

Celiac disease and upper tract Crohn's disease – A rare association

Doença celíaca e doença de Crohn do tubo digestivo superior – Uma rara associação

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Abstract | The authors present the case of a 47 years old female, with no past or familial history, hospitalized due to vomiting and significant weight loss over the last 9 months, without abdominal pain, blood loss, constipation or diarrhoea. Blood tests results revealed iron deficiency anaemia, seropositivity for ASCA, anti-transglutaminase antibody and HLA-DQ2.

Upper GI endoscopy showed several ulcers in duodenal mucosa and an ulcerated stricture in D3; biopsies were taken and histopathology revealed transmural inflammatory chronic infiltrate, crypt loss and some areas of villous atrophy and intraepithelial lymphocytosis. The small bowel follow through confirmed 2 main strictures in duodenum and proximal jejunum. She was started on prednisolone, azathioprine and a gluten-free diet with an initial good response although relapse was detected one month later. In this last admission, parenteral nutrition was necessary due to her deteriorated nutritional state and she also started infliximab, with subsequent significant clinical and endoscopic improvement. *GE-J Port-Gastroenterol 2012;19:33-35.*

KEY-WORDS: Crohn's disease, celiac disease, association, small bowel stricture, infliximab

RESUMO | Os autores apresentam o caso clínico de uma mulher de 47 anos, sem antecedentes pessoais ou familiares, internada por vômitos e emagrecimento significativo nos últimos 9 meses; sem dor abdominal, perdas hemáticas, obstipação ou diarreia. Laboratorialmente, de destacar anemia ferropénica, seropositividade para ASCA, anticorpo anti-transglutaminase e para HLA-DQ2.

A endoscopia digestiva alta mostrou várias úlceras na mucosa duodenal e estenose ulcerada em D3, cuja histologia revelou infiltrado inflamatório crónico transmural, atrofia de criptas e áreas com atrofia vilositária e linfocitose intra-epitelial.

O estudo baritado do intestino delgado confirmou a presença de 2 estenoses no duodeno e jejuno proximal. A doente foi medicada com prednisolona, azatioprina e dieta sem glúten, inicialmente com boa resposta, mas com recidiva após

1 mês. Foi readmitida, com necessidade de alimentação parentérica devido ao mau estado nutricional. Começou infliximab, com melhora clínica e endoscópica subsequente. *GE-J Port-Gastroenterol 2012;19:33-35.*

PALAVRAS-CHAVE: Doença celíaca, doença de Crohn, associação, estenose do intestino delgado, infliximab

INTRODUCTION

Both Crohn's and Celiac diseases are chronic and immune diseases of the small bowel that share some features.

Celiac disease is a small bowel disorder with mucosal inflammation, crypt hyperplasia and villous atrophy, induced by gluten ingestion in genetically predisposed individuals. Crohn's disease is a chronic inflammatory immunomediated disease potentially affecting the entire digestive system but with predilection sites in the terminal ileum and colon^{1,2}.

Some authors suggest that they may be related to each other, although there are only a few reports in literature concerning their simultaneous occurrence in the same patient^{1,2}.

CASE REPORT

A 47 years old caucasian woman, without personal or familial priors, was admitted in our department due to nausea, vomiting and weight loss of 35% in the last 9 months. She had no abdominal pain or blood loss and her bowel habits remained regular, without constipation or diarrhea. The physical examination only showed a thin woman, weighting 35 Kg, body mass index of 15, with digital hypocratism.

The initial blood samples revealed: iron deficiency anaemia (haemoglobin:10g/dL; mean corpuscular volume:73fl; iron:27 µg/dL; transferrin: 192 µg/dL; ferritin:50 ng/dL), sedimentation rate: 55mm; C reactive protein: 11.6 mg/dL; albumin: 2.1 mg/dL. Cultures from blood and faeces, Human Immunodeficiency Virus, immunoglobulin profile and Mantoux test were either negative or normal.

An upper endoscopy was performed showing gastric stasis, hyperemia and multiple aftoid ulcers in the duodenum and a stricture in D3 with ulcerated mucosa (Figures 1, 2 and 3). The biopsies of the aftoid ulcers and ulcerated stricture

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revealed crypt loss and transmural chronic inflammatory infiltrate without granulomas. In areas of normal mucosa, some villous atrophy and intra-epithelial lymphocytosis were observed (Figure 4). Cytomegalovirus was excluded by immunohistochemistry techniques.

She started ciprofloxacin and metronidazol to rule out bacterial proliferation that was stopped later on.

A normal ileocolonoscopy with normal biopsies was also performed as well as a small bowel follow through. In this last exam two main strictures with irregular mucosa were observed, one in the duodenum and the other in the proximal jejunum.

Abdominal ultrasound and computed tomography showed small mesenteric lymphadenopathies and densification of adipose tissue and mesentery.

This time, new blood samples revealed positive serology for celiac disease (anti tissue transglutaminase IgG and IgA) and positive anti *Saccharomyces cerevisiae* (ASCA). The HLA-DQ2 was also positive.

We assumed that the patient had Crohn's disease (the aftoid ulcers were typical, there was a stricture and densification of adipose tissue in CT scan and a positive ASCA) and also a celiac disease (positive and specific serology and intraepithelial lymphocytosis). Lymphoproliferative disease was excluded by repeated negative histology and also by a normal immunohistochemistry profile of the mucosal lymphocytes without any clonal proliferation.

She was put on a gluten free diet, prednisolone 40 mg/daily (with progressive tapering after two weeks) and azathioprine (2,5 mg/kg/d) due to the severity of her symptoms. She was discharged with clinical improvement. About one month later she was readmitted with the same complaints, after intake of diclofenac for back pain and poor adherence to a gluten-free diet.

Infectious complications, such as intraabdominal abscess, were ruled out. An enteroscopy revealed the same lesions, persisting aftoid ulcers and D3 stricture. Due to her deteriorated nutritional state, both enteral (gluten-free) and parenteral nutrition were undertaken for almost 3 weeks, with a good clinical response. By this time, 10 weeks after the beginning of azathioprine, another enteroscopy was performed showing a duodenal mucosa in healing process with a significant improvement of the stricture with no need

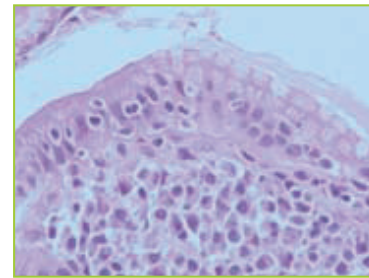


Figure 4 In the areas of normal mucosa the histology revealed villous atrophy and intra-epithelial lymphocytosis.

for endoscopic dilation. A small bowel follow through was repeated revealing the persistence of the two main strictures. We decided to maintain azathioprine and start infliximab (0, 2 and 6 weeks and then maintenance q8 weeks). The patient remained symptom free and gained 8 Kg in a 6 months' period.

DISCUSSION

We presented the clinical case of a patient with Crohn's and celiac disease.

Both are genetically predisposed diseases that share a similar immune-mediated Th1 inflammatory cascade in response to loss of tolerance to external antigens (gluten for celiac disease and intestinal flora to Crohn's disease)^{1,2}.

This may be responsible for the concomitant occurrence of both diseases. In several studies the association with ulcerative colitis is almost absent, probably because the last one has a Th2 pattern¹, although some studies related exactly the contrary³.

Celiac patients and their relatives have a greater predisposition to Crohn's disease compared to the control population^{1,2,4}, with equal predisposition to other autoimmune diseases such as insulin-dependent diabetes mellitus or thyroiditis². In contrast, the prevalence of celiac disease among inflammatory bowel disease (IBD) patients was comparable with general population⁵.

Moreover, the auto antibody profile of both diseases may be crossed. Anti-tissue transglutaminase antibody has high sensitivity and specificity for celiac disease⁶. Despite the high specificity of ASCA for Crohn's disease, they can also be positive in some patients with celiac disease⁷.



Figure 1 Multiple aftoid ulcers in the duodenum



Figures 2 and 3 Multiple aftoid ulcers in the duodenum and a stricture in D3 with ulcerated mucosa.



In spite of these explanations and the relatively high prevalence of both diseases, there are only a few reports describing the association between Crohn's and celiac disease^{1,2,8,9,10}.

In the majority of the published cases, Celiac disease preceded the diagnosis of Crohn's disease^{2,8,9}. Furthermore, most patients had symptomatic Celiac disease² and colonic or terminal ileum Crohn's disease². We think that our patient fits the rare profile of a latent celiac with an active upper tract Crohn's disease with stricturing behaviour (A3, B2, L4 according to Montreal's classification).

The use of azathioprine and infliximab is recommended in both diseases when they are too severe or refractory¹¹. Despite the latent celiac disease pattern, we are convinced that it's reasonable to continue a gluten-free diet, even lifelong, to prevent relapses.

CONCLUSION

The occurrence of celiac disease and upper Crohn's disease in the same patient is an extremely rare association, although they share some features as previously described. By having both conditions affecting the duodenum and proximal jejunum, the nutritional status of this patient was severely compromised, demanding a challenging treatment strategy, with step-up drug therapy. Because this was successful, we prevented more aggressive therapy, such as endoscopic dilation or surgery.

REFERENCES

- Masachs M, Casellas F, Malagelada R. Inflammatory bowel disease in celiac patients. *Rev Esp Enferm Dig* 2007;99:446-450.
- Schedel J, Rockmann F, Bongartz T, *et al.* Association of crohn's disease and latent celiac disease: a case report and review of the literature. *Int J Colorectal Dis* 2005;20:376-380.
- Cottone M, Marrone C, Casà A, *et al.* Familiar occurrence of inflammatory bowel disease in celiac disease. *Inflamm Bowel Dis* 2003;9:321-323.
- Yang A, Chen Y, Scherl E, *et al.* Inflammatory bowel disease in patients with celiac disease. *Inflamm Bowel Dis* 2005; 11:528-532.
- Leeds J, Horoldt B, Sidhu R, *et al.* Is there an association between celiac disease and inflammatory bowel diseases? A study of relative prevalence in comparison with population controls. *Scand J Gastroenterol* 2007;42:1214-1220.
- Di Tola M, Sabbatella L, Anania MC, *et al.* Anti-tissue transglutaminase antibodies in inflammatory bowel disease : new evidence. *Clin Chem Lab Med* 2004;42:1092-1097.
- Barta Z, Csípő I, Szabó GG, *et al.* Seroreactivity against *saccharomyces cerevisiae* in patients with crohn's disease and celiac disease. *World J Gastroenterol* 2003;9:2308-2312.
- Kitis G, Holmes GK, Cooper BT, *et al.* Association of celiac disease and inflammatory bowel disease. *Gut* 1980;21:636-641.
- Curtis WD, Schuman BM, Griffin JW. Association of gluten-sensitive enteropathy and crohn's colitis. *Am J Gastroenterol* 1992;87:1634-1637.
- Karoui S, Boubaker J, Hamzaoui S, *et al.* Association of asymptomatic celiac disease and crohn's disease [article in french]. *Ann Med Interne (Paris)* 2000;151:411-412.
- Gillett H, Arnott ID, McIntyre M, *et al.* Successful infliximab treatment for steroid-refractory celiac disease: a case report. *Gastroenterology* 2002;122:800-805.