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SCIENTIFIC LETTER

A 61-year-old patient with Crohn's disease and severe postoperative recurrence responding to JAK inhibitor ruxolitinib for polycythemia vera treatment

Varón de 61 años con enfermedad de Crohn y recurrencia postquirúrgica severa con respuesta a inhibidor JAK ruxolitinib indicado para tratamiento de policitemia vera

Treatment for Crohn's disease (CD) does not include JAK/STAT pathway inhibition. Nevertheless, two JAK inhibitors (filgotinib and upadacitinib) have shown positive results in phase II clinical trials for the induction treatment in CD,[1,2] and are being tested for CD in phase III trials. Ruxolitinib is an orally administered inhibitor of JAK 1 and 2, approved for the treatment of primary or secondary myelofibrosis, polycythemia vera and acute graft-versus-host disease.[3,4] No description between its potential effect in inflammatory bowel disease has been reported.

We present the case of a 61-year-old male, former smoker, with history of polycythemia vera (JAK2 positive) since 2012, hepatosplenomegaly and an extensive venous splanchnic system thrombosis. He had been in need for periodic phlebotomies, anticoagulation and hydroxyurea treatment. Endoscopic signs of portal hypertension have been always absent. He had typical blood test findings in this condition: low ferritin, high red blood and platelet counts, and high lactate dehydrogenase.

In 2013, he was diagnosed with inflammatory ileal Crohn's disease, with partial response to azathioprine. In 2015 he was admitted due to penetrating ileal disease complicated with abdominal abscess. He underwent open ileal resection and right hemicolectomy. The anatomopathological exam confirmed CD diagnosis and revealed a diffuse large B-cell intestinal lymphoma with regional nodal invasion. He received chemotherapy with six cycles of R-CHOP scheme (Rituximab plus cyclophosphamide, doxorubicin, vincristine and prednisolone) achieving a complete remission after treatment. Regarding CD, he completed 3 months with metronidazole for postoperative recurrence prevention. Immediate treatment with azathioprine was ruled out because of intestinal lymphoma. Thereafter, the patient denied any biologic treatment, and for three years, when having mild diarrhea or abdominal cramps, he only received budesonide cycles and oral cholestyramine, with good clinical response and remaining regularly with no abdominal pain, 3 bowel movements per day, no bloody diarrhea and undernormal but stable body weight. Nevertheless, he had persistent elevated fecal calprotectin (FC) from 500 to 1000 mg/kg, normal C-reactive protein (CRP) and was in need for intermittent enteral protein supplementation. He also had recurrent iron deficiency without anemia attributable to both CD and polycythemia vera. Due to patient's avoidance behavior, no colonoscopies had been performed until 2019, revealing mild postoperative recurrence (Rutgeerts score i2b), with no histological evidence of intestinal lymphoma. Immunosuppressive treatment was rejected by the patient, given his steady clinical state.

In September 2020, the patient showed up with a 3-week history of clinical relapse with up to 10 bowel movements per day and bloody diarrhea. Infectious agents were ruled out. Blood tests revealed CRP of <2 mg/dL, FC of 1300 mg/kg, hypoproteinemia of 5.91 mg/dL, mild leukocytosis (12,220 $\times$ 10e9/L) and normal hemoglobin (13.9 g/dL). Parallely, treatment with ruxolitinib 10-mg every 12 h prescribed by Hematology Department for giant progressive splenomegaly associated with polycythemia vera. A new 2-month budesonide cycle was initiated and a new colonoscopy was performed in October 2020, showing severe postoperative recurrence with diffuse ileitis and extensive ulceration (>75% of the circumference) of the anastomosis and neoterminal ileum up to 15-cm (Rutgeerts score i4). Histopathology showed severe inflammation related to active Crohn's disease, with no evidence of intestinal lymphoma. Ustekinumab treatment was raised to the patient but, at that time, he was already in 6-week treatment with ruxolitinib and was referring clinical improvement to his baseline: 3 non-bloody bowel movements per day. An added immunosuppressive treatment was again refused and close clinical and biochemical follow-ups were agreed with the patient.

Six months after ruxolitinib treatment was started, blood tests normalized and FC showed a progressive drop to 323 mg/kg. He also showed a weight gain of 5-kg. No further budesonide cycles were needed. Colonoscopy showed diffuse ulcerative ileitis affecting 25% of the circumference of the anastomosis, and erythema and aphthous lesions in the neoterminal ileum up to 5-cm (Rutgeerts score i3). In addition, polycythemia vera was showing satisfactory evolution with significant decrease in splenomegaly.

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We want to emphasize the patient's inflammatory activity background when reporting this evolution since ruxolitinib was started. As exposed, we could observe a steady clinical remission for six months and an obvious endoscopic improvement related to ruxolitinib treatment, with more than 50% reduction of ulcerated mucosa in both ileocolonic anastomosis and neoileum. Despite these favorable results, due to persistent Crohn's disease activity, the patient's past evolution and comorbidity, we raised again to the patient the need for active treatment. Ustekinumab was chosen because of its security profile and no remarkable interactions with ruxolitinib when checking both data sheets. After multidisciplinary consensus and with the patient approval, ustekinumab treatment was started without stopping ruxolitinib.

References

1. Vermeire S, Schreiber S, Petryka R, Kuehbacher T, Hebuterne X, Roblin X, et al. Clinical remission in patients with moderate-to-severe Crohn's disease treated with fi lgotinib (the FITZROY study): results from a phase 2, double-blind, randomised, placebo-controlled trial. Lancet. 2017;389:266–75.
2. Sandborn WJ, Feagan BG, Loftus EV Jr, Peyrin-Biroulet L, Van Assche G, Armuzzi A, et al. Efficacy and safety of upadacitinib in a randomized trial of patients with Crohn's disease. Gastroenterology. 2020;158:2123–38.
3. Bryan JC, Verstovsek S. Overcoming treatment challenges in myelofibrosis and polycythemia vera: the role of ruxoilitinib. Cancer Chemother Pharmacol. 2016;77:1125–42.
4. Zeiser R, von Budnoff N, Butler J, Mohty M, Niedervwieser D, Or R, et al. Ruxolitinib for glucocorticoid-refractory acute graft-versus-host disease. N Eng J Med. 2020;382:1800–10.

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