Olmesartan-associated sprue-like enteropathy

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DESCRIPTION

A woman in her 80s was admitted to our hospital due to dehydration caused by >10 watery diarrhoea stools/day for nearly 2 months. She had been taking olmesartan, an angiotensin II receptor blocker (ARB), for about 8 years to treat hypertension. Prior workup, including stool culture, abdominal computed tomography (CT), and upper and lower gastrointestinal endoscopy, was negative per her previous physician. She was treated with probiotics and antibacterial agents, but there was no improvement in her symptoms. After hospitalisation, blood test findings showed hypoalbuminaemia (albumin 2.7 g/dL (reference range 4.1–5.1)) and electrolyte abnormalities (sodium 127 mEq/L (reference range 138–145), potassium 4.6 mEq/L (reference range 3.6–4.8), chloride 96 mEq/L (reference range 101–108) and calcium 8.0 mg/dL (reference range 8.8–10.1)) reflecting poor oral intake and severe malabsorption. Slightly elevated inflammatory response was noted (white blood cell count 10.7×10^9/L (reference range 3.3×10^9–8.6×10^9) and C reactive protein 0.24 mg/dL (reference range <0.14)), but all of the various infections were negative. Antinuclear antibodies were positive (1280 times (reference range <40)). Upper gastrointestinal endoscopy was performed again. It revealed multiple granular protrusion in the duodenal bulb and mucosal atrophy from descending to transverse part of the duodenum (figure 1). Antegrade double-balloon enteroscopy (DBE) revealed diffuse villous atrophy throughout the duodenum and ileum with patchy reddening and erosions (figure 2). Endoscopic findings did not rule out malignant lymphoma with diffuse changes, and capsule endoscopy was performed to further examine the anorectal side. There was diffuse villous atrophy, a finding similar to that seen on antegrade DBE (figure 3). A biopsy from duodenum showed villous atrophy and disappearance of the crypts (figure 4), and cytomegalovirus or tuberculosis infection and lymphoma of the small intestine were ruled out by immunohistochemistry. Olmesartan-associated sprue-like enteropathy or coeliac disease was suspected. Human leucocyte antigen (HLA) testing was HLA-DQ6/6, and she did not have HLA-DQ2 or HLA-DQ8 haplotypes, which are strongly associated with coeliac disease. After discontinuation

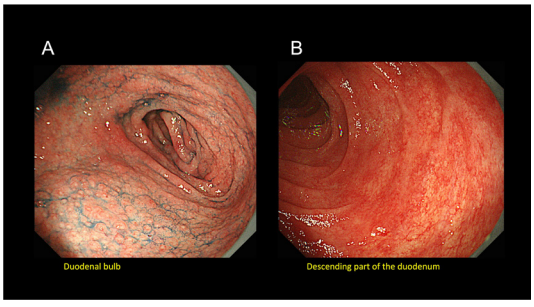

Figure 1 Upper gastrointestinal endoscopy reveals multiple granular protrusion in the duodenal bulb (A) and mucosal atrophy from descending to transverse part of the duodenum (B).

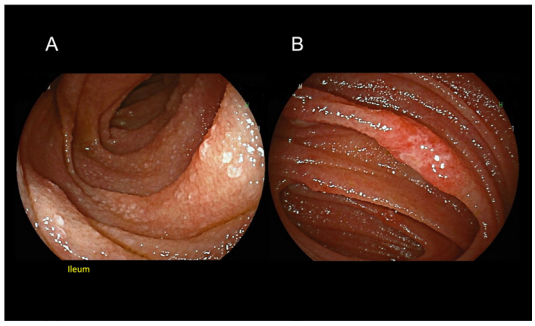

Figure 2 Antegrade double-balloon enteroscopy reveals diffuse villous atrophy (A) throughout the duodenum and ileum with patchy reddening and erosions (B).

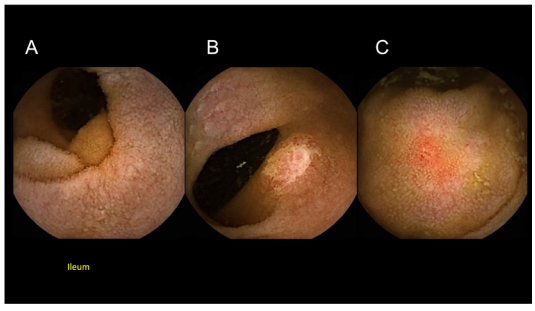

Figure 3 Capsule endoscopy shows diffuse villous atrophy (A), erosions (B) and patchy reddening (C).

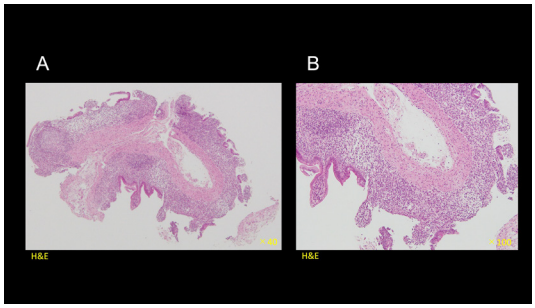

Figure 4 A biopsy from duodenum is performed. H&E staining reveals villous atrophy and disappearance of the crypts (A, B).

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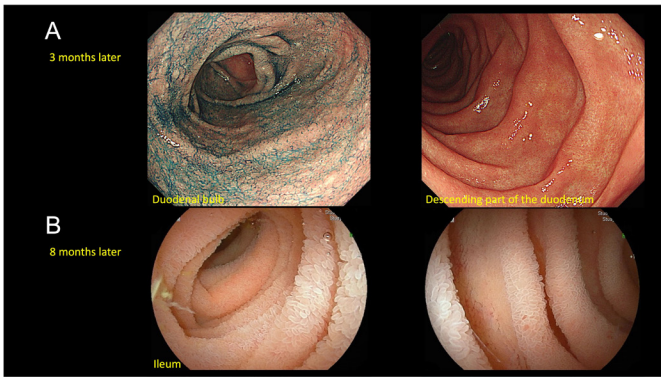

Figure 5 Upper gastrointestinal endoscopy (A) and antegrade double-balloon enteroscopy (B) show the largely healed state of mucosal atrophy.

of olmesartan, her symptoms rapidly improved, although her diet was not gluten-free. Based on all these results, a diagnosis of olmesartan-associated sprue-like enteropathy was confirmed. Upper gastrointestinal endoscopy and antegrade DBE were performed after 3 and 8 months, respectively. They showed that mucosal atrophy was largely healed (figure 5).

Kamal *et al* reviewed ARB-associated sprue-like enteropathy.[1] In this review, a total of 248 cases were selected and analysed and olmesartan-associated sprue-like enteropathy accounts for 94.0% of them (233 cases). Age at diagnosis ranged from 45 to 89 years old and 57.3% of them were women. The periods between ARB initiation and onset of symptoms ranged from 2 weeks to 13 years. Villous atrophy was the most prevalent histopathological findings (192/204 olmesartan users). In practice, the finding of duodenal villus atrophy on upper gastrointestinal endoscopy might be a clue to the diagnosis, although Marthey reported that 52% of the cases (15/29) showed normal duodenum endoscopically.[2] In most cases, discontinuation of ARB resulted in complete remission of symptoms (233/239 cases, 97.4%).

Olmesartan-associated sprue-like enteropathy should be considered on the differential diagnosis in the patient with chronic persistent diarrhoea.

Learning points

- In cases of persistent diarrhoea with hypertension, olmesartan-associated sprue-like enteropathy should be considered in the differential diagnosis.
- Olmesartan-associated sprue-like enteropathy can arise even long after initiation of treatment with olmesartan.
- The finding of duodenal mucosal atrophy on upper gastrointestinal endoscopy is helpful for diagnosis, but only in about half of patients. The most important step in the diagnosis of this disease is to obtain the patient's medical history.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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REFERENCES

1 Kamal A, Fain C, Park A, *et al*. Angiotensin II receptor blockers and gastrointestinal adverse events of resembling sprue-like enteropathy: a systematic review. *Gastroenterol Rep* 2019;7:162–7.
2 Marthey L, Cadiot G, Seksik P, *et al*. Olmesartan-associated enteropathy: results of a national survey. *Aliment Pharmacol Ther* 2014;40:1103–9.