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JEJUNAL THICKENING IN SERONEGATIVE CELIAC DISEASE: CASE REPORT

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Abstract: Introduction: Celiac disease (CD) is an immune-mediated systemic disease induced by gluten ingestion in patients with a genetic predisposition, leading to nutrient-losing enteropathy. Given the high sensitivity of serological tests, only 1% of celiac patients are seronegative. Case Report: 14-year-old patient hospitalized in a critical condition of malnutrition for about 4 months with weight loss of 15 kilograms, associated with liquid diarrhea with mucus, nausea, vomiting, epigastralgia and feeling of gastric fullness. Evolved with dehydration, intense asthenia and anasarca. Clinical and laboratory investigation was carried out: severe hypoalbuminemia, anemia and stool coprology with mucus, undigested muscle fibers, neutral fats and excess fatty acids. Upper digestive endoscopy with duodenal biopsy showing histological grading of Marsh III villous atrophy and CT enterography with circumferential wall thickening of the proximal jejunal segment, hyper uptake of contrast in the wall and luminal reduction of the proximal jejunum. Serological tests for celiac disease (anti-transglutaminase and anti-endomysium) were negative. Due to the clinical picture associated with imaging and histopathological findings, a hypothesis of seronegative celiac disease was raised. A gluten-free diet was started with complete symptomatic improvement after therapy and reversal of malnutrition. She maintained clinical follow-up with the team for a period of 12 months, remaining asymptomatic with gluten restriction. Discussion: Seronegative celiac disease is uncommon (1%) and its diagnosis is challenging due to the high sensitivity of serological tests (greater than 95%), which are even used as a screening for the condition, indicating the performance of duodenal biopsy. It is not associated with a worse prognosis. The clinical association with radiological and histopathological findings favors the diagnosis even with negative serological tests.

Keywords: Celiac disease; jejunal thickening; seronegative; gluten; diarrhea.

INTRODUCTION

Celiac disease (CD) is an immune-mediated systemic disease induced by the ingestion of gluten in genetically predisposed patients (Ludvigsson, 2012). It is characterized by a nutrient-losing enteropathy that occurs after gluten ingestion (Sleisenger and Fordtran, 2014).

Celiac disease is the result of the association of genetic, immunological and environmental factors (Hill, 2005). The DQ-2 allele is present in more than 90% of celiac patients and the DQ-8 allele in approximately 10%, the main triggering factor being exposure to the gluten protein (Mäki, 2004).

The immune response occurs when gluten is absorbed by the small intestine mucosa and, in the presence of the HLA-DQ2 or DQ8 molecule, gliadin is deaminated by tissue transglutaminase with T cell activation, generating cytokines that damage enterocytes and lead to villous atrophy and infiltration of intraepithelial lymphocytes (IELs) (SLEISENGER, 2014).

The diagnosis is based on the clinical picture, serological tests (anti-gliadin antibody, anti-endomysium antibody and anti-transglutaminase antibody), small intestine biopsy and HLA-DQ2 and DQ8 tests (Carvalho, 2008).

The gluten-free diet is the only proven treatment for celiac disease (Marsh, 1992). Celiac patients have proven symptomatic, serological, and histopathological remission after initiation of a gluten-free diet (Nachman, 2011).

CASE REPORT

HCWC, female, 14 years old, student, born and resident of Cuiabá, previously healthy, started with epigastralgia and postprandial gastric fullness, sought emergency service in May/2018 in her municipality, being treated with symptoms and being discharged soon after.

During the following 3 months, the patient evolved with progressive weight loss, around 15 kg, associated with liquid diarrhea, on average of 8 episodes a day, with the presence of fat and food residues, and nausea and vomiting. On this occasion, the patient was hospitalized in her municipality due to dehydration, and was referred to the ICU. After clinical stabilization, she was discharged from the ICU and transferred to the Hospital de Base de São José do Rio Preto/SP to be evaluated by the Liver Transplant team.

Admitted with worsening symptoms of diarrhea, nausea and vomiting, abdominal pain in the right hypochondrium region, intense asthenia and edema, in regular general condition, anasarcada, pale 2+/4+ and dehydrated 2+/4+. She also had periorbital edema, reduced muscle strength 3 + / 5 +, lower limb edema 4 + / 4 +, upper limb edema 4 + / 4 +, abdomen with wall edema and diffuse pain on palpation. In laboratory tests on admission, Hb: 7.6, Ht: 23.8, Albumin: 1.19, Creatinine: 0.3, Sodium: 137, Potassium: 3.4, Urea: 21, TGO: 33, TGP: 27, GT gamma: 299 and alkaline phosphatase: 168.

Complementary tests were performed to investigate the condition. Serum ceruloplasmin and copper, hemoglobin electrophoresis, direct coombs test, and anti-nuclear factor (ANA) with negative results. The functional coprological examination showed a normal search for reducing substances, leukocytes absent, fats absent, mucus 2+/3+, erythrocytes absent, undigested muscle fiber 2+/3+, negative parasitology.

I requested anti-transglutaminase IgA and anti-endomysium IgA serological tests, which were also negative.

The abdominal ultrasound showed a liver with normal dimensions and contours, with solid echotexture, and diffuse increase in the echogenicity of its parenchyma, a small amount of free fluid in the abdominal cavity. Upper digestive endoscopy with increased vascular network of the distal esophagus, gastric-bilious reflux, half-open pylorus, preserved duodenum; duodenal biopsy was performed. The histopathological examination of the biopsy of the second duodenal portion showed moderate chronic duodenitis, with atrophy and flattening of the villi, Marsh stage III, moderate lymphocytic infiltrate in the lamina propria, increased glandular mitotic activity, areas of loss of the striated border of glandular cells and moderate lymphocytic aggression to the superficial mucosal epithelium (about 30 lymphocytes/100 enterocytes), as shown in figures 1, 2 and 3.

Due to the findings described, a hypothesis of celiac disease was raised and a gluten-free diet was started, but the patient progressed with worsening of the general condition, maintaining diarrhea, with steatorrhea and food residues, without the presence of blood, and severe hypoalbuminemia (2.15), with sluggishness, difficulty of ambulation and additional weight loss of 6 kg in the period.

Parenteral diet was then started and an enterotomography was requested: jejunal-proximal segment with circumferential wall thickening, increased contrast uptake, reduced lumen, distensibility, accompanied by lymphadenopathy, altered follow-up measures approximately 15 cm and lymphadenopathy in the mesenteric root, as per figure 4 and 5.

A gluten-free diet was maintained. The patient evolved with progressive

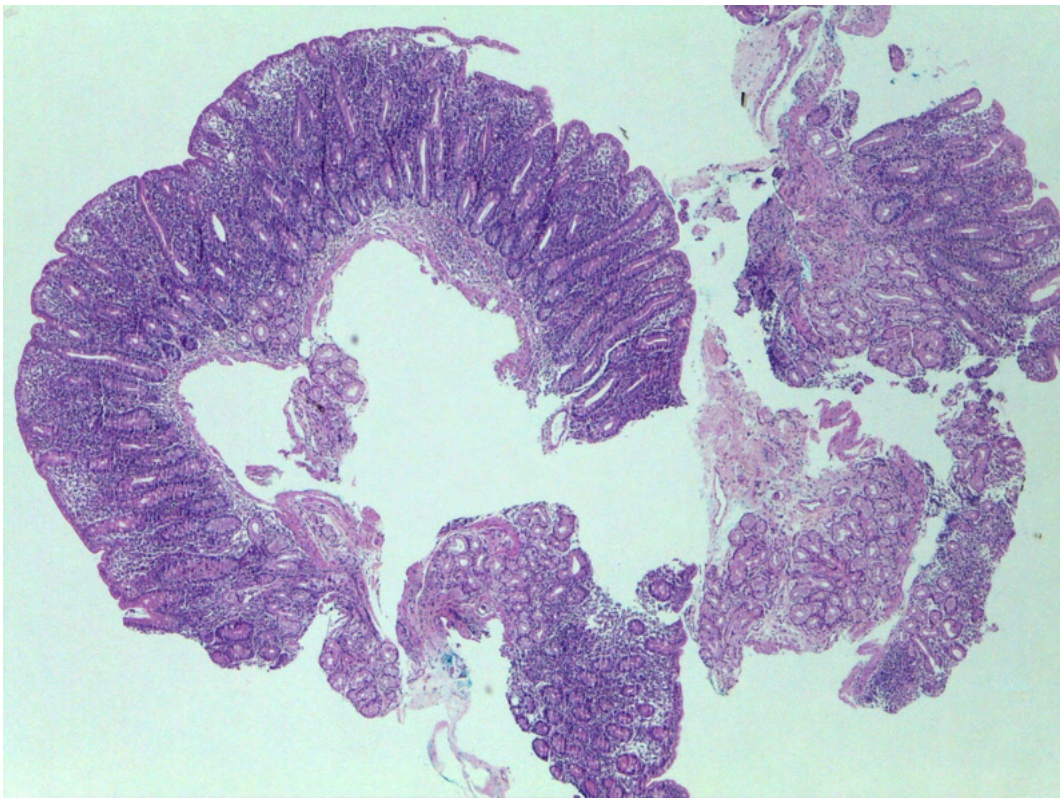

Figure 1 - Histological section of the 2nd duodenal portion stained with hematoxylin and eosin.

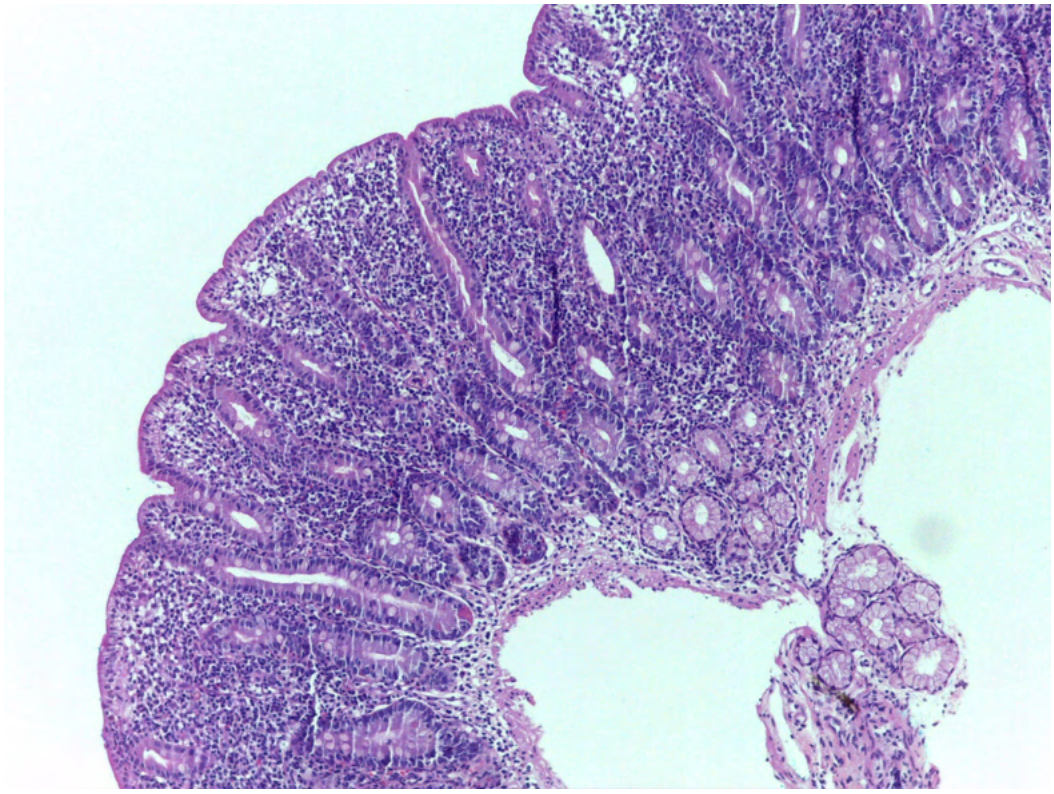

Figure 2 - Histological section of biopsy of the 2nd duodenal portion stained with hematoxycillin and eosin demonstrating Marsh III villous atrophy.

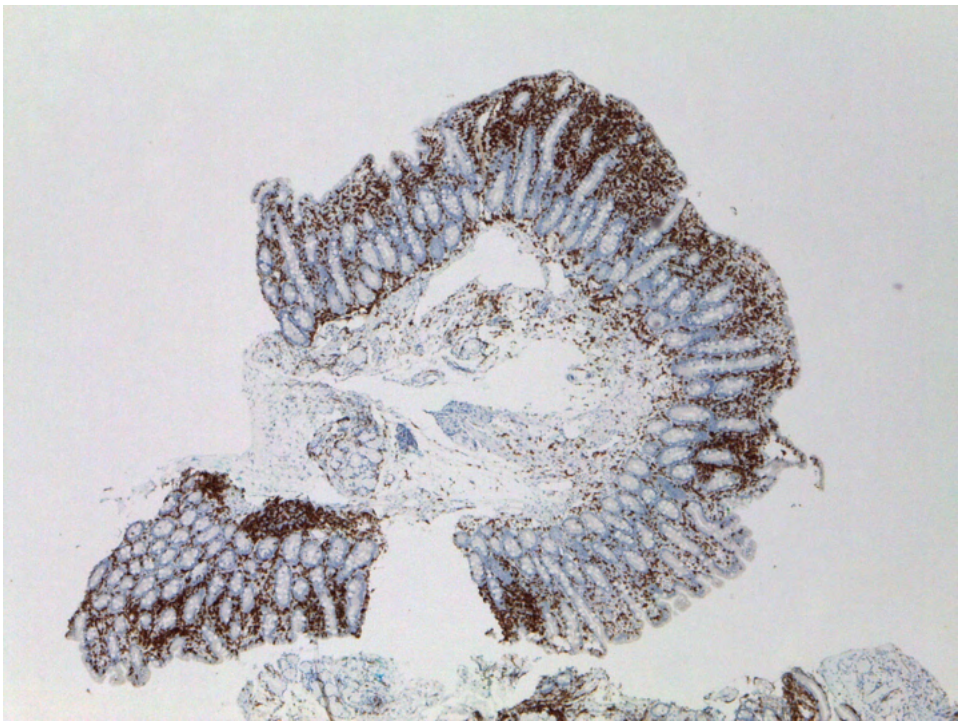

Figure 3 - Histological section of biopsy of the 2nd duodenal portion stained with argentic impregnation.

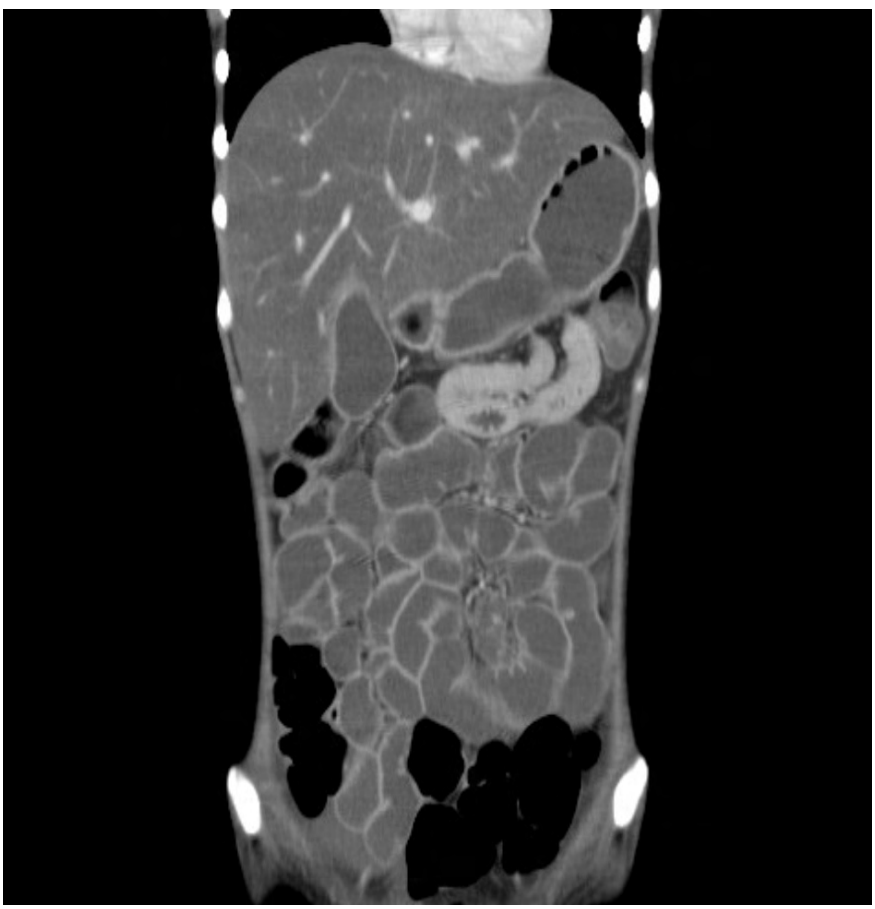

Figure 4 - Coronal tomography image of the total abdomen in venous phase contrast.

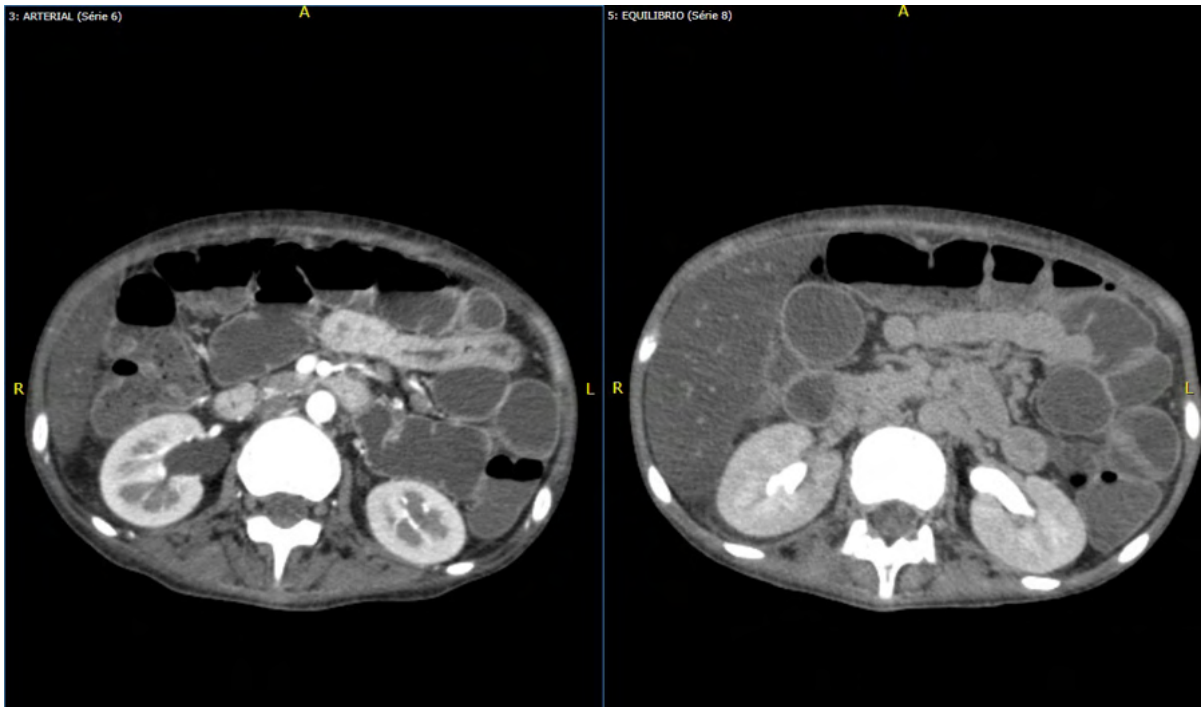

Figure 5 - Image A: Cross-sectional tomography of the abdomen with contrast in arterial phase; Image B: same exam in late phase.

improvement of the clinical picture after 15 days of hospitalization, accepting an oral diet, weight gain and maintaining a daily evacuation of pasty consistency, without blood or mucus, without other complaints and improvement in muscle strength. The patient maintained the dietary guidelines and there was complete remission of the clinical picture, laboratory and radiological changes in a regular outpatient follow-up with the team during the initial 12 months. After the period, she continued to follow up in the city of origin.

DISCUSSION

Celiac disease (CD) is a chronic form of enteropathy, resulting from the interaction of environmental, genetic factors (presence of HHLA DQ2/DQ8) and an abnormal adaptive immune response against gluten-containing foods, leading to compromise of the intestinal mucosal surface and, consequently, abnormal absorption of nutrients (Carvalho, Green, Ludvigsson).

The prevalence of CD affects from 1:100 to 1:300 individuals in the world (Bai) and in Brazil, an incidence of 1:681 in Brasília, 1:273 in Ribeirão Preto, 1:417 in Curitiba, and 1:214 in Sao Paulo (Gandolfi).

For the definitive diagnosis of CD, UDE with biopsy is essential. Findings include: infiltrates, patterns of hyperplasia and atrophy. The Marsh classification is used for histological characterization, with Marsh II-III being compatible with CD (Ludvigsson, 2014).

Serological tests for CD are important to select patients who must undergo biopsy and to confirm the diagnosis, the main tests being antigliadin antibody, antiendomysium antibody and antitransglutaminase antibody (Bai, 2013).

The choice of IgA anti-transglutamine antibody assay as screening is due to its high sensitivity (95%), specificity (95%) and low cost (Bai, 2013). Among the imaging findings, we can find small bowel wall thickening in any segment, as a consequence of lymphocytic inflammatory activity. Observed in the early stages in the jejunum progressing later to the ileum (Francis, 2011).

Due to the high sensitivity of serological tests, a minority of patients with celiac disease are seronegative, with a prevalence of approximately 1.03% (Giorgio, 2015). Patients with a clinical picture compatible with seronegative celiac disease and normal levels of IgA can undergo duodenal biopsy for histological investigation (Kotze, 2021).

The only treatment available to date for CD is a gluten-free diet (wheat, barley and rye). Such deletion must be permanent and final. In most patients, gluten-freedom is sufficient to improve symptoms and prevent complications from CD (Hill, 2005).

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