ARVC specific autoantibody identifies cardiac sarcoidosis and correlates with inflammation activity

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Introduction: Cardiac sarcoidosis (CS) is an inflammatory granulomatous disease of unknown origin. CS and arrhythmogenic right ventricular cardiomyopathy (ARVC) are overlapping syndromes. With both, patients are at increased risk of ventricular arrhythmias and sudden cardiac death. However, the diagnosis of CS is challenging, especially in patients with no extracardiac involvement, but correct diagnosis has large therapeutic impact. Recently, a novel diagnostic autoantibody (anti-DSG2 Ab) was identified in ARVC. We sought to identify this antibody in CS patients and correlate its levels with inflammation activity using cardiac positron-emission-tomography (18-FDG-PET).

Methods: Recombinant human desmoglein-2 (DSG2) proteins on western blots were exposed to sera as well as purified IgG of 14 patients with sarcoidosis (all confirmed by histology) and 6 controls (1 ARVC patient (positive control) and 5 healthy control subjects (negative control)). Clinical patient characteristics were correlated to detected antibody intensity levels.

Results: The sarcoidosis cohort comprised 43% (6/14) male patients and the average age was 50±12 years. Anti-DSG2 Abs were identified in 43% (6/14) and were detected faintly (below cut off level) in 21% (3/14) of all sarcoidosis patients. Antibody was also present in the ARVC patient (1/1) and was absent in all control subjects (5/5). Myocardial inflammation was present in 18-FDG PET imaging in all CS patients with positive anti-DSG2 Abs, corresponding to an average SUV (standardized uptake value) of 8.1±4.2. In patients with faint or no antibody, the SUV values were significantly lower with 1.2±2.1 and 3.2±4.0, respectively (P=0.044, one-way ANOVA). The Pearson correlation coefficient (R) was 0.6 (P=0.037) for SUV vs. higher antibody levels assessed by pixel count of the western blot bands for purified IgG.

Conclusions: Anti-DSG2 Abs are not only a specific biomarker for ARVC, but are also found in CS, suggesting a similar pathophysiological mechanism in these overlapping syndromes, both involving cardiac inflammation and myocyte cell death. Moreover, antibody levels correlate with disease activity on cardiac PET imaging. Larger cohorts are necessary to confirm these findings.

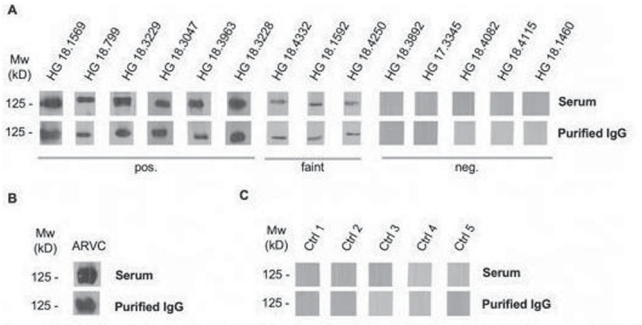

Figure 1 (**A**) Different levels of anti-DSG2 Ab detection in sarcoidosis patients. (**B**) Strong anti-DSG2 Ab detection in an ARVC patient. (**C**) No antibodies are present in control subjects.

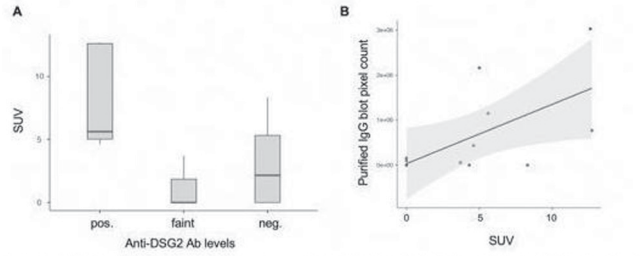

Figure 2 (**A**) Correlation of SUV values assessed by 18-FDG cardiac PET imaging to different levels of anti-DSG2 Ab detection (*P*=0.044, one-way ANOVA). (**B**) Pearson correlation coefficient (R) = 0.6 (*P*=0.037) for SUV vs. Ab levels assessed by pixel count of the western blot bands for purified IgG.