be noted that the initial episode and all recurrences were mild, not meeting criteria for severity, and accompanied by diarrhoea and mild worsening of kidney function on every occasion.

Several risk factors for recurrence of CDI converged in our patient: advanced age, immunosuppression, chronic kidney disease, PPI use and numerous recurrent episodes with exhaustion of available treatment options, including two FMTs. Treatment with bezlotoxumab is indicated in patients 18 years of age and older receiving treatment for CDI and at high risk of recurrence[5]; in our case, these criteria were fulfilled. Bezlotoxumab is the first drug authorised to prevent rCDI, and the results of the clinical trials conducted[5] confirm that it reduces recurrence rates. However, there is still no experience with repeat administration of the drug and there are still no data comparing it to other drugs.

Solid organ transplant recipients are under-represented in the majority of clinical trials and registry studies.[3] They also have higher rates of morbidity and mortality due to their clinical condition, their treatments and factors such as more frequent hospitalisations and greater use of antibiotics.[4] The choice of a specific treatment should be tailored to each patient's condition and risk of recurrence.

References

1. Czepiel J, Drozdz M, Pituch H, Kuijper EJ, Perucki W, Mielimonka A, et al. *Clostridium difficile* infection: review. Eur J Clin Microbiol Infect Dis. 2019;38:1211–21.
2. Avni T, Babitch T, Ben-Zvi H, Hijazi R, Ayada G, Atamna A, et al. *Clostridioides difficile* infection in immunocompromised hospitalized patients is associated with a high recurrence rate. Int J Infect Dis. 2020;90:237–42.
3. Cheng Y-W, Phelps E, Ganapini V, Khan N, Ouyang F, Xu H, et al. Fecal microbiota transplantation for the treatment of recurrent and severe *Clostridium difficile* infection in solid organ transplant recipients: a multicenter experience. Am J Transplant. 2019;19:501–11.
4. Schneider KM, Wirtz T, Kroy D, Albers S, Neumann UP, Strowig T, et al. Successful fecal microbiota transplantation in a patient with severe complicated *Clostridium difficile* infection after liver transplantation. Case Rep Gastroenterol. 2018;12:76–84.
5. Wilcox MH, Gerding DN, Poxton IR, Kelly C, Nathan R, Birch T, et al. Bezlotoxumab for prevention of recurrent *Clostridium difficile* infection. N Engl J Med. 2017;376:305–17.

María Hernández[a,*], Nuria Saura[a], Sandra García[a], Raúl Velamazán[a], Daniel Abad[a], Gonzalo Hijos[a], Enrique Alfaro[a], Pablo Cañamares[b], Viviana Laredo[a], Sara Lorente[a]

[a] *Servicio de Aparato Digestivo, Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain*
[b] *Servicio de Aparato Digestivo, Hospital General San Jorge, Huesca, Spain*

* Corresponding author.
E-mail address: mhernandezainsa@gmail.com (M. Hernández).

Pericardial effusion associated with mesalamine treatment in a patient with ulcerative colitis☆

Derrame pericárdico asociado al tratamiento con mesalazina en un paciente con colitis ulcerosa

Mesalazine (5-aminosalicylic acid or 5-ASA) is the standard treatment for the induction and maintenance of mild/moderate flare-ups of ulcerative colitis (UC). The anti-inflammatory mechanism is not known; it is postulated that there is an increase in the expression of peroxisome proliferator-activated receptors in the intestinal mucosa and the cyclooxygenase pathway is inhibited.[1] Mesalazine is a safe drug that is widely used in clinical practice. Various adverse effects have been described with a low incidence and variable severity, which may lead to the drug being withdrawn. The most frequent are: arthromyalgia, abdominal pain, nausea, diarrhoea and headache. These side effects are not dose-dependent; they are due to hypersensitivity reactions and not to cumulative toxicity.[1]

We present the case of a 53-year-old woman, with no relevant history, diagnosed with ulcerative proctitis at another medical centre in February 2020. Treatment with oral mesalazine (500 mg/8 h) and mesalazine foam (one nocturnal application) was started at that time. She was admitted to the centre in May 2020 due to a moderate outbreak of left UC, undergoing abdominal pelvic computed tomography (CT). The CT scan showed proximal extension of the disease to the sigmoid area and a small pericardial effusion (PE). She was transferred to our hospital after a lack of response to intravenous corticosteroids for 10 days (methylprednisolone 60 mg/24 h). Cytomegalovirus infection was ruled out by rectal biopsy as the cause of corticosteroid refractoriness and treatment was started with infliximab (5 mg/kg), maintaining oral mesalazine (4 g/24 h). Given her good clinical response and test results, she was discharged from hospital. She came to the emergency department two weeks later having had fever for three days, with evening peaks of up to 38.5 °C without other associated symptoms or abdominal symptoms, and without an increase in the number of stools or bleeding. Laboratory tests showed an elevation of acute phase reactants (C-reactive protein of up to 8.9 mg/dl). An urgent abdominal CT scan was performed which identified proctosigmoiditis without local complications and worsening of the pericardial effusion. The study was completed with a transthoracic echocardiogram with a finding of a moder-

☆ Please cite this article as: Ezquerra A, Resina E, Montes Á, Álvarez-Malé T, Gisbert JP. Derrame pericárdico asociado al tratamiento con mesalazina en un paciente con colitis ulcerosa. Gastroenterol Hepatol. 2021;44:721–723.

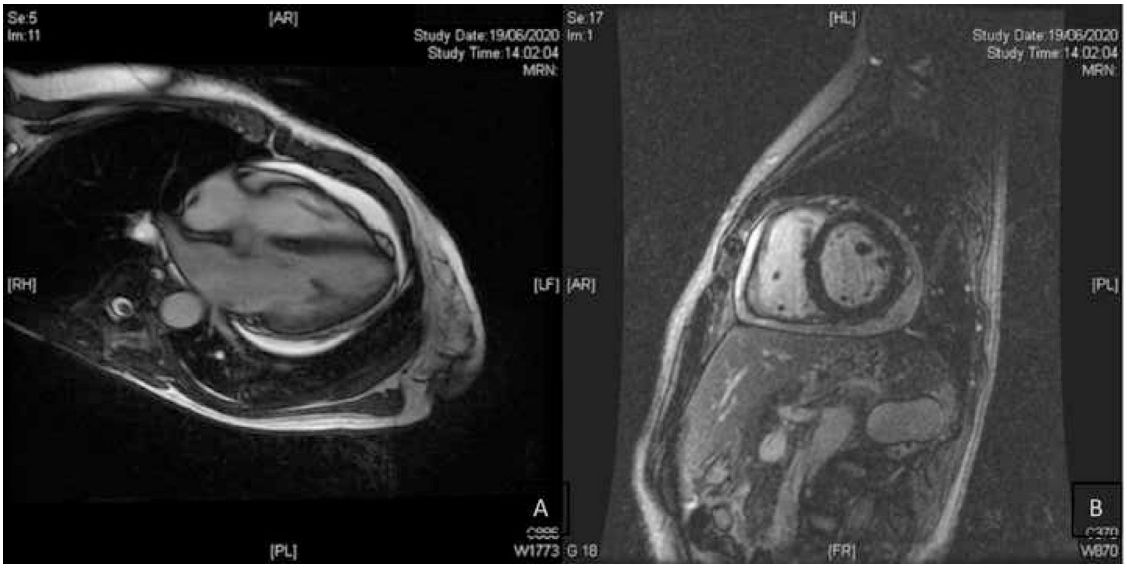

Figure 1 (A) Four-chamber cine sequence showing normal-thickness pericardium with mild-moderate pericardial effusion. (B) Late enhancement sequence showing absence of enhancement in pericardial leaves, compatible with absence of active inflammation.

ate effusion (17 mm) without haemodynamic compromise. The patient was admitted for study of fever without focus and PE. A rectoscopy was performed, in which a clear improvement was observed compared to the previous examination, so, given the absence of compatible symptoms, UC activity was ruled out as a cause of the fever and elevation of acute phase reactants. The PE study ruled out an infectious cause (negative PCR for respiratory viruses, including SARS-CoV-2, in nasopharyngeal exudate), as well as tumour and autoimmune causes. In the autoimmunity study, there was positivity only for p-ANCA. Cardiac magnetic resonance imaging (Fig. 1) confirmed moderate effusion and ruled out acute pericarditis or other pericardial involvement. Mesalazine was suspended as a possible causative drug and infliximab was ruled out as a cause of PE, since it was observed weeks before the drug was started. During admission, after suspension of mesalazine, the patient remained afebrile without antibiotics, antipyretics and normalisation of acute phase reactants. A follow-up echocardiogram one month after hospital discharge showed the practical resolution of PE (minimum effusion <5 mm). The patient remained afebrile after discontinuation of mesalazine two months after admission.

Cardiac side effects related to mesalazine are reported with a frequency from 0 to 0.3%.[1] Among them are: cardiomyopathy, acute myocardial infarction and atrioventricular blocks.[1] Involvement of the pericardium, myocardium, or both (myopericarditis) is rare, but can be potentially serious and requires early detection and treatment.[2] The pathophysiology of cardiac toxicity due to mesalazine is not known, and humoral (IgE-mediated) and cellular mechanisms or direct toxicity are postulated.[3]

In our patient, the finding of PE was incidental, since the clinical, laboratory and electrocardiogram findings were not compatible with myopericarditis. It was not accompanied by pleural effusion, positive autoimmunity (except p-ANCA, relatively common in patients with UC), or any other extraintestinal manifestation compatible with mesalazine-induced lupus. The cases of PE described in the literature are exceptional. The diagnosis is made by exclusion and from the temporal relationship with the introduction of the drug.[4]

In summary, mesalazine is an effective and safe drug, although cardiac side effects have been reported exceptionally. There should be a high clinical suspicion and a broad differential diagnosis should be made and, in the event of a potential causal relationship, the drug should be discontinued and not reintroduced due to the high risk of recurrence.[5]

Conflicts of interest

Javier Gisbert has provided scientific advice and support for research and/or training activities for MSD, Abbvie, Pfizer, Kern Pharma, Biogen, Mylan, Takeda, Janssen, Roche, Sandoz, Celgene, Gilead, Ferring, Faes Farma, Shire Pharmaceuticals, Dr Falk Pharma, Tillotts Pharma, Chiesi, Casen Fleet, Gebro Pharma, Otsuka Pharmaceutical and Vifor Pharma.

References

1. Sehgal P, Colombel J-F, Aboubakr A, Narula N. Systematic review: safety of mesalazine in ulcerative colitis. Aliment Pharmacol Ther. 2018;47:1597–609, http://dx.doi.org/10.1111/apt.14688.
2. Dias T, Santos A, Santos RM, Carvalho A. Recurrent mesalazine-induced myopericarditis in a patient with ulcerative colitis. BMJ Case Rep. 2019;12:e228037, http://dx.doi.org/10.1136/bcr-2018-228037.
3. Taha ME, Abdalla A, Al-Khafaji J, Malik S. Mesalamine-induced myopericarditis: a case report and literature review. Cardiol Res. 2019;10:59–62, http://dx.doi.org/10.14740/cr820.
4. Kaiser GC, Milov DE, Erhart NA, Bailey DJ. Massive pericardial effusion in a child following the administration of mesalamine. J Pediatr Gastroenterol Nutr. 1997;25:435–8, http://dx.doi.org/10.1097/00005176-199710000-00015.
5. Brown G. 5-Aminosalicylic acid-associated myocarditis and pericarditis: a narrative review. Can J Hosp Pharm. 2016;69:466–72.

Alberto Ezquerra[a,*], Elena Resina[a], Álvaro Montes[b], Tomás Álvarez-Malé[a], Javier P. Gisbert[a]

[a] *Servicio de Aparato Digestivo, Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-IP), Universidad Autónoma de Madrid (UAM), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Madrid, Spain*

[b] *Servicio de Cardiología, Hospital Universitario de La Princesa, Madrid, Spain*

[*] Corresponding author.
E-mail address: ezquerra93@gmail.com (A. Ezquerra).

2444-3824/