RESPONSE TO USTEKINUMAB IN PATIENT WITH CROHN’S DISEASE AND PSORIASIS INDUCED BY ANTI-TNF

INTRODUCTION

• Therapy with tumour necrosis factor α (TNF) inhibitors have revolutionized the treatment of Crohn’s disease no responders or intolerant to classic immunosuppressants and also in the management of perianal disease. Only infliximab and adalimumab are authorized for use in patients with inflammatory bowel disease. However, different paradoxical cutaneous side effects have been described for anti-TNF α therapy such as psoriasis. Treatment of these instances of paradoxical psoriasis often requires withdrawal of the drug, which may lead to recurrence or persistence of the rash and loss of the therapeutic effect on underlying disease.

• Ustekinumab is a monoclonal antibody approved for the treatment of moderate-severe psoriasis in plaques that binds to the interleukin 12 and 23 p40 subunit, these interleukins are also involved in the pathophysiology of Crohn's disease.

• Our case adds to another few cases described in the literature, outside clinical trials, patients with Crohn's disease and anti-TNF-induced psoriasis treated with ustekinumab, supporting the effectiveness of the use of this drug in the control of both entities.
• 39-year-old woman who developed in July 2011 itchy scaly lesions on external auditory canals, oral comissures, perinasal region, genital region, interglutea region and lower limbs after 12 months of treatment with adalimumab for Crohn’s disease.

• Physical examination showed scaly plaques on both ears, nostrils, genital area and knees (fig 1A, 2A, 3A). The histology of the lesions was compatible with psoriasis. The rest of the complementary studies were normal. Anti-TNF-induced psoriasis were suspected, so adalimumab was stopped.

• She received several treatments since she was diagnosed. She tried topical corticosteroids. She also began treatment with acitretin 10 mg per day that was suspended for digestive intolerance. Methotrexate 7.5 mg per week was increased up to 15 mg/week without improvement. In January 2012 she iniciated with cyclosporin 200 mg once a day for 2 months with large clearance of lesions, but it must be abandoned due to intense headache. At this time, gastrointestinal disease worsened with increased of daily bowel movements. Thus, in April 2012 a decision was made to start ustekinumab treatment to initial dose of 45 mg subcutaneous (s.c), followed by 45 mg 4 weeks later and later every 12 weeks. 3 weeks after starting the drug, she showed an almost complete disappearance of the cutaneous lesions, maintaining a complete remission of the digestive disease and cutaneous lesions after 8 weeks (fig. 1B, 2B, 3B). Due to recurrence of scaly lesions on ears, dosage of 45 mg was increased every 8 weeks with complete resolution of them.

• 15 months after starting ustekinumab, the patient has no digestive of cutaneous symptoms.


DISCUSSION

- Since the introduction of anti-TNF inhibitors in the treatment of inflammatory bowel, rheumatic and skin diseases, several cases of adverse skin reactions have been reported.

- The mechanism by which occurs is not well elucidated. Psoriasis induction or exacerbation of a pre-existing psoriasis is one of the most common cutaneous side effects. It is postulated that inhibition of TNF-α can induce overexpression of cutaneous IFN-α, which lead to predispose to psoriasis.

- In the majority of cases topical treatment is effective in the treatment of cutaneous lesions, however, it can be necessary to stop anti-TNF drug with the risk of relapse of inflammatory bowel disease.

- Ustekinumab is a human monoclonal antibody anti-interleukins 12 and 23 approved for the treatment of moderate-severe plaque psoriasis, currently is being conducted a clinical trial phase III of ustekinumab in Crohn's disease, with higher doses to those used in psoriasis, demonstrating its efficacy in this disease. In our case, given the persistence of psoriasis despite oral and topical treatment and evidence of poor control of Crohn's disease, we decided the administration of ustekinumab. Our patient has controlled gastrointestinal underlying disease and achieved clinical clearance of cutaneous lesions with ustekinumab 45 mg subcutaneous every 8 weeks.
CONCLUSION

Ustekinumab may be an effective therapeutic alternative in the treatment of patients with multi-drug resistant Crohn's disease who develop paradoxical psoriasis by anti-TNF, gaining control of cutaneous and gastrointestinal symptoms.

References.-