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Letters to the Editor

Collagenous sprue with associated features of refractory celiac disease

Key words: Celiac disease. Histology. Refractory sprue. T lymphocytes.

Dear Editor,

Collagenous sprue is a rare entity, and slightly more than 60 sporadic cases have been reported worldwide since it first description (1). Its relationship with classic celiac disease and other sprue-like intestinal disorders remains to date controversial (1).

Although we have a specific interest in the field of celiac disease and although we see more than 200 cases/year, collagenous sprue has been only diagnosed recently in one case, here described.

Case report

A 75 years old man was admitted to our Hospital due diarrhea, rapid onset weight loss (about 5 kg in 40 days), fatigue and malaise. The patient had no history of previous gastrointestinal disorders, alcohol abuse, and travels in tropical/subtropical areas. His past medical history was remarkable for chronic ischemic heart disease, and he was in therapy with ASA and ACE inhibitors. Physical examination revealed modest dehydration, peripheral edema, and a fissured tongue. Blood chemistry showed microcytic anemia, low serum levels of iron, calcium, magnesium, and cholesterol, hypoprotidemia with hypoalbuminemia, and abnormal coagulation. Microbiological tests (including CMV, EBV, HIV, and the search for parasites and *Clostridium difficile* in stool) were repeatedly negative. The dosage of anti- IgA transglutaminases were weakly positive (EU 12/mL) compared with low levels of total IgA (98 mg/dL). HLA haplotype showed the presence of HLA-DQ2.

The patient underwent upper panendoscopy with multiple duodenal biopsies. Histological examination revealed total villous atrophy. Enteroscopy and capsule endoscopy demonstrated non-ulcerative lesions of the small intestine and a colonoscopy showed diverticulosis of the sigmoid colon. The patient was discharged with a diagnosis of celiac disease and started a gluten free diet.

After an initial period of well-being the patient had a relapse of diarrhea, accompanied by peripheral edema and fever. Due to the suspicion of a lymphoproliferative disease a CT scan was performed, that showed no thickening of the wall of the small intestine and lymph nodes enlargement distributed below the root of the mesentery and right iliac area. An upper endoscopy with multiple biopsies in the duodenum was repeated, that confirmed the histological diagnosis of villous atrophy. The patient's conditions worsened, with profuse watery diarrhea, weight loss and peripheral edema, as well as vomiting and nausea, and total parenteral nutrition was started. *S. aureus* sepsis developed, and it was treated with intensive antibiotic therapy. Due to the suspicion of refractory sprue, the histological slides were reviewed by another pathologist. Severe villous atrophy (Marsh-Oberhuber grade 3C, Corazza-Villanacci classification grade B2) (2) with evident subepithelial collagen deposition was present, whereas immunohistochemistry revealed an increased number of intraepithelial lymphocytes, CD3 positive and CD8 negative, an immunophenotype of refractory sprue (3) (Fig. 1). TCRβ monoclonal rearrangement disclosed no significative abnormalities.

The patient was treated with strict gluten free diet, prednisone 1 mg/kg body weight for 4 weeks and then slowly tapered with rapid clinical response and improvement of nutritional parameters. Presently, he enjoys good health.

Discussion

We describe a case of refractory celiac disease type I associated to collagenous sprue.

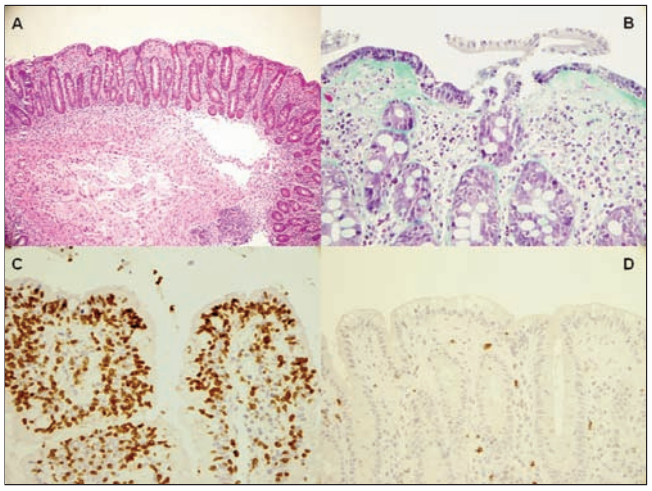

Fig. 1. Severe atrophy of villi and evident sub-epithelial collagen deposition. A. H&E. B. Trichrome stain. Original magnification x20. C. Positivity for CD3 and D. Negativity for CD8. Original magnification x40.

This entity is very rare and our experience, even though ours is a referral center for celiac disease, is limited to the present report. Some points are however worth discussing.

Firstly, collagenous sprue, as well as refractory CD, is typical of elderly patient, and must be always suspected when the patients, notwithstanding a strict adherence to a gluten-free diet, are not responsive or worsen. Of course, in such instances the presence of lymphoproliferative disorders (4), a well know complication of refractory celiac disease, must be accurately excluded.

Secondly, immunohistochemical typing for CD3 and CD8 intraepithelial lymphocytes is important in celiac disease, and may help in establish prognosis for refractory cases (5). Although widely investigated, monoclonal rearrangement may be of some utility in patients with refractory disease, but its real value still remain to be established (6).

However, a better definition of refractory and collagenous sprue is desirable, since these entities are generally thought to have a poor prognosis, with severe morbidity and mortality. Indeed, there is recent evidence that these patients may be successfully treated (7), and the vast majority of patients with collagenous sprue (that sometimes display associated celiac disease) may have relatively good clinical outcomes (8).

In conclusion, we report a case of collagenous sprue with associated celiac disease from Italy, and want to stress the diagnostic difficulties often encountered in this setting. However, a high grade of suspicion, coupled to clinical-pathological investigation, often is the clue factor in individuating, diagnosing, and treating these patients.

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