non-responsive to a gluten-free diet, or refractory coeliac disease. No relation between the length of exposure to olmesartan and enteropathy has been described. The intestinal epithelium damage could be related to the immune-mediated cellular response secondary to an imbalance between anti-inflammatory and pro-inflammatory factors. The most frequent symptoms are diarrhoea and weight-loss; other possible symptoms are: fatigue, nausea and abdominal pain. Although the histopathological findings are not specific, it is worth mentioning that most patients present the symptoms described in the anatomopathological study undergone by our patient (villi atrophy with variable inflammation). The gluten-free diet and treatments for other types of enteropathy (glucocorticoids, anti-diarrhoeal, pancreatic enzymes, antibiotics, etc.) tend to be ineffective. It has been observed that once olmesartan is suspended, there is a remission of symptoms and histological disorders. Intestinal biopsy has not been repeated for this patient.

In view of the abovementioned, we conclude that the clinical condition presented by our patient was secondary to the intake of olmesartan. According to the Naranjo algorithm, causality is considered probable (7 points). This adverse reaction has been notified to the Spanish Agency of Medicines and Medical Devices.

References


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Enteropatía by olmesartan

Dear Editor,

Olmesartan medoxomil is a drug belonging to the angiotensin II type 1 receptor antagonist, which was approved in 2002 as a treatment for arterial hypertension. Although diarrhoea is a very frequent adverse effect in patients undergoing chronic drug treatment, the mechanisms by which it develops are mostly unknown. Enteropathy with villous atrophy has been previously associated with certain drugs, such as some immunosuppressants. In June 2012, Rubio-Tapia et al. reported 22 cases of enteropathy with villous atrophy in patients who were being treated with olmesartan medoxomil and later, in May 2013, DeGaetani et al. described the case of a series of patients with intestinal villous atrophy with absence of coeliac disease, in some of which patients, with no defined aetiology, either had been or were being treated with olmesartan. To date, there are few documented cases in the medical literature associating this drug with the onset of severe diarrhoea with significant weight loss, and most of these have histological analyses of the duodenum showing villous atrophy. As a result, in July 2013, the U.S. Food and Drug Administration issued an alert listing enteropathy as a severe side effect caused by olmesartan. In the following paragraphs, we describe a case diagnosed at our centre that presented severe diarrhoea with associated malnutrition.

The patient was a 78-year-old male who, in March 2013, consulted about diarrhoea of about one month evolution. His pathological history included longstanding, essential arterial hypertension that had been treated, for 8 years with 40 mg olmesartan administered on a daily basis. The patient had diarrhoea with 4 to 5 daily defecations, which were abundant and watery, but did not present blood, pus or mucous. Diarrhoea episodes intensified after meals and did not subside during the night sleep. He had lost 10 kg over the previous 2 months and presented incapacitating asthenia. He had not travelled abroad or been in contact with people presenting similar symptoms. Physical examination indicated that his weight was 53.8 kg, with a BMI of 21. No lesions were detected on his skin or oral cavity. His blood test levels indicated: creatinine 4.2 mg/dl (0.5–1.1 mg/dl), potassium 2.7 mM/l (3.5–4.5 mM/l), pH 7.2 (7.35–7.45) and bicarbonate 13.8 mM/dl. Laboratory tests also indicated total proteins of 4.4 g/dl (6.4–8.3), retinol binding protein 2.95 mg/dl (3.0–6.0), albumin 2.57 g/dl (3.3–5.2), prealbumin 13.3 mg/dl (20.0–40.0), phosphorus 1.6 mg/dl (2.7–4.5), calcium 7.4 mg/dl (8.7–10.3), iron 23 ug/dl (65–175), with magnesium, folic acid and vitamin B12, all within normal ranges. The haemogram showed anaemia, with Hb 9.8 g/dl (12–18). We ordered a complete microbiological study including the following: a total of 3 stool cultures, which showed regular flora for the sample, toxin and culture for Clostridium difficile, which were negative; no parasites were detected in the faeces. The serology for rotavirus and HIV, as well the serum DNA test for cytomegalovirus (CMV) were all negative; IgG through indirect immunofluorescence for Leishmania, negative; 3 determinations through immunochromatography for Giardia Lamblia, negative. Elastase and faecal calprotectin determination were within normal ranges. Alfa-1-antitrypsin clearance was 15.6 mg/g (<24), which, in the presence of diarrhoea, was...
not considered pathological. The patient underwent a colonoscopy, showing no signs of macroscopic disease, except for 2 small tubular adenomas with low grade dysplasia. His thyroid hormones, TSH, and blood sugar levels were within normal ranges, autoantibodies (ANA and anti-DNA) and tumour markers (CEA and CA 19-9) were all normal, and the complete serology for coeliac disease (IgA and IgG anti-transglutaminase and antiendomysial antibodies) was negative. The colon biopsies reported lymphocyte infiltration of the mucosa. The upper digestive endoscopy showed no macroscopic lesion and no *Helicobacter pylori* was detected in gastric antrum biopsies. Both the X-ray study of the small intestine with barium contrast and the computed tomography of the abdomen with intravenous contrast were normal. The hydrogen breath test with glucose did not find bacterial overgrowth. Histological analysis of the duodenum confirmed the presence of subtotal villous atrophy, crypt hyperplasia, intraepithelial lymphocytes increase and lamina propria plasmacytosis, all of these findings being compatible with type ia coeliac disease in the modified Marsh classification. The immunophenotypic study conducted on the intraepithelial lymphocytes of the patient’s duodenal mucosa confirmed an increased percentage of lymphocytes of up to 24.9% (8%-12%) with respect to the total epithelium, whereas the TCR lymphocyte percentage was within the normal range, and the CD3 - CD103+ lymphocyte percentage was 1.8% (>20%), thus indicating an absence off coeliac disease. However, and despite presenting histological and serological findings not conclusive of coeliac disease, the patient was put on a gluten-free diet but showed no improvement after a month. Consequently, the patient underwent further tests for IgA and IgG anti-enterocyte and anti-globlet cells and the results obtained were normal. The patient’s HLA was DQB1*03 DQB1*13, ruling out coeliac disease. Given the lack of response to a gluten-free diet, the progressive weight loss of up to 20 kg, and the significant impact on blood test levels, the patient was instructed to resume a regular diet and to suspend treatment with olmesartan. Three weeks after having suspended the treatment, the patient remained asymptomatic, and blood test levels normalised. Six months later, the patient remains completely asymptomatic from a digestive viewpoint, without anaemia, and with a weight gain of 5 kg; he had an upper digestive endoscopy performed with duodenal biopsies that confirmed a normal pattern of intestinal villus, and an intraepithelial lymphocyte immunophenotypic study, all of them within normal ranges.

In conclusion, enteropathy induced by olmesartan is an infrequent entity, probably not widely known and, therefore, underdiagnosed. As confirmed by the case presented here, which was diagnosed at our centre, and from our review of the medical literature published to date, the patient had chronic diarrhoea that developed months or even years after initiating olmesartan treatment, associated with significant weight loss and fundamental histological changes in the duodenum, with villous atrophy, in the colon and digestive organs. Drug discontinuation results in a clinical improvement, seen in weeks, and histological normalisation of the intestinal mucosa, although the latter is not necessary to confirm the diagnosis. In light of the above, it is crucial to include chronic treatment with olmesartan in the differential diagnosis of unexplained chronic diarrhoea and intestinal villous atrophy refractory to a gluten-free diet.

**References**


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**Hermansky-Pudlak syndrome: A case report**

**Síndrome de Hermansky-Pudlak: descripción de un caso**

Dear Editor,

Hermansky-Pudlak syndrome is a recessive autosomal genetic disease characterised by ocularcutaneous albinism, associated with a tendency to haemorrhage due to the absence of platelet granules and lysosomal dysfunction resulting from ceroid material accumulation. Additionally, patients commonly develop interstitial pneumopathy, which is a pulmonary affection. Given that this syndrome is highly uncommon—only some 200 cases have been described—we believe that the presentation of this case is of clinical interest.

A 50-year old female patient with ocuocutaneous albinism, with no other history of interest, had undergone a uterine fibroid procedure with hysterectomy and adnexectomy. The patient had several drug allergies (metamizole, aycetysalicic acid, butyloxypheno-lamine, deschlorpheniramime and cefixime). The patient had never smoked and did not consume toxic substances. She had no occupational or environmental exposure to toxic substances. She did not have regular contact with animals; she lives in a rural convent. Her family history revealed that her father died from an unspecified pulmonary disease and she had an albino brother who also died from a respiratory disease that was not studied. As regular medication, she had amitryptilina and benzodiazepines for the treatment of migraines episodes. She had dry cough and moderate effort dyspnoea of one year of progression, occasional night sweats and slight weight loss of about 5–6 kg during this period. The patient had no other related symptoms. Her physical

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