

Title:

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Duodenal villous atrophy with a negative serology induced by mycophenolate mofetil: not everything is celiac disease

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Dear Editor,

We present the case of a 35-year-old kidney transplant patient under chronic therapy with mycophenolate mofetil (MMF) and diagnostic workup due to chronic diarrhea with associated malnutrition. Viral and enterobacteria serology studies, pancreas function tests, parasite examination, bacteria stool culture, *C. difficile* test, abdomen/pelvis computed tomography (CT) scan and colonoscopy were performed without abnormal findings. A gastrointestinal endoscopy showed a marked villous atrophy (VA) in the second duodenal portion, which was confirmed by the pathology report (MARSH IIIc). There was no evidence of microorganisms or cytomegalovirus infection. A PET-CT was performed in order to rule out lymphoproliferative syndrome. MMF was discontinued, due to negative serological tests (anti-endomysial antibody, anti-tissue transglutaminase antibody and normal IgA) for celiac disease and the persistent gastrointestinal symptoms. A clinical improvement with a decrease in the number of bowel movements and proper food tolerance was observed after MMF was discontinued.

Discussion

Celiac disease is the main cause of VA. However, VA with negative celiac serology is uncommon, assuming a therapeutic challenge, and is mainly induced by drugs (1).

Antibodies used for the diagnosis of celiac disease, despite their high sensitivity and specificity, may lead to false negative results such as lymphoproliferative syndromes. Thus, it is necessary to rule out these syndromes and a complete genetic study is recommended.

MFM is an immunosuppressive agent that is used in transplant patients. The main adverse effects associated with the administration of MFM include diarrhea, leucopenia and vomiting, as well as a higher frequency of infection, predominantly due to cytomegalovirus (2). The adverse effects induced by MFM in the colon are well known. However, there are few studies that describe the isolated involvement of the small intestine, which may include inflammation of the mucosa, erosions and ulcerations. Villous atrophy induced by MFM is a very infrequent adverse effect, which is barely reported in the literature and manifests as chronic diarrhea and malabsorption. The mechanism of mucosal damage is not clear; a direct toxicity effect and an impaired immunological environment have been proposed (3). It is important to rule out an infectious etiology or graft *versus* host disease (GVHD) in these patients. Treatment involves suppression or dose reduction of the immunosuppressive agent, although the villous atrophy may remain for a long time (4).

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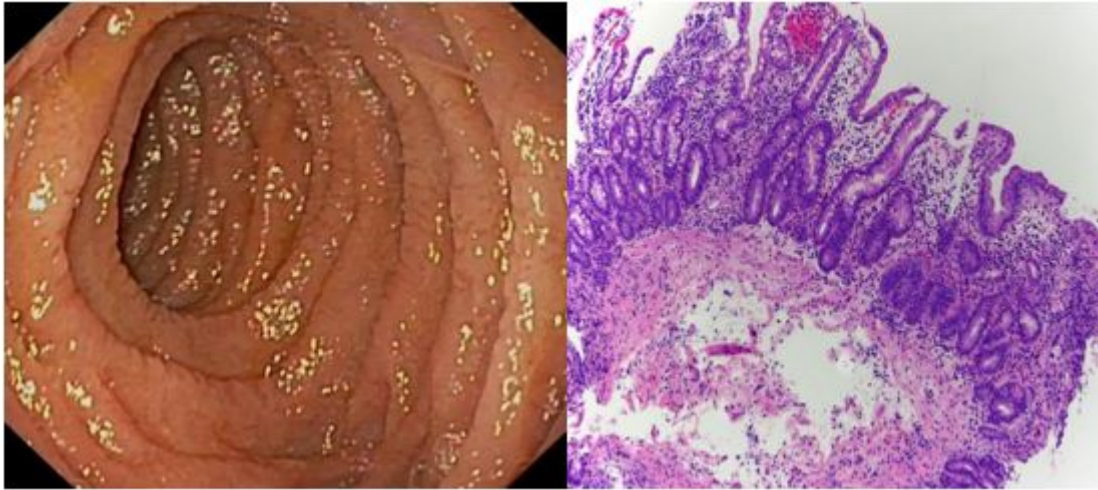


Fig. 1. A. Gastroscopy. The second duodenal portion where marked flattening of the duodenal mucosa is observed, with atrophy of the duodenal villi. B. Pathological anatomy. Biopsy of the second duodenal portion with an important decrease in the height of the villi, which are atrophic and widened at the expense of a mixed infiltrate with lymphocytes, plasma cells, eosinophils. However, it does not significantly penetrate the surface epithelium.

Accepted