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Original article

Autoantibodies in systemic sclerosis and their clinical correlation in patients from a Midwestern region of Brazil

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ABSTRACT

Introduction: Systemic sclerosis (SSc) is a connective tissue disease of autoimmune nature characterized by the triad of vascular injury, autoimmunity (cellular and humoral) and tissue fibrosis. Autoantibodies do not seem to be simply epiphenomena, but are involved in disease pathogenesis. It is believed that the SSc-specific autoantibodies are responsible both for amplifying immune response and targeting cell types that are relevant in the pathophysiology of SSc.

Objectives: To correlate the profile of the following specific autoantibodies: anti-centromere (ACA), anti-topoisomerase I (topo I) and anti-RNA polymerase III (RNAP III) with clinical and laboratory manifestations were observed in 46 patients with SSc in the Midwest region of Brazil.

Methods: The occurrence of specific autoantibodies in 46 patients with SSc was investigated, correlating the type of autoantibody with clinical and laboratory manifestations found.

Results: Among all patients evaluated, we found a predominance of females (97.8%), mean age 50.21 years old, Caucasian (50%), limited cutaneous SSc (47.8%), time of diagnosis between 5 and 10 years (50%), and disease duration of 9.38 years. According to the specific autoantibody profile, 24 patients were ACA-positive (52.2%), 15 were positive for anti-topo I (32.6%), and 7 showed positive anti-RNAP III (15.2%). The anti-topo I autoantibody correlated with diffuse scleroderma, with greater disease severity and activity, with worse quality of life measured by the SHAQ index, with a higher prevalence of objective Raynaud's phenomenon and digital pitting scars of fingertips. The ACA correlated with limited scleroderma, with earlier onset of disease, as well as higher prevalence of telangiectasias. The anti-RNAP III correlated with diffuse scleroderma, with a higher occurrence of subjective Raynaud's phenomenon and muscle atrophy. There was no association between the positivity for anti-topo I, ACA and anti-RNAP III antibodies and other variables related to laboratory abnormalities, as well as Rodnan skin score and skin, vascular, musculoskeletal, gastrointestinal, cardiopulmonary and renal manifestations.

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Conclusions: The clinical subtype of the disease and some clinical manifestations in SSc may correlate positively with the presence of specific autoantibodies.

Autoanticorpos em esclerose sistêmica e sua correlação com as manifestações clínicas da doença em pacientes do Centro-Oeste do Brasil

Palavras-chave:
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RESUMO

Introdução: a esclerose sistêmica (ES) é uma enfermidade do tecido conjuntivo de caráter autoimune caracterizada pela tríade de injúria vascular, autoimunidade (celular e humoral) e fibrose tecidual. Os autoanticorpos não parecem ser simplesmente epifenômenos, mas sim estarem envolvidos na patogênese da doença. Acredita-se que os autoanticorpos específicos da ES são responsáveis tanto pela amplificação da resposta imune quanto por alvejar os tipos celulares que são relevantes na fisiopatologia da ES.
Objetivos: correlacionar o perfil de autoanticorpos específicos (anti-SCL70, ACA, anti-POL3) com as manifestações clínicas e laboratoriais observadas em 46 pacientes com ES da região Centro-Oeste do Brasil.
Métodos: pesquisou-se a ocorrência de autoanticorpos específicos em 46 pacientes com diagnóstico de ES e correlacionou-se o tipo de autoanticorpo com as manifestações clínicas e laboratoriais encontradas.
Resultados: dentre todos os pacientes avaliados, encontrou-se predomínio feminino (97,8%), idade média de 50,21 anos, cor branca (50%), forma limitada da doença (47,8%), tempo de diagnóstico entre cinco e 10 anos (50%) e tempo de evolução da doença de 9,38 anos. De acordo com o autoanticorpo específico, 24 pacientes apresentavam ACA positivo (52,2%), 15 apresentavam positividade para anti-SCL70 (32,6%) e sete apresentavam anti-POL3 positivo (15,2%). O autoanticorpo anti-SCL70 se correlacionou com a forma difusa da doença, com maior gravidade e atividade da doença, com pior qualidade de vida medida pelo índice HAQ, com maior prevalência de fenômeno de Raynaud objetivo e microcicatrizes de polpas digitais. O ACA se correlacionou com a forma limitada da doença, com o início mais precoce da enfermidade, bem como com maior prevalência de telangiectasias nos pacientes. Já o anti-POL3 se correlacionou com a forma difusa da doença, com maior ocorrência de fenômeno de Raynaud subjetivo e de atrofia muscular. Para as demais variáveis relacionadas às alterações laboratoriais, bem como em relação ao escore cutâneo de Rodnan e às manifestações cutâneas, vasculares, musculoesqueléticas, gastrintestinais, cardiopulmonares e renais, não houve associação entre elas e a positividade para os anticorpos anti-SCL70, ACA e anti-POL3.
Conclusões: a forma clínica da doença e algumas manifestações clínicas na ES podem se correlacionar positivamente com a presença de autoanticorpos específicos.

Introduction

Systemic sclerosis (SSc) is a connective tissue disease of autoimmune nature, extremely heterogeneous in its clinical presentation, with involvement of multiple systems, and following a variable and unpredictable course.[1] Its etiology remains unknown, with a multifactorial cause being suggested, possibly triggered by environmental factors in a genetically predisposed individual.[2]

The hallmark of SSc is microvasculopathy, activation of fibroblasts and excessive collagen production.[3] It is a unique disease as it has features of three distinct pathophysiological processes; it consists of the triad of vascular injury, autoimmunity (cellular and humoral) and tissue fibrosis, leading to involvement of skin, in addition to several internal organs such as lungs, heart, gastrointestinal tract, among others.[3,4]

It is believed that the link between initial vascular involvement and the final consequence of the disease (tissue fibrosis) could be represented by autoimmunity. Circulating antibodies, alteration of immune mediators and infiltration of mononuclear cells in affected organs represent a positive argument for the hypothesis that dysfunction of the immune system leads to illness.[5,6]

It is described that highly specific antibodies can be detected in the sera of virtually all patients with SSc.[7] A review article by Zimmermann and Pizzichini highlights that specific antibodies represent one of the hallmarks of the disease and constitute the most evident expression of the