Association between celiac disease and Crohn’s disease – a challenge to the coloproctologist

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INTRODUCTION

The celiac disease (CD) is characterized as an autoimmune disease caused by the permanent gluten intolerance in genetically susceptible individuals1. In the past few years, its clinical and ethiopathogenic features have been cleared. Nowadays, it is known that in order for it to occur the association of three factors is determinant: genetic changes, exposure to gluten and altered immune response3.

Histocompatibility antigens class II, HLA-DQ2 and HLA-DQ8 present changes in celiac patients3,5. When these subjects are exposed to gluten, their immune response is exaggerated, with increase in intraepithelial T lymphocytes – in the proximal intestine mucosa – and inflammatory cytokines, leading to the villous atrophy and poor absorption of nutrients6. Excluding gluten from the diet usually leads to the regression of morphological changes in the proximal intestine7. Such changes result in the

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clinical variants of the disease and its intensity, so the onset of early symptoms can occur during childhood or adulthood. Thus, CD fits the differential diagnosis of other pathologies that present pain and abdominal distension, vomit, iron deficiency and malnutrition.

In adult subjects, the diagnosis of CD should include detailed anamnesis, serological and histopathological studies. However, in this age group the disease can be subclinical, and diagnosis can be late – sometimes, after surgical approaches, since it seems like a picture of acute abdomen, or after other therapies that provided no benefits to the patient. The immunological characteristics of CD establish a relation with other autoimmune conditions, such as dermatitis herpetiformis, thyroid diseases, Addison’s disease, autoimmune thrombocytopenia, sarcoidosis, IgA nephropathy and selective IgA deficiency. Approximately 2 to 4% of the insulin dependent patients with diabetes mellitus present with CD.

The relation with other autoimmune diseases led to studies on the association between CD and inflammatory bowel diseases (IBD) in the past few years (proctocolitis and Crohn’s disease). Crohn’s disease is more common in the terminal ileum. It presents segmental lesions in the digestive tract, affecting all the layers of the organ wall and possibly leading to stenosis or fistula. Proctocolitis is the IBD more commonly associated with these diseases, such as sclerosing cholangitis, and other vasculitis. Anemia and malnutrition are systemic repercussions that are present in most patients with the disease. The iron-deficiency anemia, which is refractory in patients with IBD, should lead to the suspicion of associated CD.

Many clinical studies and case reports have been described in the past few years to relate CD and IBD. The prevalence of IBD in CD has been described as five to ten times higher in the general population. Shah et al. described a risk of proctocolitis five times higher in first-degree relatives of patients with CD. Likewise, Cottone et al. described the high incidence of proctocolitis in 600 first-degree relatives of patients with CD.

Between January 2002 and December 2004, the Italian Group of Inflammatory Bowel Diseases performed a multicentric study aiming to establish the prevalence of IBD among celiac patients. Out of the 1,711 patients, 9 (0.5%) serological and histological results that were compatible with the CD diagnosis – 6 patients presented with proctocolitis and three with Crohn’s disease, lower prevalence in comparison to the general population.

In 2007, during 1 year period, Masachs et al. followed-up three groups of celiac patients, their first-degree relatives and a control group, in order to identify the prevalence of IBD in celiac patients and their relatives. Three cases of Crohn’s disease were reported in 86 celiac patients; four cases of Crohn’s disease in first-degree relatives; and one case in the control group (809 people); no case of proctocolitis was reported, which led to the conclusion that celiac patients and their first-degree relatives have higher chances of having Crohn’s disease if compared to the general population.

Lopez-Vasquez et al. identified mutations in the A MICA gene (major histocompatibility complex class I chain related gene A) expressed in the gastrointestinal epithelium of patients with IBD. Changes in the MYOIXB gene, responsible for the production of myosins and for the intestinal epithelial integrity, are found in celiac patients and these mutations can also be found in 40% of the patients with IBD.

The presence of binding regions shared by these diseases, such as 5q31-33 (IBD5 and CELIAC2) and 19p13 (IBD6 and CELIAC4) has supported this idea. Recently, the description of polymorphisms in the genes IL2, region IL21, in 4q27 and in the gene IL18RAP, in 2q12, reinforces the evidence of association between CD and IBD. Besides, the well established relation between Crohn’s disease and the gene IL23R has been associated to CD in the Finn and Spanish population. Based on these findings, Dena et al. studied the genes NKX2-3, IRGM and ATG16L1, whose changes are clearly defined in the IBDs, in patients with CD and first-degree relatives; however, no evidence has been established among celiac patients.

In the service of Hospital das Clínicas de Ribeirão Preto (HCRP) at Universidade de São Paulo, we had a case of association between CD and Crohn’s disease. The patient was 37 years old at the time, and in the first appointment she presented with history of...
pain and abdominal distension, vomit, weight loss (10 kg in 3 months) and refractory anemia to treatments prescribed in other medical services.

There had been an intestinal subocclusion (referred to enterectomy), however, there were no reports concerning the removed piece. She had the report of an upper digestive endoscopy (UDE) with a duodenal biopsy compatible with CD. However, up until then she had not been advised to rule out gluten from her diet. We repeated the UDE with new biopsies of the second part of the duodenum, and the CD diagnosis was confirmed. Admitted to our nursery for clinical and nutritional rehabilitation, her picture of intestinal occlusion got worse, and traffic demonstrated areas of stenosis and dilatation of the small intestine (Figure 1). After being submitted to exploratory laparotomy, segments of the jejunum and ileum were shown with stenosis and dilatation (Figure 2). The exploration of the surgical piece demonstrated an inflammatory infiltrate in the mesentery, intestinal wall thickening with ulcers and fibrin deposition (Figures 3 and 4). The surgical piece was analyzed twice at the Department of Pathological Anatomy at HCRP and the diagnosis of Crohn’s disease was confirmed. At the postoperative, we initiated nutritional guidance and suspended gluten from the diet. Thirty days after the surgery, we started treating the patient for Crohn’s disease. An immunomodulator was prescribed and, nowadays, the patient had significant clinical improvement, without new intercurrences.
CONCLUSION

In the past few years, with the advances in diagnostic methods and molecular evaluations, the analysis between diseases whose ethiopathogens involve genetic changes and autoimmune mechanisms has improved. Thus, we can cite the studies that tried to relate CD and IBDs. It is important to remember that similarities are not restricted to genetics and immunology, because their similar clinical pictures can lead to diagnostic mistakes and incorrect treatments. The association of both pathologies in the same patient should be brought up in cases of severe malnutrition and refractory anemia to treatment. However, even though most clinical studies demonstrate this association, we are still waiting for the description of the real genetic link between these pathologies.

REFERENCES

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