Clinical and Autoantibody Associations in ANA-Positive Systemic Sclerosis

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Introduction

- Systemic sclerosis (SSc) is a fibritic disease which is clinically, immunologically, and molecularly heterogeneous.
- The majority of patients have positive anti-nuclear antibodies (ANA) and most have prototypic SS-related autoantibodies, including anti-centromere (ACA), anti-Scl-70 (ATA), or anti-RNA polymerase-III (RNP), each of which has strong clinical associations and are predictive of outcomes.
- The subset of ANA-positive patients with SSc who lack prototypic autoantibodies has been poorly characterized.
- The purpose of this study was to:
  - Identify ANA positive and triple negative SSc patients and assess their demographic and clinical characteristics.
  - Investigate the presence of specific autoantibodies not routinely clinically assessed and determine their clinical associations.

Materials and Methods

Study Population & Clinical Characteristics
- 280 patients from the URMID and Northwestern scleroderma registries available for clinical evaluation were considered evaluable.
- Patients were assessed for disease subset, skin involvement (modified Rodnan * skin score), digital ulcers, telangiectasias, CK, levels, interstitial lung disease * (ILD) on chest CT (as defined by honeycombing, ground glass opacities, and *), and pulmonary arterial hypertension (PAH) as assessed by right heart catheterization.

Immunofluorescence and Immunoblot
- Sera from 57 clinically triple negative patients were screened for ANA by Immunofluorescence and Immunoblot
- 29 additional autoantibodies were assessed using EUROLINESSc and
- The purpose of this study was to:
  - Investigate the presence of specific autoantibodies not routinely clinically assed, many of which were associated with specific clinical manifestations.
  - Triple negative patients demonstrated an equal prevalence of limited and diffuse cutaneous SSc, high prevalence of digital ulcers, myopathy, and ILD.
  - Ro-52 was the most prevalent antibody (50%) and was associated with increased risk of ILD and elevated CK, confirming previous studies which showed association of Ro-52 with ILD and inflammatory myositis. Additional * autoantibodies in this subset included: Th/To, Scl-70, PM-75, and Mi-2b, fibrillarin.
  - Many patients had multiple autoantibodies and this was associated with more severe lung disease.
  - There was a high prevalence of myositis specific antibodies.
  - ANA positive triple negative SSc is a relatively common but clinically diverse * entity and clinicians should recognize these patients as high risk for ILD and muscle disease.

Results

Patient Characteristics (Table 1)
- 14% of two well described SSc populations were characterized as ANA+ triple negative SSc.
- ANA positive patients negative for the prototypic SSc antibodies were clinically heterogeneous, demonstrated a variety of autoantibodies which was not routinely clinically assessed, many of which were associated with specific clinical manifestations.
- Triple negative patients demonstrated an equal prevalence of limited and skin involvement (modified Rodnan * skin score), digital ulcers, telangiectasias, CK, levels, interstitial lung disease * (ILD) on chest CT (as defined by honeycombing, ground glass opacities, and *), and pulmonary arterial hypertension (PAH) as assessed by right heart catheterization.

Antibody Prevalence by Immunoblot
- Presence of autoantibodies was assessed by immunoblot in the triple negative cohort (*). Antibodies with a prevalence >5% were assessed in the entire cohort (*).
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Table 2. Antibody prevalence by immunoblot. Presence of autoantibodies was assessed by immunoblot in the triple negative cohort (*). Antibodies with a prevalence >5% were assessed in the entire cohort (*).

References