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Letters to the Editor

Clinical, laboratory, serological, and histological profile of sprue-like enteropathy associated with olmesartan use

Key words: Enteropathy. Diarrhea. Olmesartan. Sprue.

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Dear Editor,

Olmesartan is one of the various angiotensin II receptor blockers (ARBs) used for the management of high blood pressure. A clinico-pathological condition that mimicked celiac disease in association with the use of olmesartan was described in 2012 and designated olmesartan-associated sprue-like enteropathy (OSLE). It was first described by Rubio-Tapia et al. (1) in a group of patients with diarrhea, weight loss, negative anti-transglutaminase antibodies, evidence of enteropathy, and no clinical response to gluten-free diet who had other enteropathy causes ruled out and finally responded both clinically and histologically to olmesartan discontinuation. A systematic review and a French study on OSLE have been recently reported, which support an association between olmesartan use and the development of the condition (2,3). The pathogenic mechanisms of the disease remain unclear as of today.

In our institution an observational, descriptive study was performed in 12 patients who met the clinical, histopathological, and evolutionary criteria of OSLE from May 2013 to December 2015. Mean age was 67 years (range: 47-87), and the series included 9 women and 3 men. Mean treatment duration was 32 months (range: 12-60). All patients had watery diarrhea, weight loss, and negative celiac serology. They were admitted with severe clinical illness including prerenal kidney failure, metabolic acidosis, water-electrolyte imbalance, and malnutrition parameters. Most common laboratory abnormalities included anemia and hypoalbuminemia. Duodenal biopsy histology revealed villous atrophy in all 12 patients. In the genetic study five patients had a DQ2/DQ8 haplotype, which represented 41.6% of the total sample. All patients responded well to drug discontinuation, and 100% of patients with a follow-up biopsy showed histological recovery (Table I).

Table I. Clinical, laboratory, genetic, and histopathological profile of patients with olmesartan-induced sprue-like enteropathy

Sex (M/F)	*Weight loss (kg)*	*Dose (mg)/ time (years)*	*Ac (t-TG)*	*Outcome after withdrawal*	*HLA DQ2 or DQ8*	*Duodenal histology*	*Histology after withdrawal*	*Colon histology*
78/F	22	40/2	Negative	Improvement	Yes (DQ-8)	Severe VA & IEL (Marsh 3c)	Mild non-atrophic chronic duodenitis	Nonspecific chronic inflammation
59/M	20	40/5	Negative	Improvement	No	Mild VA Eosinophilia Lymphoid follicular hyperplasia (Marsh 3a)	Mild non-atrophic chronic duodenitis	Collagenous colitis

(Continue in the next page)

Table I (Cont.). Clinical, laboratory, genetic, and histopathological profile of patients with olmesartan-induced sprue-like enteropathy

Sex (M/F)	*Weight loss (kg)*	*Dose (mg)/ time (years)*	*Ac (t-TG)*	*Outcome after withdrawal*	*HLA DQ2 or DQ8*	*Duodenal histology*	*Histology after withdrawal*	*Colon histology*
63/M	15	20/3	Negative	Partial improvement	No	Mild VA (Marsh 3a)	Chronic duodenitis with mild VA and crypt hyperplasia	Not performed
53/F	15	40/2	Negative	Improvement	No	Partial VA Crypt hyperplasia IEL (Marsh 3b)	Mínimal inflammatory changes	Chronic colitis with nonspecific changes Melanosis Coli
74/F	12	40/3	Negative	Improvement	Yes (DQ-2)	Mild VA IEL (Marsh 3a)	Non-atrophic chronic duodenitis	Chronic colitis with eosinophilic component
82/M	11	40/3	Negative	Improvement	No	Severe VA with IEL & eosinophilic component (Marsh 3c)	Non-atrophic chronic duodenitis	No lesions
68/F	24	40/2	Negative	Improvement	Yes (DQ-8)	Mild VA (Marsh 3a)	Normal mucosa	Chronic colitis with eosinophilic component
47/F	9	40/3	Negative	Improvement	No	Mild VA & IEL (Marsh 3a)	Non-atrophic chronic duodenitis	No lesions
69/F	4	40/3	Negative	Improvement	Yes (DQ-8)	Mild VA & IEL (Marsh 3a)	Normal mucosa	Collagenous colitis
87/F	7	40/1	Negative	Improvement	No	Severe VA & IEL (Marsh 3c)	Not performed	Not performed
64/F	12	40/2	Negative	Improvement	No	Severe VA (Marsh 3c)	Non-atrophic chronic duodenitis	Collagenous colitis
65/F	5	20/3	Negative	Improvement	Yes (DQ8)	Mild VA with eosinophilic component (Marsh 3a)	Non-atrophic chronic duodenitis	Not performed

VA: Villous atrophy; IEL: Intraepithelial lymphocytosis. Marsh scale for the classification of duodenal biopsy findings.

While the causing mechanism remains unknown, the long latency seen from drug exposure to symptom onset, the finding of lymphocytes and collagenous colitis, and the condition's high association rate with HLA-DQ2/8 all suggest a cell-mediated delayed hypersensitivity reaction (2,4). This would speak against a class effect of ARBs. However, an alternate hypothesis suggests that the mechanism of action would involve the inhibition of the transforming growth factor beta (TGF-β), an important mediator of intestinal immune homeostasis, as seen with all ARBs (3). Since this enteropathy has been strongly linked to olmesartan use alone, the delayed hypersensitivity reaction hypothesis seems more plausible. Two cases of sprue-like enteropathy potentially associated with ARBs other than olmesartan were reported last year (3,5). The first case was included in a French study and was related to irbesartan use, whereas the second case involves a patient with severe enteropathy associated with valsartan. As of today, however, evidence is insufficient to confirm this enteropathy type in association with ARBs other than olmesartan. Therefore, considering the data reported by our team on these 12 patients with OSLE and the reviewed literature, we may conclude that olmesartan must be considered as a cause of severe diarrhea in order to facilitate an early identification of OSLE patients, particularly of those with severe diarrhea, duodenal villous atrophy, and negative celiac serology. Drug discontinuation is vital for suspected olmesartan-induced sprue-like enteropathy as it results in rapid clinical improvement and slower histological recovery.

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