GE Port J Gastroenterol. 2016;23(2):96–100

Portuguese Journal of Gastroenterology

www.elsevier.pt/ge

CLINICAL CASE

Enteropathy Associated with Olmesartan

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Received 3 September 2015; accepted 25 October 2015
Available online 3 December 2015

KEYWORDS
Gastrointestinal Diseases;
Olmesartan

Abstract The recognition of an enteropathy caused by olmesartan is recent. It was first described in 2012 by the Mayo Clinic, which presented 22 clinical cases. Olmesartan is a highly prescribed drug and the differential diagnosis of a sprue-like enteropathy is very wide, so it is important to be aware of this pathology.

We report a case of a 67-years-old man, with arterial hypertension under treatment with olmesartan, with a 4-months history of diarrhea and weight lost. He was admitted three times in our Department during this period of time. An initial diagnosis was made of lymphocytic colitis but he did not respond to treatment with corticosteroids. There was a high suspicion of celiac disease, so the patient started a gluten-free diet but still there were no symptomatic changes. The patient underwent several blood and imaging tests which were negative. Due to the suspicion of an enteropathy caused by drugs, olmesartan was stopped and the patient showed a significant improvement of his symptoms.

The exact pathophysiology of this entity remains to be elucidated. It may affect all gastrointestinal tract and mimic a refractory celiac disease as well as a lymphocytic colitis due to similar symptoms and histology. It is expected more cases like this in the future due to high use of olmesartan in current clinical practice.

So, it is important to all gastroenterologists to be aware of this pathology and take it into consideration when putting together a differential diagnosis.

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http://dx.doi.org/10.1016/j.jpge.2015.10.007

PALAVRAS-CHAVE
Doenças Gastrointestinais;
Olmesartan

Enteropatia por Olmesartan

Resumo A enteropatia por Olmesartan não estava reconhecida até ao ano de 2012 quando a ''Mayo Clinic'' apresentou 22 casos. Apesar de existirem poucos casos publicados, é importante familiarizar os clínicos com aspectos referentes a esta patologia, visto tratar-se de um fármaco muito prescrito e o diagnóstico diferencial da enteropatia ''sprue-like'' ser muito amplo.

Apresentamos o caso de um paciente em tratamento com Olmesartan por hipertensão arterial. É internado 3 vezes num prazo de 4 meses por quadro de diarreia e perda importante de peso. Inicialmente, é diagnosticado de colite linfocítica que não responde ao tratamento com corticóides e, posteriormente, de provável doença celíaca que não responde a dieta sem glúten. Realizam-se inúmeros exames complementários, analíticos e de imagem, sem concluir-se nenhum diagnóstico. Perante a suspeita de uma enteropatia por Olmesartan, retira-se o fármaco definitivamente e reinicia-se o glúten na dieta, confirmando-se uma melhoria espectacular do quadro clínico. Durante os internamentos não tomava Olmesartan, sendo o motivo da melhoria clínica durante os mesmos.

Os mecanismos associados a esta patologia são desconhecidos. Pode afectar todo o aparelho digestivo e mimetizar uma doença celíaca refractária e/ou colite linfocítica devido a semelhança dos sintomas e da anatomia patológica. Devido à elevada prescrição deste medicamento, é esperável que no futuro se diagnostiquem mais casos, motivo pelo qual, os clínicos, principalmente os gastroenterologistas, devem de considera-la no diagnóstico diferencial.

1. Introduction

Sprue-like enteropathy is characterized by diarrhea, villous atrophy of the small bowel with lymphocyte infiltration, intestinal malabsorption, significant weight loss and negative celiac disease serology. This entity remains a challenge to all gastroenterologists due to a wide differential diagnosis, such as bacterial overgrowth, jejunitis, lymphoma, tropical sprue, protein-losing enteropathy or immunosuppressive drugs such as methotrexate, azathioprine and mycophenolate.[1,2]

Olmesartan is an angiotensin II receptor antagonist indicated for the treatment of hypertension since 2002. Olmesartan-associated enteropathy was first described in 2012 by Rubio-Tapia et al. of the Mayo Clinic when they reported 22 clinical cases.[1]

We describe a case of a sprue-like enteropathy due to olmesartan to draw attention to this disease, given the high frequency of use of this drug and the difficulty of diagnosis if the entity it is not known.

2. Case report

We report a case of a 67-years-old man, with hypertension under treatment with olmesartan 40 mg/day. He presented with a 4-months history of diarrhea and significant weight loss of 22 kg. He was hospitalised three times in our Gastroenterology Department during this period of time. At first, the patient described a 1-month history of diarrhea with a bowel frequency of 10 times/day, mostly by night, absence of blood or mucous in stools and a weight loss of 7 kg. He had no abdominal pain, nausea, vomiting or fever. His blood tests were normal, with no changes in his complete blood cell count, coagulation, ionogram, hepatic or renal function. Stool culture and Clostridium difficile toxin were negative. Colonoscopy showed no macroscopic changes but the histological features of the biopsies showed intraepithelial lymphocytosis. The findings were suggestive of lymphocytic colitis. He started treatment with budesonide 9 mg/day with good symptomatic improvement. He was then discharged and follow-up was made in clinic.

After one month, the patient was once again admitted in our Department due to symptomatic recurrence. He presented a total of 15 kg weight loss. Blood tests showed hypokalemia of 2.9 mmol/l, hypomagnesemia of 1.3 mmol/l and hypoalbuminemia of 2.3 g/dL. Complete blood cell count was normal. There were no changes in his D-Xylose absorption test as well as fecal pancreatic elastase and stool cultures. Abdominal CT and gastrointestinal transit showed significant dilatation of the small bowel but no stricture or stenosis were found. An endoscopic ultrasound showed an atrophic pancreas with a normal duct of Wirsung. Celiac disease serology (IgA anti-transglutaminase, anti-endomysial and anti-gliadin antibodies) was negative and the genetic test for HLA DQ2/DQ8 was positive. An endoscopy was also performed and duodenal biopsies showed increased intraepithelial lymphocytes, crypt hyperplasia and villous atrophy (grade IIIC according to the modified Marsh classification) (Fig. 1). Meanwhile, the patient showed clinical improvement and he was discharge with the diagnosis of celiac disease. His eating habits were changed during this admission and he started a gluten-free diet.

After approximately 45 days, the patient was admitted due to severe recurrence of symptoms. He had a total weight loss of 22 kg then. The blood tests showed a prothrombin time of 50%, total cholesterol of 85 mg/dL, triglycerides of 73 mg/dL, hypoalbuminemia of 1.9 g/dL and transferrin of