



Case report

Celiac disease in 3 patients with Takayasu's arteritis

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ABSTRACT

Takayasu's arteritis (TA) is a chronic vasculitis of unknown etiology. Celiac disease (CD) is an autoimmune disease caused by the ingestion of gluten. TA and CD have been associated with many other autoimmune conditions. However, only five cases with this association have been reported. In this series, three patients with TA and CD were included; all were female, 21, 30 and 54 years old. TA clinical manifestations preceded CD diagnosis in all patients. Aortic arch branches were affected in all of them. Serologic markers were positive and a small intestine biopsy showed typical findings of CD in the three patients. Special attention should be given to this possible association because these entities may be asymptomatic; the recognition of new disease variants modifies treatment, and sometimes CD constitutes a differential diagnosis of mesenteric ischemia.

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Enfermedad celíaca en 3 pacientes con arteritis de Takayasu

RESUMEN

La arteritis de Takayasu (AT) es una vasculitis de causa incierta. La enfermedad celíaca (EC) es una enfermedad autoinmunitaria provocada por la exposición al gluten. Ambas entidades se relacionan con distintas enfermedades autoinmunitarias, pero hasta la fecha sólo hay 5 casos descritos de asociación entre ellas. Se presentan tres casos clínicos con EC y AT. Los tres son mujeres de 21, 30 y 54 años. En todas ellas las manifestaciones de la AT precedieron a las de la EC y en todos los casos había compromiso de los vasos supraaórticos al diagnóstico. La EC fue diagnosticada por marcadores serológicos y biopsia duodenal en los tres casos. Reconocer esta asociación tiene importancia porque ambas entidades pueden cursar largo tiempo sin ser diagnosticadas, el diagnóstico de una nueva entidad modifica la terapéutica y la EC en un paciente con AT puede simular a la isquemia mesentérica.

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Palabras clave:

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Introduction

Takayasu's Arteritis (TA) is a vasculitis of unknown etiology which affects the aorta and its branches.¹ Celiac disease (CD) is an autoimmune disease caused by exposure to gluten.² There are only 5 cases currently described with the association of these diseases.³⁻⁷

The objective of these report is to describe the characteristics of three patients with both diagnoses.

Clinical observation

Case 1

A 21-year-old female patient was diagnosed with TA in 1995. She came to the clinic with joint pain and claudication of the upper left extremity, which had lasted for 4 months. Upon examination she had

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Table 1
General characteristics of the patients

	Age	Gender	Physical examination	DA
Case 1	21	Female	Diastolic murmur with maximum intensity in 2nd intercostal space, right parasternal line Absence of left radial pulse BP 130/0 mmHg	Stenosis of 50% of right primitive carotid artery and 95% of left primitive carotid artery and 99% of left subclavian artery
Case 2	30	Female	Absence of both radial pulses	Brachiocephalic trunk stenosis, both vertebral artery, primitive carotid artery and left subclavian
Case 3	54	Female	Diastolic murmur with maximum intensity in 2nd intercostal space, right parasternal line Reduction in amplitude of right radial pulse Bilateral carotid bruit	Stenosis of brachiocephalic trunk, right external carotid carotid, left subclavian and right subclavian artery

no left radial pulse and aortic insufficiency. A Digital Angiography (DA) showed findings typical of TA (Table). After no improvement with treatment based on prednisone, a left primitive carotid artery angioplasty was performed and was treated with aspirin and methotrexate, showing clinical improvement. In 2009 she presented diarrhea lasting 4 weeks and accompanied by abdominal pain. An abdominal magnetic resonance angiography showed no alterations; immunoglobulin A anti-endomysium antibodies were positive and a duodenal biopsy showed diffuse atrophy of the villi and a dense inflammatory infiltrate of the lamina propria. A gluten-free diet was indicated and clinical improvement ensued.

Case 2

A 30-year-old patient was diagnosed with TA in 1998 after presenting an ischemic stroke at age 19. In 2005 she presented weight loss, headache and claudication of the left upper extremity. Upon examination, no radial pulses were found. A DA was performed which found supra-aortic vessel stenosis (Table). Treatment with prednisone and aspirin was started. 6 months after the initial visit she presented diarrhea which had lasted for 5 months. An abdominal magnetic resonance angiography was performed and no vascular alterations were seen; anti-endomysial IgA was positive and duodenal biopsy revealed showed an inflammatory lesion with complete villous atrophy. She underwent treatment with gluten free diet and showed clinical improvement.

Case 3

A 54-year-old female patient, who had an ischemic stroke at age 26, was diagnosed with CD at age 46. She presented fatigue and headache in 2009. Upon examination she presented a diastolic aortic murmur, a reduction in right radial pulse and a systolic bruit on both carotid arteries. A DA showed changes typical of TA (Table). A biopsy of both temporal arteries was performed to rule out temporal artery arteritis, showing no alterations. Treatment with glucocorticoids, aspirin and methotrexate was installed with clinical improvement.

Discussion

The three cases presented were diagnosed with TA and CD. We have only found 5 published patients showing this association.³⁻⁷ Considering the elevated presence of CD in the population, the presence of concomitant TA may be casual; however, the coexistence of both autoimmune diseases leads to questions on whether both physiopathological processes could be related. CD is an immunologic disorder (mediated by T lymphocytes; TL) triggered by an environmental factor (gladin) in genetically susceptible individuals (human leucocytary antigen [HLA] DQ2 and/or DQ8). The destruction of the enterocytes and subsequent villous atrophy may be explained

by the activation of gladin reactive TL which generates a favorable cytokine milieu and collaborate in the generation of antibodies on the part of B-lymphocytes. In addition, gladin produces direct damage of the enterocyte through the liberation of interleukin 15, in which the presence of lymphocytes generate cell lysis through NKG2D/MIC-A interaction. It is important to mention that in the presence of tissue inflammation, transglutaminase liberation may occur; this enzyme generates glutamic acid from glutamine, increasing binding to gladin peptides to HLA-DQ2 and DQ8. Although it is known that gladin may activate these mechanisms, the underlying mechanisms are unknown.²

In TA, CD4, CD8 TL and *natural killer* cells compose the inflammatory infiltrate that originates in the vasa vasorum and later invades the media, adventitia and the arterial intima. Because the TL receptors involved present a limited antigen repertoire, it could be possible that a yet unidentified antigen could be responsible of unleashing the response.^{8,9} With respect to what has previously has been mentioned, both diseases are T CD4 mediated autoimmune diseases, in which the presence of a non specific antigen could unleash an abnormal immune reaction.⁴ In the case of CD, the causal antigen was identified as gladin, but in TA it remains unknown. Patients with CD show an increase of intestinal epithelium permeability due to great chronic inflammation; this situation favors the interaction between TL and antigens. Due to this, recognition of an exogenous antigen similar to a vascular tissue component in predisposed patients (due to a lack in immune tolerance mechanisms) could unleash an inappropriate immune response against blood vessels. However, with the data presented a casual relationship between these entities may not be established and even less if such physiopathological speculation is real.

Conclusions

The presentation of this series may result useful because, if this association were real, recognizing the presence of one or the other in patients with TA or CD would allow the reduction in diagnostic and modify the therapeutic approach.

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