A Case of Sprue-like Enteropathy Associated With Valsartan and Irbesartan

Introduction

Sprue-like enteropathy in association with olmesartan was first described in 2012. Several study results have since further supported the association between angiotensin II receptor blockers (ARBs) and sprue-like enteropathy, characterized by chronic diarrhea and weight loss in combination with villous atrophy that has been shown to improve after drug withdrawal across Western countries. Herein, we report the first case of sprue-like enteropathy associated with valsartan and irbesartan in Korea.

Case Report

A 73-year-old man with hypertension and variant angina presented with chronic diarrhea and weight loss of 7 kg persisting for several months. He reported up to 10 watery evacuations accompanied by abdominal pain daily. He had visited 2 other Korean tertiary care centers without a diagnosis before being transferred to our hospital. Following empiric treatment with a 2-week course of steroids and ganciclovir for suspected eosinophilic and Cytomegalovirus gastroenteritis, respectively, at another hospital, there was no improvement. He had anemia (hemoglobin: 8.3 g/dL) and hypoalbuminemia (with serum albumin: 1.0 g/dL).

Routine stool examinations, Clostridium difficile toxin assays, PCR test, and stool cultures, were negative for Salmonella spp., Shigella spp., Yersinia spp., and Vibrio spp. He showed an elevated fecal alpha-1-antitrypsin clearance rate if 403.58 mL/24 hours. Abdominal and pelvic computerized tomography (CT) imaging showed diffuse wall thickening in the area extending from the stomach to the ileal loop. Esophagogastroduodenoscopy revealed scalloping, grooving with nodularity, and frailty in the duodenum along with a hyperemic change in the stomach and mid-esophagus (Fig. 1). Colonoscopy showed mild mucosal edema in the colon. Histological evaluation of duodenum biopsy specimens showed marked blunting of the duodenal villi, relative crypt hyperplasia, goblet cell depletion, increased inflammatory infiltration, and patchy eosinophilic infiltration (Fig. 2). Stomach and esophagus biopsies were non-specific, but mild eosinophilic infiltration was noted.

Figure 1. Findings of CT scan and endoscopy. (A) Abdominopelvic CT scan shows diffuse thickening of the small bowel wall. Esophagogastroduodenoscopy images reveal (B) diffuse edematous and hyperemic change in the stomach and (C, D) scalloping and grooving in duodenal mucosa. (E) Follow-up endoscopy shows improvement in scalloping and grooving of the duodenum 2 weeks after discontinuing angiotensin II receptor blockers.
The patient had been taking 160 mg valsartan and 20 mg irbesartan daily for the past 10 years and 2 years, respectively, to treat hypertension. As drug-related enteropathy was suspected, the use of both valsartan and irbesartan was suspended. Diarrhea subsided immediately following drug discontinuation. Follow-up endoscopy 2 weeks later showed improvement in duodenal scallops and grooves (Fig. 1E). Five months after the withdrawal of both ARBs, serum albumin level improved to 3.8 g/dL, and body weight increased from 44 kg to 56 kg.

Discussion

The clinicopathologic features of our case correspond with those of previously reported cases of olmesartan-associated enteropathy.\(^2\)-\(^4\) The average duration of drug exposure typically ranges from months to years; however, cases occur up to 13 years after drug exposure.\(^5\)-\(^6\) Our patient had been taking 2 types of ARBs and developed symptoms 10 years and 2 years after the initiation of valsartan and irbesartan, respectively. Although the pathogenesis of ARB-associated enteropathy is unclear, it may be mediated by the binding of angiotensin II to the angiotensin II receptor, resulting in intestinal epithelial apoptosis.\(^7\)

Endoscopic findings are non-specific, so pathologic diagnosis is important. In this case, the most common pathologic findings were sprue-like mucosal injuries, namely, villous blunting and crypt hyperplasia. Villous blunting is the most important feature that distinguishes sprue-like enteropathy from eosinophilic gastroenteritis. In addition, in ARB-associated enteropathy, eosinophils may locally increase without predominance, whereas diffuse eosinophilic infiltration is characterized in eosinophilic gastroenteritis. Although histologic findings alone are not sufficient for the diagnosis of ARB-associated enteropathy, they can lead to an accurate diagnosis in an appropriate clinical context.

Recent studies and systematic reviews showed the association between enteropathy and olmesartan\(^8\) and other ARBs including telmisartan, valsartan, irbesartan, losartan, and eprosartan. To date, ARBs have not been shown to increase the risk of intestinal malabsorption in the Korean population.\(^7\) To the best of our knowledge, this is the first case of ARB-induced sprue-like enteropathy reported in Korea. Given that ARB-associated enteropathy is rarely suspected, it may currently be underdiagnosed in Korea. Therefore, it should be considered in patients with diarrhea and weight loss,
particularly in those taking hypertensive medication.

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