Pitfall in diagnosing refractory coeliac disease: a case of losartan-induced enteropathy

T. van Gils
R.J. Robijn
G. Bouma
E.A. Neefjes-Borst
C.J.J. Mulder

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The main cause of villous atrophy in western countries is coeliac disease (CD). In case of negative CD antibodies, other causes of villous atrophy, such as collagenous sprue and drug-induced enteropathy have to be excluded before a patient can be diagnosed with seronegative CD. Several studies reported the entity of olmesartan-induced enteropathy. However, only a limited number of patients with enteropathy caused by other angiotensin II receptor blockers, such as irbesartan and valsartan, has been reported 1, with only 1 well-described case of losartan-induced enteropathy 2. As losartan is often prescribed with 226,990 users of Lasonox ® out of 16.9 million Dutch citizens in 2015 3, it is important to be aware of adverse events which could be caused by this drug. We report a patient with losartan-induced enteropathy who was initially suspected for refractory CD type II (RCD II), a rare condition with 50% of the patients developing an enteropathy associated T-cell lymphoma within 4–6 years after diagnosis 4. For this report, an expert pathologist specialized in the gastrointestinal tract (EAN-B) reviewed the histological features of all duodenal biopsies reported.

Our patient is a a 56-year-old male with hypertension. He was initially diagnosed with CD based on Marsh IIIb despite negative transglutaminase and endomysial IgA antibodies in the absence of IgA deficiency. Five months after CD diagnosis he presented with persisting frequent fatty diarrhea, nausea and weight loss (initially 78 kg, dropped to 64 kg) despite a gluten-free diet. Biopsies showed again Marsh IIIb with loss of CD8 on intra-epithelial lymphocytes (IEL), which could be indicative for RCD II. He was referred to our tertiary CD center for RCD II diagnostic work-up and budesonide was started. Laboratory tests showed that the patient was HLA-DQ2.2 heterozygote positive in the absence of CD antibodies, enterocyte antibodies and immunoglobulin deficiency. As work-up for RCD II, medication was reviewed. The patient reported the use of losartan (50 mg daily) since two years. Because we hypothesized losartan as a potential cause for villous atrophy, the drug was discontinued. Duodenal biopsies and flowcytometric analysis of subsets of IELs, presented as percentages of total IELs, three weeks after discontinuing losartan, showed no clues for CD or RCD II (Marsh 0, 0.5% γδ T-cell receptor positive IEL and 6% aberrant, i.e., RCD II-specific, IEL). We re-introduced a gluten-containing diet and discontinued budesonide. Duodenal biopsies 5 months later still showed Marsh 0. Clinically, the patient gained weight (78kg) in the absence of any symptoms (Figure 1).

This case showed a rare but severe adverse event caused by a commonly used antihypertensive drug which became clinically significant several months after starting Losartan and with fast recovery of villi and symptoms after discontinuing the drug. This case was not as severe as some presentations of olmesartan-induced enteropathy previously described resulting in hospitalization of a significant part of these patients 1. We showed the importance of the careful work-up of seronegative CD, a diagnosis only possible after extensive work-up, and the awareness of rare adverse events caused by ‘innocent’ frequently used medication.

Fig 1. Summary of clinical course.
EMA; endomysial antibodies, RCD II; refractory coeliac disease type II, TGA; tissue transglutaminase antibodies

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The authors declare no conflict of interest.
REFERENCES


3. National Health Care Institute (the Netherlands), [www.gipdatabank.nl](http://www.gipdatabank.nl)
