Anti-SSA/Ro52 autoantibodies in scleroderma: results of an observational, cross-sectional study

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ABSTRACT

Objective. *To date, the diagnostic utility of anti-SSA/Ro52 autoantibodies in scleroderma and the association of them with certain clinical manifestations, particularly inflammatory myositis, are still controversial. This paper aims to assess the correlation between the presence of anti-SSA/Ro52 antibodies and the demographic, clinical and prognosis characteristics of patients with systemic sclerosis (SSc).*

Methods. *This is a retrospective, cross-sectional and observational study in patients with SSc. Baseline demographic and clinical characteristics were recorded. Presence of anti-SSA/Ro52, anti-SSA/Ro, anti-SSB/La, snRNP/Sm, anti-centromere, anti-Scl-70 and anti-PM-Scl were analysed by immunoblot, and antinuclear antibodies (ANA) by indirect immunofluorescence. Statistical analysis was performed with PASW Statics 18 software.*

Results. *A total of 132 consecutive patients with analysis of anti-SSA/Ro52 antibodies were selected from a Spanish cohort of 408 patients with SSc, 87.1% of them being women. About half of patients had the limited form (51.5%), followed by diffused form (18.9%), sclerosis sine scleroderma (22.7%), and prescleroderma (6.8%). Prevalence of anti-SSA/Ro52 was 35.6%. No association between anti-SSA/Ro52 and clinical manifestations was found, while detection of anti-SSA/Ro52 was significantly associated with the presence of anti-Ro.*

Conclusion. *The results of our study show that anti-SSA/Ro52 antibodies are often found in SSc patients. No clinical manifestations, including inflammatory myopathy, were related with anti-SSA/Ro antibodies.*

Introduction

Systemic sclerosis (SSc) or scleroderma is a complex autoimmune disorder, characterised by small vessel vasculopathy, production of autoantibodies and fibroblast dysfunction leading to increased deposition of extracellular matrix (1-4) and resulting in the progressive fibrotic replacement of normal tissue architecture, producing the failure of affected organs, such as the kidney, heart and lungs (3-5).

The clinical manifestations include a wide scope of vascular (Raynaud's phenomenon and ischaemic ulcers), visceral involvement (oesophageal and intestinal dysmotility, gastroesophageal reflux, interstitial lung disease, pulmonary hypertension, scleroderma renal crisis, myocardial sclerosis, and heart arrhythmias) (4, 6) and, in a subset of patients, increase risk of haematological malignancies (7).

The natural history of SSc embraces from a relatively benign condition to a rapidly progressive disease with high mortality (1, 4). Based on this, SSc can be classified into different subsets: limited cutaneous SSc (lcSSc), diffuse cutaneous SSc (dcSSc), and SSc without skin involvement (SSc sine scleroderma) (1, 4, 8).

At the present time, no therapy has been shown to reverse or arrest the progression of fibrosis, representing a major unmet medical need (3), being the treatment of SSc based on organ-specific strategies (4).

Nowadays, antinuclear autoantibodies (ANA) represent a serologic hallmark of the disease and have proven value as diagnostic and prognostic biomarkers and are also important tools for planning treatment and disease management (4, 9, 10, 11). Recently, autoantibodies have been included among the new classification criteria for SSc by American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) (2). Indeed, up to 95% of SSc patients have circu-

lating autoantibodies directed against one or more autoantigens (11), including topoisomerase I (formerly called Scl-70), centromere proteins (CENPs), RNA polymerase III, the PM/Scl complex, also known as the human exosome (10, 12) and U1RNP (ribonucleoprotein complex) (13). Autoantibodies against U3RNP (fibrillarin) (14, 4) and Ro-ribonucleoprotein complex (including SSB/La, SSA/Ro52 and anti-SSA/Ro60) (10, 15-29) have also been detected in patients with SSc.

Classically, cutaneous subsets have been associated with the development of organ complications. However, new evidence suggests that specific autoantibodies could predict better organ involvement and clinical patterns in patients with SSc (9, 20).

Ro antigens consist of two different proteins, SSA/Ro60 and SSA/Ro52, located in two different cell compartments. Anti-SSA/Ro antibodies have been assessed in patients with autoinmune conditions, including SSc (17, 18).

While the association of Ro60 antibodies with autoimmune conditions is well established, particularly in systemic lupus erythematosus (SLE), subacute cutaneous lupus, and Sjögren's syndrome (SjS), the role of SSA/Ro52 antibodies still is unclear, although they have been reported in a wide variety of autoimmune diseases (as systemic lupus erythematosus and primary Sjögren's syndrome) (10, 15, 19).

To date, however, the diagnostic utility of 'monospecific' or 'isolated' anti-SSA/Ro52 autoantibodies (anti-SSA/Ro52 reactivity without concomitant anti-SSA/Ro60 reactivity) and the association of anti-SSA/Ro52 with certain clinical manifestations of SSc, particularly inflammatory myositis, are still controversial (21, 22).

In this context, we designed this study to assess the possible relationship between the presence of anti-SSA/Ro52 with different clinical variables and autoantibody profiles in patients with SSc.

Methods

Study design, patients and data collection

This is an observational and cross-sectional study to analyse the correlation between the presence of anti-SSA/Ro52 antibodies and the demographic, clinical and prognosis parameters in a group of patients selected from a cohort diagnosed with scleroderma or systemic sclerosis (SSc) in the Internal Medicine Department of Vall d'Hebron Hospital (Barcelona, Spain), a referral centre for this disease. A modification of the classification proposed by LeRoy and Medsger (6) was used to classify patients in four subsets: preSSc, was defined by the presence of Raynaud's phenomenon, characteristic SSc nailfold capillaroscopic changes and/or disease-specific autoantibodies but no skin thickening; lcSSc was defined when skin sclerosis was confined distally to the elbows and knees or the face; dcSSc was defined when skin thickening extended proximally to the elbows and knees or included the trunk; and ssSSc was defined by the presence of Raynaud's phenomenon or equivalents, scleroderma clinical features and antinuclear autoantibodies but no skin sclerosis. Selection criteria were determined by the availability of anti-SSA/Ro52 test in serum, regardless of the clinical condition of the patient. Anti-SSA/Ro52 assay became available at our institution in March 2008. So, all patients diagnosed since then until May 2011 were consecutively included in the present study. Clinical characteristics of this selected group of patients did not differ from the cohort.

The study protocol was approved by the Ethical Review Board of our institution and procedures were in accordance with the ethical standards laid down in Helsinki Declaration, as revised in 2000.

The following demographic and clinical data were collected: age, sex, time of disease onset (defined as the self- reported date of the first symptom attributable to the disease, Raynaud's phenomenon in the majority of patients), time of diagnosis, type of scleroderma (limited, diffuse, sine scleroderma, and pre scleroderma), presence of Raynaud's phenomenon, ulcers, musculoskeletal pain, arthralgia, arthritis, non-inflammatory myopathies, inflammatory myopathies, oesophageal dysmotility, primary biliary cirrhosis, diffuse parenchymal lung disease, pulmonary hypertension, cardiac dysfunction, renal dysfunction, renal crisis, Sjögren's syndrome and capillaroscopic abnormalities.

Clinical features

Peripheral vascular manifestations. They are defined by the presence of Raynaud's phenomenon, with or without ischaemic digital ulcerations.

Digestive tract involvement. Any of the following diagnoses were considered related to SSc: oesophageal involvement, when hypomotility of the lower two thirds of the oesophagus and/or decreased peristalsis were confirmed by manometry or cine-radiographic study; gastric involvement, when gastric hypomotility was detected by radiographic or radionuclide study or when gastric antral vascular ectasia was identified by endoscopy; intestinal involvement, when an intestinal motility disturbance was confirmed by manometry or cine-radiographic study, when malabsorption syndrome was diagnosed by Breath test, or when intestinal pseudo-obstruction was identified by simple radiology or computerised tomography scan.

Hepatic involvement: diagnoses of primary biliary cirrhosis, autoimmune hepatitis or nodular regenerative hyperplasia of the liver.

Pulmonary involvement. It was defined by the presence of interstitial lung disease (ILD) or pulmonary arterial hypertension (PAH). The ILD was established if any of the following criteria were identified: (a) restrictive pulmonary pattern with forced vital capacity (FVC) below 80% of expected value on pulmonary function tests and (b) pulmonary interstitial pattern evidenced by chest radiograph or high-resolution CT Scan (HRCT), or (c) alveolitis confirmed by bronchoalveolar lavage. PAH was diagnosed when systolic pulmonary arterial pressure was estimated to be above 40 mm Hg by Doppler echocardiogram or when mean pulmonary arterial pressure was found to be higher than 25 mmHg by right-sided heart catheterisation. PAH was considered to be isolated when ILD was not identified.

Muscle involvement. It was defined as

the presence of proximal muscle weakness or myalgias and at least one of the following abnormalities: a serum creatin quinase over the normal value or results of an electromyogram consistent with myopathy.

Joint involvement. It was defined by the presence of any of the following: arthralgia, arthritis, tendon friction rubs or acro-osteolysis.

Heart involvement. It was established by one or more of the following: pericarditis, ischaemic cardiopathy of unknown cause, reversible thallium perfusion defects after cold stimulation, any disturbance on colour-Doppler echocardiography, electrocardiographic alterations with no other cause, left ventricular ejection fraction lower than 50% or right ventricular ejection fraction lower than 40% on echocardiography or radionuclide ventriculography.

Sclerodermal renal crisis: as was defined by Traub *et al*. (23).

Sjögren's syndrome: as defined by the American-European Consensus Criteria 2002 (24).

Immunoblot assay (LIA)

Line immunoassay (Euroline ANA profile No. 3, Euroimmun, Lübeck, Germany) was used to analyse the presence of autoimmune antibodies in the panel of 132 serum samples, according to the manufacturer's instructions. Briefly, each immunoblot strip containing nRNP/Sm, Sm, Ro60/SS-A, Ro-52, La/SS-B, Scl70, Jo-1, CENP B, dsDNA, nucleosomes, histones and ribosomal P-proteins antigens, coated separately, was incubated with a 1:101 diluted serum sample for 30 minutes. Later on, the attached antibodies were bounded by anti-human antibodies labelled with alkaline-phosphatase enzyme in a second 30 minutes incubation. Finally, the addition of a substrate along with chromogen allowed visualising the staining bands corresponding to specific antigen-antibody unions in the strip. The whole process was performed at room temperature.

Indirect immunefluorescence

An indirect immunofluorescence (IIF) assay of Nova Lite (IFA) ANA plus Mouse Kidney & Stomach (Inova Diagnostics, San Diego CA, Inc) was used for screening of ANA IgG antibodies, according to the manufacture's instructions. The screening dilution was 1:40.

To analyse the ANA titters, positive samples was tested by IIF using HEp-2 cells (Inova Diagnostics, San Diego CA, Inc) using secondary anti-human IgG (H + L) according to the manufacturer's instructions. Two-fold serum dilutions (from 1/40 to 1/2560) in PBS were analysed. Briefly, ANA HEp-2 substrate slides were incubated with patient's serum samples. After the appropriate washes, a FITC-coupled anti-human IgG antibody was added. The results were visualised through of fluorescent microscope and compared with the negative and positive controls provided by the assay. Several immunofluorescence patterns were expected: homogeneous, speckled, centromere, nucleolar and peripheral. An expert technician read fluorescence patterns; when doubts appeared, the result was contrasted with a second technician.

Capillaroscopic technic

Nailfold capillaroscopy was performed on each finger of both hands with a Wild M3 stereomicroscope and the use of a cold light lamp Intralux 5000 Volpi (Urdorf, Zurich, Switzerland), as previously described (1). According to Maricq *et al*. (24), two capillaroscopic patterns were distinguished: an active pattern characterised by predominance of capillary loss, and a slow pattern characterised by megacapillaries with no capillary loss.

Statistical analysis

Data were analysed with PASW Statics 18 (v.18.0.0) software. Mean and standard deviation (SD) was calculated for quantitative variables (age, time of disease onset and time of diagnosis) and percentage of patients was calculated for qualitative variable. Chi-square test, Fisher exact test and odds ratios and their 95% confidence limits were performed for comparative analysis of percentages. Tests were considered significant when p-value was <0.05.

Results

A total of 132 patients with anti-SSA/Ro52 antibodies assay performed were selected from a cohort of 408 patients with SSc. One hundred fifteen of these patients (87.1%) were women and 17 (12.9%) male. Sixty-eight (51.5%) had limited SSc, 25 (18.9%) diffused SSc, 9 (6.8%) pre-scleroderma and 30 (22.7%) SSc sine scleroderma (Table I).

The prevalence of patients with anti-SSA/Ro52 antibodies was 35.6%. Non-statistically significant differences were found between anti-SSA/Ro52 positive patients and anti-SSA/Ro52 negative patients neither in the demographic characteristics nor in the clinical manifestations (Table I).

Most of patients had capillaroscopic slow pattern, regardless of the presence/absence of anti-SSA/Ro52 antibodies, (OR 0.58, 95%CI 0.16–2.08, p=0.401).

ANAs were detected in 93.1% of the patients analysed (Table II). The highest ANA titter found was 1/2560 in the 3.6% of 84 anti-SSA/Ro52 negative patients, followed by the ANA titter 1/1280 (10.6% of 47 anti-SSA/Ro52 positive patients and 4.8% of 84 anti-SSA/Ro52 negative patients). Near half of the patients analysed in each group had 1/640 ANA titter (53.2% of anti-SSA/Ro52 positive patients and 42.9% of anti-SSA/Ro52 negative patients). Altogether, ANAs titter was not statistically different between both groups (p=0.591) (Table II).

Staining pattern of IIF on Hep2 cells was analysed in 118 patients (Table II). Most of patients showed centromere staining (50% of 42 anti-SSA/Ro52 positive patients and 27.6% of 76 anti-SSA/Ro52 negative patients) with speckled pattern (38.1% of anti-SSA/Ro52 positive patients and 50% of anti-SSA/Ro52 negative patients). Non-statistically significant differences were found in the staining pattern on Hep2 cells between both groups (p=0.149).

Table III shows the percentages of patients with specific autoantibodies associated with scleroderma. Anti-centromere antibodies were present in 44.8%, anti-Scl70 in 19.0%, anti-RNP in 2.2%, anti-Ro60 in 10.5%, anti-La 1.2% and anti-PMScl in 3.4% of patients. According to the anti-SSA/Ro52 detection, 61.9% of patients presented anti-centromere antibodies concomitantly with anti-SSA/Ro52 antibodies,

Table I. Demographic and basic clinical characteristics. Comparison between anti-SSA/Ro52 positive patients and anti-SSA/Ro52 negative patients.

	Total	Anti SSA/Ro52 positive	Anti SSA/Ro52 negative	OR (95%CI)	*p*-value
Patients, n (%)	132 (100)	47	85		
Age, Mean (years) ± SD		59.63±15.41	56.15±14.37	0.99 (0.96–1.01)	0.197
Time of disease onset, mean (years) ± SD		16.61±11.85	16.46±12.18	1.00 (0.97–1.03)	0.947
Time of diagnosis, mean (years) ± SD		9.3±6.78	8.76±7.35	1.00 (0.94–1.04)	0.685
Women, n (%)	115 (87.1)	42 (89.4)	73 (85.3)	0.72 (0.24–2.20)	0.568
Male, n (%)	17 (12.9)				
Type of scleroderma,					0.104
Limited, n (%)	68 (51.5)	31 (66)	37 (43.5)		
Diffuse, n (%)	25 (18.9)	6 (19)	19 (22.4)		
Pre-scleroderma, n (%)	9 (6.8)	2 (4.3)	7 (8.2)		
Sine scleroderma, n (%)	30 (22.7)	8 (17)	22 (25.9)		
Raynaud's phenomenon, n (%)	124 (94)	43 (91.5)	81 (95.3)	1.88 (0.45–7.91)	0.380
Ulcers, n (%)	55 (41.6)	18 (38.3)	37 (43.5)	1.24 (0.60–2.57)	0.559
Musculoskeletal pain, n (%)	79 (59.8)	25 (53.2)	54 (63.5)	1.53 (0.74–3.16)	0.246
Arthralgia, n (%)	64 (48.5)	22 (46.8)	42 (49.4)	1.11 (0.54–2.27)	0.774
Arthritis, n (%)	19 (14.4)	7 (14.9)	12 (14.1)	0.94 (0.34–2.57)	0.903
Non-inflammatory myopathies, n (%)	9 (6.8)	4 (8.5)	5 (5.9)	0.67 (0.17–2.63)	0.566
Inflammatory myopathies, n (%)	8 (6.0)	2 (4.3)	6 (7.1)	1.71 (0.33–8.82)	0.518
Oesophageal dysmotility, n (%)	73 (55.3)	25 (53.2)	48 (56.5)	1.14 (0.56–2.34)	0.717
Primary biliary cirrhosis, n (%)	3 (2.3)	2 (4.3)	1 (1.2)	0.27 (0.02–3.03)	0.256
Diffuse parenchymal lung disease (ILD), n (%)	44 (33.3)	15 (31.9)	29 (34.1)	1.1 (0.52–2.36)	0.797
Pulmonary hypertension, n (%)	22 (16.6)	5 (10.6)	17 (20)	2.1 (0.72–6.12)	0.167
Cardiac dysfunction, n (%)	49 (37.1)	16 (34)	33 (38.8)	1.23 (0.58–2.59)	0.586
Renal dysfunction, n (%)	3 (2.3)	1 (2.1)	2 (2.4)	1.11 (0.1–12.56)	0.934
Renal crisis, n (%)	2 (1.5)	1 (2.1)	1 (1.2)	0.54 (0.03–8.96)	0.668
Sicca syndrome, n (%)	36 (27.3)	15 (31.9)	21 (24.7)	0.7 (0.3–1.54)	0.373
Capillaroscopic slow pattern, n (%)	84 (63.6)	30 (83.3)	43 (89.6)	0.58 (0.16–2.08)	0.401

n: number of patients.

while 35.1% of patients with anti-centromere antibodies were anti-SSA/Ro52 negative, being the odds ratio three times higher in the group of patients with anti-SSA/Ro52 (OR 3.0, 95%IC 1.37–6.57, p=0.05). There were 10 patients who had anti-SSA/Ro52 positive antibodies in the absence of Scl70, anticentromere or RNP, this subset of patients did not show any statistically association with any clinical sign, although there was a trend of increase inflammatory myopathy (p=0.056).

Additionally, the odds of having anti-SSA/Ro60 antibodies was 25.2 times higher in the group of anti-SSA/Ro52 positive patients (OR 25.2, 95%CI 3.1–203.7, p<0.001). On the other hand, we found that the odds of having anti-Scl70 antibodies was higher in the group of anti-SSA/Ro52 negative patients, although this result did not reach statistical significance (OR 0.36, 95%CI 0.11–1.14, p=0.074). The percentages of patients having anti-RNP, anti-La (SSB) or anti-PM-Scl antibodies were very low in both groups of patients (Table III).

Discussion

In the last decades, the knowledge of the prevalence of anti-Ro/SSA antibodies in various autoimmune diseases has been expanded, and the clinical importance of these antibodies is increasing. Nonetheless, the pathological role of the antibodies is still poorly understood (19).

In this context, we evaluated the association of anti-SSA/Ro52 autoantibodies with the clinical features and autoantibodies profile of our SSc cohort.

The results of our study show that anti-SSA/Ro52 antibodies are often found in SSc patients. No clinical manifestations, including inflammatory myopathy, were related with anti-SSA/Ro antibodies. A high percentage of patients presented anti-centromere antibodies concomitantly with anti-SSA/Ro52.

Of note, we found a global prevalence of anti-SSA/Ro52 antibodies of 35.6%, similar to that reported in patients with myositis (35.4%) (20, 29), but lower than that found in patients with SLE-SCLE (systemic lupus erythematosus-subacute cutaneous lupus erythematosus) (53.0%) (15, 26), Sjögren's syndrome (63.2%) (17, 26) or patients with SLE (17, 26).

In a study using the consensus of three independent methods (LIA, ALBIA and ELISA), the frequency of anti-Ro52 antibodies was 19% in cohort of 100 patients with SSc (17), in line with previous studies (11, 27). The frequency of isolated anti-Ro52 antibodies was higher than the frequency of anti-Ro60 (11, 17), as we also reported in our study using only one of the three methods – LIA. The use of only one method to determine anti-Ro52 antibodies could explain the higher positivity rate.

Similarly, the prevalence of anti-SSA/Ro52 reactivity was also significantly higher than anti-Ro60 reactivity in patients with idiopathic inflammatory myopathies, primary biliary cirrhosis, mixed essential cryoglobulinaemia and primary Sjögren's syndrome (22). Some recent studies have shown that anti-SSA/Ro52, in absence of anti-SSA/Ro60, is the most common immune marker in patients with idiopathic inflammatory myopathies and interstitial lung diseases (10, 22, 28).

We did not find any differences between groups in the frequencies of Scl-70, SSB/La and PM-Scl. U1 RNP was only positive in two patients, both of them in the anti-SSA/Ro52 group, although it was not statistically significant.

Anti-centromere antibodies are classically associated with the limited form of the disease (60–82%) (29). In a re-

Table II. ANAs titter, immunofluorescence pattern and capillaroscopic pattern. Comparison between anti-SSA/Ro52 positive patients and anti-SSA/Ro52 negative patients.

	Total	Anti SSA/Ro52 positive	Anti SSA/Ro52 negative	*p*-value
ANA titter (1/x), n (%)	131	47	84	0.591
0		3 (6.4)	6 (7.1)	
40		1 (2.1)	4 (4.8)	
80		1 (2.1)	5 (6)	
120		0 (0)	1 (1.2)	
160		5 (10.3)	13 (15.5)	
320		7 (14.9)	12 (14.3)	
640		25 (53.2)	36 (42.9)	
1280		5 (10.6)	4 (4.8)	
2560		0 (0)	3 (3.6)	
Immuno-fluorescence (IIF), n	118	42	76	0.149
Centromere, n (%)		21 (50)	21 (27.6)	
Homogeneous, n (%)		2 (4.8)	5 (6.6)	
Speckled, n (%)		16 (38.1)	38 (50)	
Nucleolar n (%)		3 (7.1)	6 (7.9)	
Homogeneous and speckled, n (%)		0 (0)	5 (6.6)	
Nucleolar and speckled, n (%)		0 (0)	1 (1.3)	

n: number of patients.

Table III. Percentages of patients with specific autoantibodies associated with scleroderma. Comparison between anti-SSA/Ro52 positive patients and anti-SSA/Ro52 negative patients.

	Total	Anti SSA/Ro52 positive n (%)	Anti SSA/Ro52 negative n (%)	OR (95%CI)	*p*-value
Patients, n	132	47	85		
Anti-centromere, n	116	42	74		
Positive, n (%)	52 (44.8)	26 (61.9)	26 (35.1)	3.0 (1.37–6.57)	00.05
Scl70, n	116	40	76		
Positive, n (%)	22 (19.0)	4 (10)	18 (23.7)	0.36 (0.11–1.14)	0.074
U1-RNP, n	104	40	64		
Positive, n (%)	2 (2.2)	2 (5)	0 (0)	Fisher's exact test	0.146
Ro n	114	42	72		
Positive, n (%)	12 (10.5)	11 (26.2)	1 (1.4)	25.2 (3.1–203.7)	<0.001
La n	114	42	72		
Positive, n (%)	2 (1.2)	1 (2.4)	1 (1.4)	1.7 (0.12–28.4)	0.697
PM-Scl, n	58	17	41		
Positive, n (%)	2 (3.4)	1 (5.9)	1 (2.4)	2.5 (0.15–42.4)	0.513

n: number of patients.

cent study with sera of 863 patients with SSc, anti-centromere antibodies were present in 35.9% of patients and co-occurrence with anti-SSA/Ro52 (in 92 patients) and anti-SSA/Ro60 (in 11 patients) was also reported (11). As suggested by the authors of this study, although the reasons of this frequent co-occurrence are unknown, it is probably that the aetiopathogenetic pathways marked by these antibodies have common components, including common genetic predispositions (11). Based on this, we think the reported association between anti-SSA/Ro52 and anti-centromere antibodies should deserve further studies, as it could foretell specific association with clinical manifestations, similarly to the association observed in others autoantibodies (9).

Similarly, we detected anti-RNP antibodies only in anti-SSA/Ro52 positive patients (n=2), although the relevance of this serendipity is still to be determined. Anti-U3RNP (fibrillarin) antibodies are more frequently detected in young, male, and black patients (4), while detection of anti-U1RNP (ribonucleoprotein complex) antibodies is mainly associated with SLE and the mixed connective tissue disease, and it is less common in SSc patients (13). The prevalence in SSc patients can vary in different ethnic groups (26, 30).

We also assessed the possible relationship between epidemiological and clinical manifestations with the detection of anti-SSA/Ro52 antibodies, without any statistically significant difference being reported between positive and negative patients. In previous studies, significant association between isolated anti-SSA/Ro52 reactivity and some clinical signs, as interstitial lung disease and myositis, has been described (26, 28), although it has not been fully proved in patients with SSc (27).

In line with our results, in a previous study with 1010 patients with SSc, no evidences were found that anti-SSA-Ro52 could be at a higher frequency in SSc patients with myositis. These findings support the hypothesis that anti-SSA/Ro52 is a general serum marker with limited linkage to myositis phenotype or other clinical manifestations in SSc (27). Notwithstanding, patients with exclusively positive anti-SSA/Ro52 showed a trend toward greater inflammatory myopathy.

With these data in mind, we were not able neither to demonstrate a clear correlation between anti-SSA/Ro52 antibodies and the occurrence of certain clinical manifestations, particularly pulmonary involvement or myopathies. We consider that, although, to date, no associations have been observed, possible relationships between anti-SSA/Ro52 antibodies and clinical manifestations should be finally ascertained in larger observational studies, and using the same standard, validated method.

Our study suffers limitations inherent to its retrospective design. Although our cohort of SSc patients is large, anti-SSA/Ro52 was only available from patients recruited after March 2008, hence our study sample was limited. On the other hand, all patients are evaluated by the same well trained physicians and data recorded is of good quality and reliable.

Conclusion

The results of our study shows that anti-SSA/Ro52 antibody can be often found in patients with diagnosis of SSc, even in the absence of anti-centromere or Scl-70 autoantibodies. A relationship between anti-SSA/Ro52 and clinical manifestations was not found in our study.

Key messages

- Anti-SSA/Ro52 is presented in 36.5% of patients with SSc in our cohort.
- Anti-SSA/Ro52 may help in the diagnosis of SSc.
- There is an absence of association between anti-SSA/Ro52 and clinical manifestations.

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