(21317) - INDUCTION OF REMISSION OF ULCERATIVE COLITIS WITH THE COMBINATION OFTACROLIMUS AND USTEKINUMAB - A CASE REPORT

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Introduction: Over time, concerns regarding the safety profile of tacrolimus have led to its decreased utilization in the treatment of ulcerative colitis (UC). However, improved understanding of its usage have highlighted its potential as a significant therapeutic option for inducing remission and the decision to its use should be made on a case-by-case basis,considering the individual patient's condition and weighing the benefits against the associated risks. Meanwhile, ustekinumab has emerged as a therapeutic option due to its demonstrated efficacy in inducing remission inUC. The synergistic action of tacrolimus and ustekinumab has shown promising results in achieving remission in patients who have not responded to other treatments. Nevertheless, the selection of appropriate cases for this combination therapy aswell as the reasons behind its potential effectiveness became a hot-topic in UC**.** Despite the growing interest in this therapeutic approach, there is a lack of formal evidence in the literature regarding the efficacy of combination therapy with oral tacrolimus and ustekinumab.

Aim: Our aim is to present a case report of a patient who experienced clinical and biochemical remission with the combination therapy of oral tacrolimus and ustekinumab, despite having failed multiple biologic therapies in the past; tohighlight the potential effectiveness of this combination therapy as an alternative for patients with refractory inflammatory bowel disease (IBD).

Case report: An 18-year-old woman with a 1-year diagnosis of left-sided UC, with multiple admissions due to disease exacerbation or infections, refractory to infliximab (with azathioprine) and currently under treatment with vedolizumaband tacrolimus, was admitted with a severe disease exacerbation. Due to a history of neuropsychiatric side effects from corticosteroids, it was decided to postpone its start and tofacitinibwas initiated as an alternative treatment. However, over the

course of 6 days, there was no clinical improvement of UC. Blood tests revealed persistent moderate peripheral eosinophilia (3000 cells/mm3) and mild acute kidney injury. As a result, tofacitinib was temporarily suspended, which led to a rapid normalization of renal function and eosinophil levels. Tofacitinib was restarted after a 2-day suspension, but the patient experienced moderate eosinophilia (2000 cells/mm3) recurrence, which was considered an adverse effect to tofacitinib, leading to its suspension with eosinophilia resolution. Given the severity of the disease, after a multidisciplinary team discussion, it was decided to start high-dose corticotherapy and ustekinumab with maintenance therapy every 4 weeks, and to add tacrolimus. Prophylactic antibiotic therapy with trimethoprim and sulfamethoxazole was also administered due to the triple immunosuppression. The patient received intravenous ustekinumab at a dose of 6 mg/kg, followed by subcutaneous ustekinumab maintenance therapy of 90 mg every 4 weeks. Oral tacrolimus was titrated to therapeutic levels, with induction doses ranging between 10 and 15 ng/mL and maintenance doses between 5 and 10 ng/mL. The initial dose of tacrolimus was gradually increased to reach the induction target, but due to neuropathic pain in the right foot, the maximum level that could be reached was 7-8 ng/mL. To address the pain, the patient was prescribed pregabalin, which successfully resolved the symptom. After therapeutic adjustment, the target maintenance doses of tacrolimus were achieved without any further events. This combination therapy resulted in the achievement of both clinical and biochemical remission, leading to the patient's discharge from the hospital. Corticosteroid therapy was gradually tapered off while maintenance therapy with tacrolimus and ustekinumab continued. After one year, the patient remained in remission and was scheduled for endoscopic reassessment to evaluate mucosalhealing.

Relevance: Despite increasing availability of biologic and small molecule treatment options for UC, non – response or lossof response remains a challenging clinical problem. Although larger scale studies are needed, this case report demonstrates the potential effectiveness of combination therapy with oral tacrolimus and ustekinumab in inducing and maintaining remission in patients with moderate to severe refractory UC. These findings suggest that combination treatment can serve as a valuable alternative for patients with refractory IBD.

Palavras-chave : Ulcerative colitis, Tacrolimus, Ustekinumab