The Novel Anti-BICD2 Autoantibody Potentially Predicts a Favorable Disease Course in Systemic Sclerosis

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Systemic sclerosis (SSc) is a systemic autoimmune disease that manifests as progressive fibrosis of the skin and internal organs. SSc is associated with the presence of several autoantibodies to intracellular targets, with the three most important SSc-specific being anti-centromere antibodies, anti-Scl70 antibodies and anti-RNA polymerase III antibodies, which occur in over 50% of SSc patients. Autoantibody specificities are strongly associated with pattern of organ involvement and disease outcome, making autoantibodies an essential tool in the clinical management of SSc. This highlights the need for additional specific and sensitive diagnostic and prognostic biomarkers in SSc. We have recently conducted high-content autoantibody profiling studies of SSc, systemic autoimmune diseases (AID), and healthy controls and found novel SSc-associated autoantibodies. These novel SSc-associated autoantibody biomarker candidates and their diagnostic value were evaluated by testing samples derived from 2 different SSc cohorts.

Clinical annotation data including age, gender, disease duration, MRSS, detailed information on organ involvement making up to a total of either >50 or >100 clinical data points (depending on the site) was available for more than 80% of all SSc serum samples included in this study. All samples were analyzed on the novel Multisil BICD2 (CE), an ELISA for the semi-quantitative detection of anti-BICD2 antibodies in human serum or plasma.

Methods

Serum samples were obtained from the biobanks of the Department of Rheumatology, University Hospital Zurich, Switzerland, and Department of Dermatology, University of Cologne, Germany. The analysis included samples collected from patients suffering from SSc (n=301) systemic lupus erythematosus (n=39), Sjögren’s syndrome (n=11), rheumatoid arthritis (n=19), idiopathic Inflammatory Myopathy (IIM; n=20) and healthy volunteers (n=99).

Results

We found anti-BICD2 with a prevalence of 28.6% in SSc patients of both cohorts, and only 2.7% prevalence in cohorts with other rheumatic diseases or healthy controls (OR=14.56). Anti-BICD2 autoantibodies were present in a subgroup of SSc patients where skin fibrosis was either from the limited cutaneous subtype (p=0.0002) or restricted to sclerodactyly (p=0.0037).

Conclusion

In this study, we were able to further confirm the diagnostic value and high specificity of the newly discovered BICD2 autoantigen. Anti-BICD2 autoantibodies were found to be elevated in patients suffering from limited SSc, and anti-BICD2 reactivity was found to be related to clinical observations of a moderate course of disease. The observations of anti-BICD2 being found in patients with limited cutaneous involvement, low MRSS, absence of pulmonary fibrosis and an only moderate impairment of lung function point towards a moderate course of disease in anti-BICD2 positive SSc patients.