Case report

Celiac disease in 3 patients with Takayasu's arteritis

Nicolás Di Benedetto, a, * Sebastián Andrés Muñoz, a Valeria Albertón, b María José Tumminello, c María Escasany, c Alberto Allievi a

a Servicio de Clínica Médica, Hospital General de Agudos Juan Antonio Fernández, Buenos Aires, Argentina
b Servicio de Anatomía Patológica, Hospital General de Agudos Juan Antonio Fernández, Buenos Aires, Argentina
c Servicio de Nutrición, Hospital General de Agudos Juan Antonio Fernández, Buenos Aires, Argentina

A B S T R A C T

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.

© 2010 Elsevier España, S.L. All rights reserved.

Introduction

Takayasu's Arteritis (TA) is a vasculitis of unknown etiology which affects the aorta and its branches. Celiac disease (CD) is an autoimmune disease caused by exposure to gluten. There are only 5 cases currently described with the association of these diseases. 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...
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 propia. A gluten-free diet was indicated and clinical improvement ensued.

Case 2

A 30-year-old female patient, who had 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. 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 propia. A gluten-free diet was indicated and clinical improvement ensued.

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). Treatment with prednisone and aspirin was started. 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.

Table 1

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

Discussion

The three cases presented were diagnosed with TA and CD. We have only found 5 published patients showing this association. 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 villious 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. 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. With respect to what has previously 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. 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 causal 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.

References