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Anti-Collagen Type V Antibody in Systemic Sclerosis: A Possible Useful Tool to Asses Disease Activity

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Abstract

Introduction: Systemic sclerosis (SSc) is an autoimmune disease characterized by vascular injury, autoimmunity and tissue fibrosis. Usually collagen type V (V Col) is found hidden between the heterotypical fibers. It was discovered in the rheumatology department at the University of São Paulo (FMUSP) that deposition of this collagen occurs, however with anomalous morphology in SSc patient's tissue, suggesting that V Col is an important molecule in fibrosis and autoimmunity process. The V Col molecule, which has atypical morphology aspect, exposed after a nonspecific inflammatory damage could result in formation of immune complexes (V Col - anti-V Col), whose deposition on the vascular endothelium, would cause a vascular damage, allowing the influx of cells of innate immunity into the extracellular matrix, resulting in an enzymatic degradation of the heterotypical fibers, with exposure of more V Col and perpetuation of the disease.

Objectives: Assess whether there is a correlation between anti-V Col's presence in the serum of patients with SSc and indexes of activity, severity and quality of life measured by sHAQ.

Methods: Were evaluated 60 patients with SSc diagnostic during the period of January to December 2014. Were applied Medsger severity criteria, Valentini activity criteria and health assessment questionnaire in SSc (sHAQ) in the patients, at initial assessment (baseline) and after 6 months, correlating the presence of anti-V Col with the clinical and laboratory manifestations found.

Results: Most patients were female (98.3%) and had the limited form of the disease (43.3%), average age 51 years, white, average duration of nine years of disease and modified Rodnan Skin Score of 13.08. The main clinical manifestations observed in each organic system of patients were: skin thickening in the hands (78.3%), Raynaud's phenomenon (100%), arthritis (33.3%), oesophageal involvement (71.7%), interstitial lung disease (45%), pulmonary arterial hypertension (PAH) (19.4%) and scleroderma renal crisis (SRC) (1.7%). The most significant laboratory abnormalities were elevation of inflammatory markers in 41.7% of patients (ESR and CRP), CPK elevation (15%), low complement (C3 and C4) (3.3%), antinuclear antibody (95%), anti-centromere (41.7%), anti-DNA topoisomerase I antibody (26.7%), anti-RNA polymerase III (11.7%), anti-U1-RNP (16.7%) and anti-Ro (SSA) in 11.7% of patients. The anti-V Col was detected in 5 cases (8.3%) and showed statistical correlation with disease activity and scleroderma renal crisis, besides tendency to association with PAH; however, did not correlate with the severity index of disease or any other clinical manifestation, or with specific SSc antibodies.

Conclusions: We suggest that disease activity in SSc patients could be determined by serological analysis, to detect the presence of V Col antibodies in the serum of patients with SSc, facilitating the approach of this serious disease. We suggest further studies with larger number of patients in order to confirm the usefulness of this new marker of disease activity in systemic sclerosis.

Keywords: Anti-V Collagen antibody; Systemic sclerosis; Pathogenesis; Health assessment questionnaire in SSc (sHAQ); Medsger of severity criteria; Valentini activity criteria

Introduction

Systemic sclerosis (SSc) is an autoimmune disease, which has heterogeneous clinical presentation, affects multiple systems and follows a variable and unpredictable course [1]. Its etiology remains unknown, multifactorial causes being suggested, such as environmental and autoimmune factors in genetically predisposed individuals [2]. Distinctive aspects of the SSc are the occurrence of microvasculopathy, abnormal activation of fibroblasts with excessive synthesis of collagen and autoimmunity [3]. The earliest events observed in the pathogenesis of SSc is the damage to endothelial cells and apoptosis, demonstrated in skin and lungs, even before any evidence of autoimmunity or tissue fibrosis [4]. From the recent

discovery of an experimental model of SSc in rabbits by immunization with type V collagen (V Col), was suggested that different forms of aggression to endothelial cells, provided that sufficiently prolonged and intense, would be able to promote damage in the endothelium - basal membrane complex, exposing the own extracellular matrix components to the immune system, triggering tissue histological alterations and autoimmunity observed in SSc [3-12].

In this context, the V Col found normally hidden between the heterotypical fibres (interlacement of collagen types I, III and V), but that is exposed when the inflammatory process occurs in the extracellular matrix. It would be the antigen itself (neo-antigen) responsible for triggering SSc animal and possibly human illness [3-12].

Other external toxic agents such as silica, similarly to V Col antigen inoculated in rabbits would cause injury of the endothelium - basal membrane complex [6,7,9] or bronchial epithelial - basal membrane complex [4,10], leading to vascular or bronchial damage, followed by intense inflammation process of the matrix, causing exposure of different antigens previously hidden from the immune system and thus would trigger the fibrosis and autoimmunity identified in SSc [4,6,7,10].

Once we found matrix disarrangement with exposure of anomalous V Col in both animals and in patients with SSc and observe the presence of changes in the histoarchitecture similar in both conditions, we suggest that the V Col endogenous (neo-antigen) performs a fundamental role in the pathogenesis of experimental and human SSc.

Therefore, we propose research anti-V Col in the serum of patients with SSc, assuming that the serological identification of this antibody could reflect what was happening at the tissue level. In other words the serological practical implementation test, easier than the immunohistochemical study, could reflect the existence of matrix disarrangement, exposure of hidden V Col antigen and synthesis of heterotypical anomalous fibres. The selected population was of SSc patients from the Midwest region of the country and laboratory data of the anti-V Col research were correlated with the clinical staging of the disease, quality of life index (sHAQ) and various laboratory parameters of disease.

Objectives

To evaluate the frequency of anti-V Col antibody in patients with SSc in the Midwest region of Brazil. Check if the anti-V Col positivity correlates with the activity and severity of disease, or with any specific clinical or laboratorial manifestation in these patients.

Methods

This is an observational, cross-sectional study.

From 72 patients previously selected from survey of medical records at the Rheumatology Department of Universidade Federal do Mato Grosso do Sul (UFMS), 60 patients fulfilled the inclusion criteria and agreed to participate of the research.

The selected patients obeyed the following criteria:

- Fill the new 2013 classification criteria for SSc [15]
- In the case of absence of skin thickening, they should fill the 2001 early SSc criteria of LeRoy and Medsger [16]
- The patients with infectious diseases or malignant neoplasias as well as children, pregnant women and indigenous patients were excluded.

The necessary information for the sociodemographic and clinical characterization of the disease were obtained from the data contained in the medical records of each patient and supplemented by interviews. At the first appointment were collected demographic and clinical data, including duration of disease, year of diagnosis, modified Rodnan Skin Score [17], autoantibody research, complete clinical examination and current treatment.

Patients were also evaluated at baseline and after 6 months, to research activity, severity and quality of life of the same. For this analysis, we used Medsger severity criteria [18], Valentini activity criteria [19], and Scleroderma Health Assessment Questionnaire (sHAQ) [20] to measure quality of life.

For laboratory research they have been using sera from patients previously selected and were properly frozen to -50°C and stored in the Laboratory of the University Hospital of UFMS. Were applied the following methodologies:

Antinuclear antibody research (ANA)

Were used indirect immune fluorescence technique [21]. The sera were considered positive when titles were greater than or equal to 160 and diluted until obtain negative fluorescence.

Research of Anti-Sm, anti-RNP, anti-Jo-1, anti-Ro (SSA) and anti-La (SSB)

It was used Immunoenzymatic assay technique (ELISA), as previously described [22], using specific substrate kits for each test, following the manufacturer specifications (Hemagen Diagnostics, Inc). It was considered positive serum with DOT above 3 times the cut-off.

For the anti-DNA research topoisomerase-1 (anti-Scl-70)

It was used Immunoenzymatic assay technique (ELISA), as previously described [23], using QUANTA LITE(TM) SCL-70 specific kit from INOVA Laboratory (INOVA Diagnostics, Inc; San Diego, CA, USA), following the manufacturer specifications. It was considered non-reactive in case the quantification in serum was less than 20 units, weakly reactive in case the quantification was between 20 and 39 units, moderately reagent between 40 and 80 units and highly reactive (high values) in case the quantification was greater than 80 units.

Anti-centromere research

Were used indirect immunofluorescence technique having as substrate HEp 2 cells according to the criteria of the II Brazilian Consensus on Antinuclear factor in Hep-2 cells (2003) [21], for the interpretation of the results.

Anti-RNA polymerase III Antibody

The research of this autoantibody was held by Rheumatology Department of the Federal University of São Paulo at Research Laboratory of the Hospital São Paulo (UNIFESP). It was used ELISA technique as previously described [24], using QUANTA LITE RNA POL III ELISA specific kit from INOVA Laboratory (INOVA Diagnostics, Inc; San Diego, CA, USA), following the manufacturer specifications. It was considered negative the values lower than 20

units, weakly reactive the values between 20 and 39 units, moderately reagent between 40 and 80 units and highly reactive (high values) values greater than 80 units.

Research of anti-collagen type V antibodies

It was used Immunoenzymatic assay technique (ELISA) [8] for IgG class antibody research and held in LIM-17 at HCFMUSP (Rheumatology Medical Research Laboratory in Hospital das Clínicas of College of Medicine of University of São Paulo) with minor modifications.

Detection of antibody to type V human collagen by ELISA

Briefly, wells of polystyrene microplates (Costar, San Diego, CA) were sensitized overnight with 50 lL of purified purified human collagen V (Sigma) (5 lg/mL) and then blocked with 100 lL of BSA 1% (Sigma) for 2 hr at room temperature. Serum samples 1: 100 diluted were added to the wells and tested in duplicate. Plates were further incubated with alkaline phosphatase-conjugated goat antirabbit IgG (Sigma) and the reaction was developed with p-nitrophenyl phosphate (p-NPP, Sigma). The optical density (OD) was read at 405 ηm (ELISA Multiskan MS, Labsystems, and Helsinki, Finland). To ensure consistency between assays, a hyper-immune rabbit serum for huCol V was systematically included in each assay and the reaction was stopped when its OD reached the value of 1.0. Positive results were defined as OD = 3 SD above the mean OD of 26 control serum samples obtained from rabbits before immunization (at day zero) and included in each assay.

Statistical Analysis

Were used the median calculation for the socio demographics data.

The evaluation of the linear correlation between sHAQ and disease activity was performed using Pearson's linear correlation test.

The comparison between patients negative for the anti-collagen V antibody, with those positive for this antibody, in relation to the sHAQ variables, score on the severity scale, score in the activity scale, duration of disease, and value of the PASP, was performed using the Student's T test. The same test was used to compare patients with the diffuse form of disease and those with limited disease, in relation to quantitative variables evaluated in this study.

The Fisher exact test was used to assess the association between the results for the anti-collagen V antibody and the variable presence renal crisis.

The chi-square test or Fisher exact tests were used to evaluate the association between the forms of the disease (diffuse and limited) with qualitative variables measured in this study.

The results of the other variables assessed in this study were presented in the form of descriptive statistics or in tables and graphs. The statistical analysis was performed using the "software" SPSS, version 20.0, considering a 5% significance level.

Results

Demographics data and monitoring of the disease

It was found total of 60 patients, 59 women (98.3%) and 1 man (1.7%) with an average age of 51.18 ± 1.56 years (average ± standard error). Of all patients, 30 patients report be white (50.0%), [27] of brown skin (45.0%) and 3 black (5.0%).

Regarding the diagnosis, all patients met the criteria for rating ACR / EULAR from 2013 (15).

In relation to the clinical forms of the disease, 26 patients were of limited form (43.3%), 20 patients with the diffuse form (33.3%), 7 patients with early form (11.7%), 7 patients in the form of overlapping (11.7%) and none with sine scleroderma form.

With respect to the time of diagnosis, 16 diagnosed patients were over 10 years (26.7%), 28 patients between 5 to 10 years (46.7%) and 16 patients less than 5 years (26.7%) . The progression of the disease in general patients was 9.28 ± 0.79 years.

The first sHAQ assessment (sHAQ1) was on average 0.63 ± 0.05, being 1.56 the highest value found and 0 the lowest. In the second sHAQ evaluation (sHAQ2) performed 6 months after first was on average 0.63 ± 0.05, and the highest value found was 1.63 and the lowest was 0.

The average value in patients Severity Score was 4.87 ± 0.37 and there was practically no difference from the second evaluation. The highest value found in one patient was 15 and the lowest was 1.

The Disease Activity Scale in the first evaluation (AS1) was on average 2.30 ± 0.17, being the highest value found 5.5 and the lowest 0. Activity Scale in the second evaluation (AS2) held after the first six months had 2.36 ± 0.19 average, being 6 the highest value found and 0 the lowest. The results are summarized in Table 1.

Variable	% (n) or average ± SE
Monitoring indices	
sHAQ 1	0.63 ± 0.05
sHAQ 2	0.63 ± 0.05
Severity scale	4.87 ± 0.37
Activity scale 1	2.30 ± 0.17
Activity scale 2	2.36 ± 0.19

Table 1: Shaq, Severity and Activity Scales of patients with SSc in the range of 6 months.

The results are presented as mean ± standard error of the mean or relative frequency (absolute frequency). Shaq 1 was obtained in the first interview and Shaq 2 was obtained after 6 months. Activity scale 1 was obtained in the first interview and activity scale 2 was obtained after 6 months.

Laboratory tests

Of the total patients evaluated, 25 (41.7%) had elevated inflammatory markers of acute phase (erythrocyte sedimentation rate > 30 mm in the first hour and / or C-reactive protein > 6 mg/dl) in the initial clinic visit.

Of the 60 patients evaluated, 9 (15.0%) had elevation of creatine phosphokinase (CPK) in the initial consultation. Of these, 3 were diagnosed with inflammatory myopathy overlap (33.3%).

Only one patient with scleroderma renal crisis presented creatinine elevation, with the amount of 1.8mg/dL (normal value from 0.6 mg/dL to 1.3 mg/dL).

Only 2 patients decreased serum complements C3 and C4 (3.3%), 1 patient in each form of the disease (diffuses / limited).

Of the total patients evaluated, 7 (11.7%) presented positive anti Ro (SSA). All patients with positive anti Ro (SSA) had Sjogren syndrome associated. Only 1 patient with diffuse form had anti La (SSB) positive (1.7%) and only one overlapping SLE patient had anti Sm positive (1.7%).

Of the total patients evaluated, 10 (16.7%) showed positive anti RNP. Of these, 6 were overlapping with other connective tissue diseases (60.0%), being represented by two SLE patients and 2 patients with Rheumatoid Arthritis and 2 patients with inflammatory myopathy with positive anti-Jo 1.

The X-ray (XR) of the hands was normal in 34 patients (56.7%). Among the 26 patients with XR changes was observed resorption of the distal phalanx in 17 of them (65.4%). Calcinosis was also observed in 9 patients (34.6%), mainly in limited form (77.8%).

Antinuclear antibody, anti-collagen V antibody and specific SSc antibodies

The antinuclear antibody (ANA) was positive in 57 patients (95%) and 3 patients with negative ANA had the early form of the disease. ANA patterns most commonly found in patients were: nuclear centromeric with positive metaphase plate in 20 patients (33.33%), nuclear fine speckled with negative metaphase plate in 13 patients (21.67%) and almost homogeneous nuclear with metaphase plate blushing 5 to 10 points in 11 patients (18.33%).

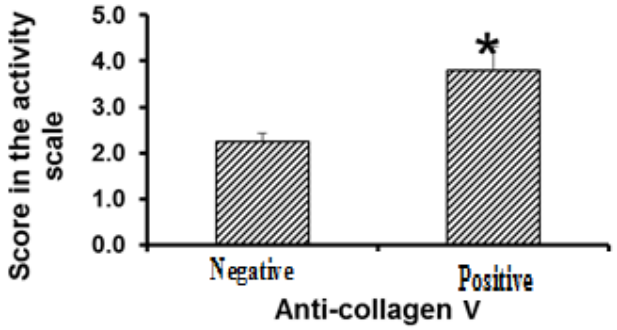

Figure 1: Graph showing the score on the scale of disease activity in patients with negative or positive for anti-collagen V. Each column represents the mean and standard error of the mean bar. * Significant difference from patients with anti-collagen negative V (t-Student test, p = 0.016).

Of the 60 patients evaluated, only 2 (3.3%) had positive anti-V Col with higher titer 1/200 at baseline, both the diffuse form. In the second evaluation, when all patients remade the anti-V Col after six months, only 3 patients (5.0%) were positive for anti COL V, 2 patients with limited form and one patient with the diffuse form. In total, 5 different patients had anti-V Col positive (8.3%), 2 patients with positivity at baseline differ from those 3 patients with positivity in the second evaluation.

The positivity of anti-V Col correlated to the clinical activity in patients with SSc, according to Valentini activity criteria (Figure 1 and Table 2). It also noted statistical significance between the positivity of antibody and scleroderma renal crisis, beyond of statistical trend between the presence of anti-V Col and the clinical manifestation of pulmonary hypertension, as shown in Table 2.

Variable	Anti-collagen V		p* value
	Negative (n=55)	Positive (n=5)	
sHAQ	0.63 ± 0.05	0.81 ± 0.21	0.33
Severity scale	4.73 ± 0.39	6.40 ± 1.25	0.22
Activity scale	2.25 ± 0.18	3.80 ±0.52	0.016 *
Disease duration (years)	8.55 ± 0.85	5.40 ± 1.12	0.274
PASP value (mmHg)	31.50 ± 3.98	39.50 ± 2.50	0.409
Pulmonary artery hypertension			
Yes	4 (6.7)	2 (3.3)	0.074
No	51 (85.0)	3 (5.0)	
Renal crisis			
Yes	0 (0.0)	1 (20.0)	0.001 *
No	55 (100.0)	4 (80.0)	

Table 2: Results of the monitoring index in patients with anti-collagen V positive or negative.

Results are presented as mean ± standard deviation or in absolute frequency (relative frequency). *P value in the t-Student test or chi-square test. sHAQ: Health Assessment Questionnaire in systemic sclerosis. PASP: estimated pulmonary artery pressure.

There was a significant positive linear correlation between the HAQ and disease activity (Pearson's linear correlation test. p <0.001; r =0.600; r2 =0.360).

Of all patients 16 (26.7%) had positive anti-topoisomerase 1. Among these patients 12 had diffuse form (75%).

Of all patients 25 (41.7%) had positive anti centromere. Among these patients 21 had limited form (84.0%) and the others had early form.

Of all patients 7 (11.7%) had positive anti RNA Polymerase III. Three of these patients had diffuse form (42.9%).

None of the patients presented positive anti PM / Scl.

There was no statistically significant association between positivity of anti-V Col and other specific antibodies present in the SSc. summarized in Table 3.

Antibody	Anti-collagen V		
	Negative (n=55)	Positive (n=5)	
Anti-centromere			
Negative	31 (56.4)	4 (80.0)	0.299
Positive	24 (43.6)	1 (20.0)	

Anti SCL 70			
Negative	41 (74.5)	3 (60.0)	0.403
Positive	14 (25.5)	2 (40.0)	
Anti POL 3			
Negative	49 (89.1)	4 (80.0)	0.475
Positive	6 (10.9)	1 (20.0)	

Table 3: Results of the association between the results for anti-collagen V antibody and the results for anti-centromere, anti SCL 70 and anti POL 3.

The results are presented in absolute frequency (relative frequency). *P value at Fisher's exact test. Anti SCL 70: anti-DNA topoisomerase I antibody anti POL 3: anti RNA polymerase 3 antibody.

Discussion

Set disease activity in SSc is much more difficult than in other rheumatic connective tissue diseases where inflammation plays an important role as in SLE and RA [25-27]. This could be explained by the fact that developments in most patients with SSc especially those with limited form has a very indolent course without obvious clinical and laboratory signs of inflammation [25,28].

Despite this difficulty, set the activity in SSc is a matter of extreme importance [27] as it enables the clinician to distinguish patients who require aggressive treatment of those in which the symptomatic treatment could be sufficient avoiding side-effects of unnecessary drugs [25]. Consequently, there is a great need to find biomarkers that can accurately reflect both global activity and organ-specific and numerous candidates have been proposed but with controversial results [26,29-31]. It is suggested from this study including anti-V Col as a biological marker for disease activity.

We note that 5 of 60 patients with SSc (8.3%) had antibodies against V Col Its presence presented correlation with criteria of disease activity and scleroderma crisis but not with disease severity as well as the quality of life of patients as measured by sHAQ.

In this study the activity scores of the patients' disease were similar to those observed in the literature [27,35] as well as the involvement of each organ in calculating the score of disease activity with higher cutaneous involvement followed by vascular and lower gastrointestinal prevalence lung and joint [36].

The sHAQ is a measure that assesses the functional capacity in patients with SSc being a useful tool for evaluating functional physical disability [37] and the impact of the disease on the physical and mental well-being of patients [38]. The utility of the sHAQ in the evaluation of patients with SSc is useful because it can predict the evolution and survival of patients [37]. The rates found in this study were similar to those described in other populations [37,39] although it was observed by sHAQ higher disability scores in patients with anti-positivity V Col. this difference was not statistically significant possibly due to the small size of patients with positive anti-V Col.

There were no significant variations in the severity scale after 6 months of follow-up of the patients with SSc so that the averages found in the two evaluation periods were identical on this research. Medsger described subgroup of patients who were followed for three years examined every six months to make the severity indexes and found little variation in the scores [29]. In another study severity and disease activity were closely related especially in the subgroup of patients with premature presentation of diffuse SSc indicating that the active disease is associated with poor prognosis [41]. Similarly, when comparing the patients in this study with greater severity it was observed that they also had significantly greater disease activity (4.03 vs. 1.38).

As previously reported the relevance of V Col study in patients with SSc arises from the fact of the molecule play possible role in the pathogenesis of the active disease especially in the early stages. When the chance to identify V Col antibodies are greater [42]. In addition late complications such as pulmonary fibrosis pulmonary hypertension and nephropathy although there histological aspects of irreversibility may indicate the occurrence of reactivation of the disease and thus showing presence of V Col exposed in tissues and generate appearance of anti-V Col in the serum of patients with SSc (4,8,10).

A previous study conducted by Riente and cols detected IgG class V Col antibodies in the serum of 31% of patients with SSc [43]. Interestingly unlike our findings antibodies were directed against the native and denatured V Col molecule. They considered that antibodies reacting against collagen IV and V could contribute to tissue damage since any damage that affects the endothelium-basal membrane complex could lead to formation of immune complexes and complement fixation against these components. They suggested that after the process of endothelial injury and basement membrane matrix inflammation could happens [43].

Our work showed low positivity frequency of anti-V Col (8.3%). We believe that the low incidence of anti-V Col found in our studied population with SSc has been reflection of the clinical disease staging that is the majority of patients were followed for a long time and found to be clinically stable. The time of medical accompaniment of the patients was 9 years and only 7 patients had the premature form of the disease.

Even though both studies have researched only anti-collagen antibodies of the IgG class another interesting aspect that can explain the disagreement of our results with those of Riente and Cols [43] was that in our research we used as antigen of ELISA assay only V Col modified after previous treatment with mercaptoethanol or denatured by heating. In our experience both the rabbit sera of the experimental model as SSc patients only reacted with COL V unstructured [5.8]. This fact reveals that both in the experimental animal model as in SSc patients only occurs exposure V Col fragments with atypical morphology in affected tissues. That is there is no way justifying the presence of V Col intact native molecule in the extracellular matrix of tissues with SSc unstructured by enzymatic action following the injury of endothelium-basal membrane complex. So pretreatment of native V Col using mercaptoethanol or heat would be simulating the enzymatic digestion and exposure of hidden epitopes that occur in tissues of patients with SSc.

We assume that the anti-V Col antibody could be a good marker to indicate vascular damage with subsequent matrix damage and exposure of hidden antigens as V Col fragments [3,6-8). We postulate that the SSc persistence of anti-V Col antibody occurs for a prolonged period lasting for a period of existence of matrix disorder with exposure of V Col anomalous which would coincide with the disease activity period. It is possible that new future research can identify anti-V Col in very premature cases of SSc even before the onset of clinical symptoms especially in the limited forms of the disease [8,27,29,42].

Interestingly Riente and Cols identified anti-V Col in 8% of patients with primary Raynaud's phenomenon [43] suggesting that the presence of this antibody could predict the appearance of SSc and in particular an active and more severe form of disease.

The observation of anti-V COL presence in the sera of patients with other rheumatic diseases suggests the occurrence of clinical inflammatory activity with endothelial damage but cannot be considered a specific marker of any diseases [44].

In this study only one patient who did not use steroids with limited form of SSc presented scleroderma renal crisis (SRC) with positivity for anti-V Col. Even being a single case and had statistical significance. We admit that the patient has presented clinical reacutization of the disease targeting the kidney organ. We recall that the destructuration of the matrix with exposure of anomalous type V collagen has also been demonstrated in large vessels in the model of experimental animals. Myofibroblasts obtained from the pulmonary artery of the rabbits when cultured in vitro synthesize increased amount of collagen especially Type V anomalous similar to what occurs with isolated fibroblasts from the skin of immunized animals (unpublished data). Increased deposition of matrix collagen would cause thickening of intimal layer and decrease vascular lumen worsening the irrigation of the bodies involved or causing pulmonary hypertension or renal crisis [45]. In addition the renal mesangium is rich in V Col [46] contributing to the pathophysiology of renal disease in SSc.

Of the six patients with pulmonary arterial hypertension (PAH) two showed anti-V Col with statistical trend by Fisher's exact test. It was also noted trend in increase of systolic pulmonary artery pressure in patients with PAH and anti-V Col. One of SSc patients in the limited form evolved with PAH during this study. Presented earlier anti-V Col negative and was asymptomatic. After six months began with symptoms of dyspnea on moderate effort when it was submitted to echocardiographic examination which proved to be compatible with mild PAH. Cardiac catheterization confirmed PAH and anti-V Col became positive.

In this study was found no statistical association between the positivity of anti-V Col with other specific SSc antibodies (ACA anti SCL 70 and anti RNA Pol3) and this data is original. Likewise Riente and Cols found greater incidence of anti-V Col in diffuse SSc however no correlation with the autoantibodies [43].

We therefore suggest that disease activity in SSc patients could be determined by serological analysis for the presence of anti-V Col antibodies in the serum of SSc patients facilitating the therapeutic approach of this serious disease.

Conclusion

Anti COL V was detected in 8.3% of patients with SSc and showed statistical correlation with disease activity and with scleroderma renal crisis. With a trend towards association with pulmonary arterial hypertension.

However their presence is not associated with the severity index of the disease and other clinical manifestations or with specific antibodies the SSc.

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