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Ulcerative colitis induced by obinutuzumab in a patient treated for a folicular lymphoma

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Dear Editor,

An increasing use of immunomodulatory drugs has led to a corresponding increase in treatment-related pathologies such as inflammatory bowel disease. Here, we present a case of ulcerative colitis due to Obinutuzumab, an antiCD20 monoclonal approved for the treatment of Non-Hodgkin lymphomas (1).

Case report

We present the case of a 61-year-old woman with a history of prolactinoma treated with cabergoline. She was diagnosed in 2018 with follicular lymphoma and began first-line treatment with Obinutuzumab-CVP (cyclophosphamide + vincristine + prednisone), completing a total of six cycles (October 2018 to February 2019), achieving complete metabolic remission. She subsequently received bimonthly maintenance treatment with Obinutuzumab for two years (April 2019 to March 2021).

From the digestive point of view, the patient reported symptoms of intermittent abdominal fullness and diarrhea after the immunotherapy cycles. The last month of maintenance treatment presented a new episode of abdominal pain associated with acute diarrhea with blood and mucus for three weeks. A colonoscopy was performed in May 2021, finding mucosa damage, erosions throughout the entire colon which were more striking in the descending-sigma colon, which are biopsied observing data compatible with severe active colitis and positive immunohistochemistry for CMV. Treatment with Famciclovir was started with disappearance of the symptoms and a new colonoscopy was performed to verify the CMV-negative status in July 2021, in which erythema, exudate and loss of vascular pattern was observed, for which a new biopsy was performed that confirm the diagnosis of an ulcerative colitis-type inflammatory bowel disease (Figure 1). She is currently asymptomatic receiving treatment with oral mesalazine.
Discussion

The approval of anti-CD-20 antibodies in 1997 for the treatment of B-cell lymphomas represented a paradigm shift in these pathologies. These antibodies can induce CD-20 B cell death by programmed cell death, sensitizing cells to chemotherapy or activating the complement cascade (2).

Decreased numbers of regulatory B cells have been observed in the peripheral blood and intestinal tissue of patients with ulcerative colitis (3). Its fundamental role is the maintenance of hemostasis of the intestinal microbiota through the production of immunoglobulins and anti-inflammatory cytokines.

The case that we present here is the first episode of ulcerative colitis due to obinutuzumab published to date; however, since the beginning of the use of anti-CD20 antibodies, associated cases of inflammatory bowel disease have been described with Rituximab (4) and Ocrelizumab (5), which is used to treat another immuno-mediated disease as multiple sclerosis, it is possible to observe this type of immune-mediated digestive pathologies in predisposed patients.

Bibliography

Fig 1. A: Rectum and distal sigma with erythema, exudate and loss of vascular pattern; B: immunohistochemical study for CMV negative; C and D: distortion of cryptic architecture caused by superficial ulceration, atrophic crypts, with loss of usual branching, and cryptitis (polymorphonuclear inflammatory infiltrate infiltrating the cryptic epithelium with the presence of abscesses and debris in its lumen). Expansion of the lamina propria due to acute lymphoplasmacytic inflammatory infiltrate.