

CELIAC DISEASE SCREENING IN PATIENTS WITH SCLERODERMA

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ABSTRACT - Both celiac disease and scleroderma have autoimmune etiology and affect the bowel causing diarrhea. As an association of autoimmune disease in a single individual is not rare, it is important to know if a patient with scleroderma may also have celiac disease. To analyze this we studied 105 scleroderma patients and 97 volunteers for IgA-EmA by indirect immunofluorescence assay. We could not find a higher prevalence of this autoantibody in scleroderma patients. The authors conclude that there is no need to screen scleroderma patients with diarrhea for celiac disease unless there is a clear clinical indication for this.

HEADINGS - Celiac disease. Scleroderma, systemic.

INTRODUCTION

Aggregation of autoimmune diseases is frequently observed in clinical practice. There is no clear cut explanation for this although it is noted that autoimmune diseases may share a genetic background. In addition, an exposure to a common etiological trigger agent is also possible⁽¹⁾.

Celiac disease (CD) is a chronic, inflammatory and immunological mediated gluten-dependent enteropathy disease that occurs in genetically susceptible individuals⁽²⁾. It appears in association with other organ specific autoimmune diseases such as thyroiditis, diabetes mellitus, dermatitis herpetiformis, autoimmune myocarditis, Addison disease, autoimmune hepatitis and primary biliary cirrhosis, etc⁽²⁾.

CD is also associated albeit occasionally with systemic autoimmune disorders such as connective tissue disorders⁽¹⁾. In this context, Sjögren syndrome is probably the connective tissue disease that bears the more convincing data. Iltanen et al.⁽¹⁾ studying 34 Sjogren's syndrome patients found that 14.7% had CD, a prevalence of 30 to 40 fold higher than observed in the normal population. It is known that Sjögren's syndrome shares the HLA DQ2 and DQ8 haplotype with CD. On the other hand, no association has been found with rheumatoid arthritis⁽¹⁾. Association of CD with polymyositis is less studied and described in case reports⁽¹⁾; as CD is a common disease, this relationship may be coincidental.

In scleroderma (SSc), association with CD is controversial. Luft et al.⁽³⁾ studying IgA antitissue transglutaminase antibody (anti-tTG) in 30 SSc patients found that 2 (7%) of them had this antibody against (2/40) 4% of normal population ($P = NS$). Rosato et

al.⁽⁴⁾ analyzing 50 SSc patients found a prevalence of anti-tTG in 5/50 of their patients although only 4 (8% of the total sample) had biopsy proven CD a value that is higher than in normal population.

SSc is associated with diarrhea due to loss of peristalsis by fibrous involvement of smooth muscle and intraluminal bacterial overgrowth and the clinical findings of diarrhea and malabsorption mimics CD⁽⁵⁾. Nevertheless, the treatment of these two entities is completely different, which emphasized the need for a correct differential diagnosis.

Nowadays, endomysium antibodies (IgA-EmA) are currently regarded as the most sensitive and specific immunologic marker of CD⁽²⁾. IgA-EmA as well as anti-tissue transglutaminase (anti-tTG) has allowed evaluating the potential risk for CD in individuals with suggestive symptoms and in high risk populations. IgA-EmA antibody has over 90% specificity and sensibility for CD diagnosis. The titer of these antibodies is related to the degree of intestinal atrophy and symptoms severity⁽²⁾.

In this context we studied 105 scleroderma patients from Southern Brazil for the presence of EmA-IgA antibodies.

METHODS

One hundred and five scleroderma patients were included in this study. In this sample 7.6% were male and 92.3% female; mean age of 43.2 years and mean disease duration of 7.7 years. In this sample, 36/105 (34.2%) had diffuse scleroderma; 9/105 (8.5%) had the mixed form (SSc plus myositis), 1 (0.9%) was sine scleroderma and 59/105 (56.2%) had the limited form (CREST syndrome).

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After formal consenting, blood was collected and the serum aliquoted and stored at -80° C until performing tests.

As control, we studied 97 healthy volunteers from the same geographical region matched for age and sex. Tests for IgA-EmA were performed by indirect immunofluorescence assay, using human umbilical cord as substrate and fluorescein conjugated goat anti-human IgA (GMK, Porto Alegre, RS, Brazil) as conjugate. Positive and negative controls were included in each test battery (Figure 1).

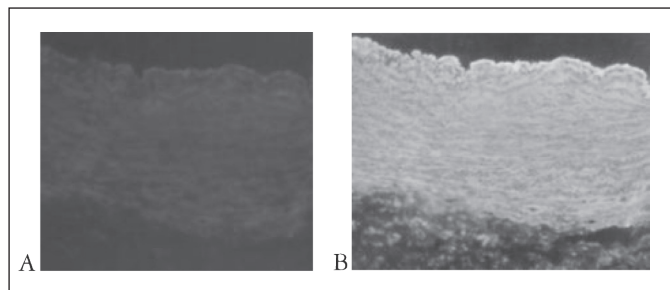


FIGURE 1. A - Negative IgA-EmA in cryostatic section of human umbilical chord (400X). B - Positive IgA-EmA in cryostatic section of human umbilical chord (400X)

RESULTS

All samples, patients and controls were negative for IgA-EmA.

DISCUSSION

Crypt hyperplasia, villous atrophy and intra epithelial lymphocytic infiltration are the main pathological characteristics

of CD. CD patients classically develop prolonged diarrhea, abdominal pain and weight loss, iron or folate deficiency, osteoporosis, chronic fatigue, milk intolerance, dental problems, neuropathy, dementia and failure to thrive. Subclinical forms are quite common; it is not rare that CD patients with minor gastroenterological symptoms are misdiagnosed as having irritable bowel disease or that CD diagnosis is only detected after the investigation of iron deficiency anemia or low bone mass (osteoporosis/osteopenia)⁽²⁾.

Bowel disease is the second most common involvement in scleroderma, next to skin, and has a high variable severity. Fibrous infiltration of small bowel results in dilated and often atonic loops that lose their propulsive function. Bacterial overgrowth causes damage of mucous layer causing malabsorption and malnutrition⁽⁵⁾.

In our study we could not prove association of SSc and CD. Our results are in contrast with those from Rosato et al.⁽⁴⁾. Differences in genetic background may be one explanation for this finding. Although the prevalence of CD in our geographical region is the same as worldwide (0.3% to 0.5%)⁽²⁾, we do not have enough knowledge of the genetic background of scleroderma Brazilian patients. One more data to be taken into account is that our sample had a small proportion of generalized SSc form – that was the only form associated with CD in the previously cited study. Sample size may be another explanation for the discordant results. SSc is a quite rare disorder, affecting 286 per million population and CD, as already mentioned, is a very common one. In this context multicentric studies with larger samples may answer this question.

Concluding, in our sample of 105 Brazilian patients there is no detected association between scleroderma and IgA-EmA presence.

Nisihara R, Utiyama SR, Azevedo PM, Skare TL. Triagem para doença celíaca em pacientes com esclerodermia. *Arq Gastroenterol.* 2011;48(2):163-4.

RESUMO - Tanto a esclerodermia como a doença celíaca são doenças de autoimunidade que causam diarreia. Como o agrupamento de doenças autoimunes em único indivíduo não é raro, é importante saber se um indivíduo com esclerodermia tem maiores chances de ter ou não doença celíaca.

Para isso, estudaram-se 105 pacientes com esclerodermia e 97 controles saudáveis para o anticorpo EmA IgA. Não foi possível detectar presença aumentada de EmA IgA em pacientes com esclerodermia. Conclui-se que não existe necessidade de busca ativa de doença celíaca em pacientes com esclerodermia e diarreia, a menos que existam evidências clínicas claras da doença.

DESCRITORES - Doença celíaca. Escleroderma, sistêmico.

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