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CASE REPORTS

A CASE OF NON-CLASSICAL CELIAC DISEASE

UM CASO DE DOENÇA CELÍACA NÃO CLÁSSICA

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ABSTRACT

Celiac disease is an immune-mediated enteropathy caused by gluten exposure, occurring in genetically susceptible individuals. Although its typical presentation mainly includes gastrointestinal symptoms, non-classical forms are becoming increasingly frequent. In this report, a case of non-classical celiac disease in a seven-year-old child presenting with severe oligoarthralgia is described. With this report, the authors aim to increase awareness of celiac disease and the variability of its presentation as a way to enable a timely diagnosis and treatment, reduce the burden of disease, and improve health-related quality of life.

Keywords: celiac disease; gluten; non-classical celiac disease

RESUMO

A doença celíaca é uma enteropatia imunomediada desencadeada pela exposição ao glúten, que ocorre em indivíduos geneticamente suscetíveis. Manifesta-se sobretudo por sintomas gastrointestinais, mas são também cada vez mais frequentes as manifestações não clássicas. Os autores descrevem um caso de doença celíaca com apresentação não clássica numa criança de sete anos com manifestações predominantemente extra-intestinais, sob a forma de oligoartralgia. Com este caso, pretende relembrar-se o desafio que constitui o diagnóstico de doença celíaca com apresentação atípica. Pretende ainda realçar-se a importância do elevado índice de suspeição para um diagnóstico e instituição de terapêutica atempados e o seu impacto positivo inequívoco na resolução dos sintomas.

Palavras-chave: doença celíaca; doença celíaca não clássica; glúten

INTRODUCTION

Celiac disease (CD) is an immune-mediated enteropathy triggered by exposure to gluten in genetically susceptible individuals.[1] Genetic and environmental factors are implicated in the disease pathogenesis.[2] Diagnosis is confirmed by the presence of jejunal histological changes compatible with CD that regress in response to a gluten-free diet,1 which represents the only available treatment.[3]

CD affects 0.6–1% of the population worldwide.[1] In Europe, its estimated prevalence is 1:200 to 1:300 children. In the Portuguese population, one study from 2002 estimated CD's prevalence at 1:134 children.[4]

Due to its significant presentation variability, CD is believed to be an underdiagnosed pathology. The condition may present with gastrointestinal symptoms, extraintestinal symptoms, or rare to no symptoms. Gastrointestinal manifestations are the most common presentation form of the

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disease in children aged between 6 and 24 months.[2] In older children and adolescents, extra-intestinal symptoms (as short stature, pubertal delay, iron-deficiency anemia, tooth enamel changes, aphthous stomatitis, and arthralgias/arthritis) are considerably more common than gastrointestinal symptoms, particularly in cases of late disease presentation, often leading to delayed diagnosis.[2]

The authors describe the case of a child with non-classical CD presentation, reinforcing the importance of an increased awareness of the disease and its variable presentation towards a timely diagnosis and treatment, reduction of disease burden, and improvement of health-related quality of life.

CASE PRESENTATION

A seven-year-old girl was admitted to the Pediatric Emergency room of Hospital de São Bernardo due to a one-month history of oligoarthralgia, abdominal pain, and mild reduction in body weight (8%). Joint symptoms started as a persistent pain and swelling of both tibiotarsal joints, which spontaneously resolved, but progressive involvement of other joints in an additive pattern was observed, with subsequent involvement of the shoulders, knees, wrists, and hips.

Additionally, the child complained of occasionally soft stools without mucus or blood in the previous months. Previous history was otherwise negative, including for vomiting, diarrhea, or other prominent gastrointestinal symptoms, as well as skin or mucous membrane alterations.

The patient had no significant past medical history and family history was also irrelevant. She was exclusively breastfed until five months of age, at which time weaning started. Introduction of gluten in the diet occurred at six months of age, without complications. Weight and height progression were constant in the 85th percentile until six years of age, when weight dropped to the 50th percentile.

Physical examination at admission showed a good general condition and nutritional status, pink and moist mucous membranes, normal adipose tissue distribution, respiratory and heart rates within the normal range, normal lung and heart sound, and no abdominal pain, distension, enlarged organs, or masses. Painful palpation of the low paraspinous region and shoulders, knees, wrists, and hips was noted, as well as discrete tenderness and soft tissue swelling of the knees, but no other inflammatory signs.

Findings from initial laboratory workup were as follows: hemoglobin 11.3 g/dL with mean globular volume of 79.8 fL; sedimentation rate (39 mm/1h) and C-reactive protein (2.13 mg/dL) compatible with inflammatory syndrome; normal liver and renal functions, with no electrolyte imbalances. Serum albumin, protein, and immunoglobulin (including IgA) levels were within the normal range. Additionally, bacteriological and parasitological stool exams were negative.

Rheumatologic diseases were excluded based on history and laboratory tests, including screening for rheumatoid factor and antinuclear antibodies, which were negative.

To investigate a suspected autoimmune etiology, an initial antibody test was performed, which included screening for CD. The test revealed high anti-transglutaminase antibody levels (164 IU/ml, with total IgA of 211 mg/dL). A duodenal biopsy was performed, showing villous atrophy and transepithelial lymphocytic infiltrate compatible with celiac disease (Marsh 3C).

Diagnosis of CD was determined and a gluten-free diet was started, with symptomatology improvement and gradual weight gain. Additional laboratory investigations were performed to exclude for autoimmune diseases associated with gluten-sensitive enteropathy, such as type I diabetes and autoimmune thyroiditis. At present, anti-transglutaminase antibodies are negative and the child is asymptomatic.

DISCUSSION

With the advent of highly sensitive and specific screening tests, an increase in the prevalence of CD has been observed over the last few decades, allowing to identify patients with minimal or no symptoms.

Although until very recently breastfeeding and timing of gluten introduction were considered influential factors in the development of CD, this association is currently being revised in light of new evidence.[5-7] In fact, a position paper from The European Society for Paediatric Gastroenterology, Hepatology and Nutrition stated that the timing and manner of gluten exposure only affect the risk of inducing CD in persons carrying at least one CD risk allele, and recommends introduction of gluten any time between 4 and 12 completed months of age.[8]

The classical presentation of CD is characterized by symptoms of intestinal malabsorption shortly after the introduction of gluten in the diet.[9] However, older children and adolescents often have an atypical presentation and, although gastrointestinal symptoms may exist, oligosymptomatic forms – or those with mainly extra-intestinal manifestations – are the main presentation form. In the present case, the child's main – and most disabling – complaint was acute oligoarthralgia. During retrieval of medical history and characterization of clinical presentation, reference to less consistent stools and occasional abdominal pain was made, but as no impact on quality of life was felt, no medical care was sought.

Current guidelines recommend serologic testing for the diagnosis of CD, specifically the IgA anti-transglutaminase antibody assay, due to its high sensitivity and specificity.[10] This is preferred over anti-gliadin antibodies (which are less specific) and anti-endomysial antibodies.[10] Patients with positive IgA anti-transglutaminase antibodies should be submitted to an intestinal biopsy to establish the diagnosis of CD. Mucosal lesion in CD has a broad spectrum of severity, ranging from intraepithelial lymphocytic infiltration without villous changes (Marsh 1) to total villous atrophy (Marsh 3C). Severity of histological changes does not correlate with the intensity of symptoms, as exemplified by the present case of a patient with CD Marsh 3C and

no severe symptoms. No HLA testing was performed, as the positive serological tests and Marsh score left no diagnostic uncertainty.

A lifelong gluten-free diet is the only effective therapeutic measure for CD.[3] In this case, the patient was started on a gluten-free diet shortly after undergoing duodenal biopsy, with an optimal adhesion to date. Only two months later, a reduction of anti-transglutaminase antibodies to non-significant values and complete symptom resolution and weight recovery were observed. Consequently, the repetition of biopsy to demonstrate histological improvement was not required.[10]

As previously noted, recognition of CD remains challenging for pediatricians, mainly due to its various and sometimes non-classical forms of presentation, as evidenced in the presented case. It is recognized that persistent intestinal damage associates with higher complication rates in CD, reinforcing the importance of a timely diagnosis and treatment.[11]

A high index of suspicion and the awareness that some forms of CD have exclusively or predominantly extra-intestinal manifestations were essential for the correct diagnosis of this case. The prompt diagnosis and rapid introduction of a gluten-free diet enabled a rapid symptom resolution and will most certainly have a very positive impact in the child's future growth and development.

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