *et al*.: The overlap ACA-positive systemic sclerosis/Sjögren's syndrome: a distinct clinical entity with mild organ involvement but a high risk for lymphoma. *Clin Exp Rheumatol* 2013; 31: 272-80.