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 (ISSc) (6).

Subsequently, a number of reports described ACA-positive Sjögren’s syndrome (SS) as a clinical entity characterised by combined features of SS and ISSc 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 SS. There were 41 patients of whom 26 derived from a database of 209 ACA-positive SS 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, parotid gland enlargement, articular involvement, leucocytopenia, hypergammaglobulinaemia, as well as anti-Ro, anti-La antibodies and rheumatoid factor (RF), as compared with the SS patients. Furthermore, 61% of the ACA-positive SS/SS overlap patients fulfilled the ARA criteria for SS implying that the remaining 39% could be defined as ACA-positive SS patients; in addition ACA-positive SS/SS overlap patients developed lymphoma significantly more often than the remaining SS 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 ISSc. 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 SS. Bournia et al., however, using Kaplan-Meier analysis showed that the probability of being free of SSC-related features such as telangiectasias, digital
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