

complications. Our patient's significant clinical improvement after starting treatment for SIBO was very striking. Moreover, this improvement has been maintained over time and was not achieved with any of the other treatments used.

Despite the limitations on the study of the intestinal microbiota, SIBO is an easily diagnosed condition thanks to aspirated hydrogen detection tests following oral glucose or lactulose solution overload. Its pathogenesis is multifactorial, with slow transit and disruption of the intestinal anatomical barriers as triggering mechanisms being particularly prominent. It is therefore related to conditions such as small-bowel diverticulosis, stenosis, inflammatory disease, irritable bowel syndrome or surgical resections.<sup>5</sup> However, its association with intestinal malrotation has not been investigated, although taking the aetiopathogenic analogies of intestinal malrotation with some of the diseases that are associated with SIBO into account, we believe that this relationship between the two conditions may exist.

In our opinion, intestinal malrotation should be taken into account in the study of nonspecific digestive symptoms and we believe it is useful to look for SIBO when symptoms are consistent or there is no improvement with other treatments. However, specific studies will be required to confirm the association of these two pathologies.

### Conflicts of interest

The authors declare that they have no conflicts of interest.

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To Dr Abel Gregorio Hernández and Ana Serrano Prats.

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## Apoptotic colitis owing to dolutegravir<sup>☆</sup>



### Colitis apoptótica por dolutegravir

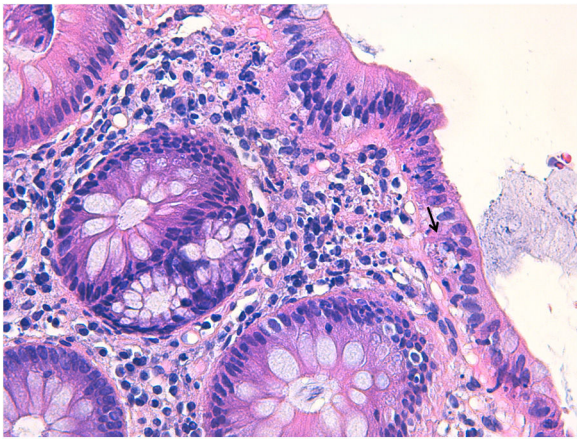
Dear Editor,

Apoptotic colitis consists of a set of histological alterations characterised by an increase in the number of apoptotic bodies in the colonic mucosa. These findings are in themselves nonspecific, since they may be due to numerous clinical conditions such as graft-versus-host disease, cytomegalovirus or adenovirus infection, common variable immunodeficiency or autoimmune enterocolopathy, as well as to the use of different drugs such as mycophenolate mofetil, CTLA-4 inhibitors (ipilimumab) and anti-PD1s (nivolumab, pembrolizumab and avelumab), although the condition has also been associated with others.<sup>1</sup> We present the case of a patient diagnosed

with apoptotic colitis secondary to antiretroviral treatment with dolutegravir.

A 54-year-old male patient with chronic human immunodeficiency virus infection for more than 20 years, without associated complications, except for a reduction in CD4 lymphocytes to a nadir of approximately 200/mm<sup>3</sup> in 1997, on antiretroviral treatment since then. His personal history shows previous parenteral drug use, chronic obstructive pulmonary disease, ischaemic heart disease, left ventricular aneurysm, paranoid schizophrenia, hepatitis C genotype 3 with sustained viral response subsequently maintaining good liver function and no evidence of fibrosis (6.8 kPa, F1), in addition to nephropathy secondary to tenofovir. In July 2018, he was being treated with darunavir, ritonavir and lamivudine, with the darunavir replaced by dolutegravir as a second drug to optimise treatment due to its lower toxicity. Approximately 2 weeks after starting on dolutegravir, the patient developed diarrhoea with more than 6 liquid stools a day, without pathological products, remaining afebrile at all times. The stool culture, including the determination of parasites in faeces, was negative, and the general blood test was also normal except for the finding of mild thrombocytopenia. The only finding on the abdominal ultrasound was hepatic steatosis. Treatment with loperamide was started and the number of stools diminished, but not so their liquid consistency, which persisted. For this reason, an

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**Figure 1** Findings consistent with apoptotic colitis, where an apoptotic body is observed in the colonic epithelium (arrow, hematoxylin-eosin x400).

ileo-colonoscopy was performed, showing a colonic mucosa without macroscopic alterations, with colonic diverticula and a 5-mm tubular adenoma in the transverse colon, which was resected. Additionally, multiple caecum/ascending, transverse, and sigmoid colon biopsies were taken to complete the diarrhoea study. The histological diagnosis of the biopsies of the different colonic segments showed a large intestine mucosa with preserved architecture, with a lamina propria with oedema and a slight inflammatory lymphoplasmacytic infiltrate, as well as frequent apoptoses in both the surface epithelium and the superficial lamina propria, with no microorganisms identified, and consistent with apoptotic colopathy (Fig. 1). The immunohistochemical technique corresponding to cytomegalovirus was negative. After dolutegravir was replaced with darunavir, the patient's condition quickly improved.

Dolutegravir is an antiretroviral belonging to the group of integrase inhibitors. Its most frequent adverse effects include diarrhoea, which can be observed in up to 18% of patients according to its summary of product characteristics. In any case, the literature describes only one case of diarrhoea due to apoptotic colitis associated with this drug,<sup>2</sup> which is why we are presenting this case, in view of the low frequency of this condition. Furthermore, this treatment

has been related to the development of lymphocytic colitis in another case, so it should also be considered among the possible causes of diarrhoea in these patients.<sup>3</sup> Apoptotic colopathy has been associated with other drugs such as mycophenolate mofetil, ipilimumab, nivolumab, pembrolizumab and avelumab.<sup>4</sup> Regarding the management of this condition, a high index of suspicion is of vital importance, followed by a detailed clinical history that permits the identification of the drug associated with this disorder and withdraw it, which is the basis of the treatment.

### Conflicts of interest

None.

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