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Successful treatment with tofacitinib in Spondyloarthritis associated Uveitis

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Vinicki JP,[1] Montagna GF[2]
[1]Unidad de Reumatología, Hospital de Quilmes, Buenos Aires, Argentina
[2]Servicio de Oftalmología, Hospital Santa Lucía, Buenos Aires, Argentina

Correspondence: Juan P Vinicki MD, Hospital address: 770, Allison Bell, Quilmes (1878), Buenos Aires, Argentina, Tel + 54 9 11 3627 2155, Email jpvinicki@hotmail.com

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Uveitis remains the third leading cause of preventable blindness in the developed countries and almost 22% of patients meet the criteria for legal blindness at some point in their follow up.[1,2] Delay in presentation to a subspecialist and therefore the start of treatment is associated with poor visual outcomes.[3] In those patients who are refractory to, or dependent on, topical glucocorticoids and have severe forms of the disease, methotrexate (MTX) is the usual first-line systemic immunosuppressive agent, followed by tumor necrosis factor inhibitor (TNFi) biologics, particularly the monoclonal antibodies infliximab and adalimumab (ADA).[4,5] There is a desperate need for new treatments in those patients who fail to reach control and remission of disease or develop treatment intolerance.

Here, we report a patient with unilateral anterior uveitis (UAU) with intolerance, adverse effect or insufficient response to 3 treatment strategies but achieving a successful therapeutic response with tofacitinib (TOF). Activity of uveitis terminology (worsening, improved and remission) applied in our daily clinical practice are according to SUN criteria.[6]

A 55-year-old patient with a diagnosis of UAU is referred by Ophthalmology to define probable association with an underlying systemic disease and initiation of immunosuppressive therapy due to insufficient response to local treatment with eye drops (anterior chamber cells grade 2+). On physical examination, the patient presented in addition to uveitis, left sacroiliitis, right plantar fasciitis and bilateral inflammation of the Achilles tendon. The MRI showed unilateral sacroiliitis. Elevated ESR and positive HLA-B35 and HLA-B44 were found in the laboratory. Colonoscopy step biopsy showed histology suggestive of ulcerative colitis (UC) despite the fact that the patient had no symptoms. The clinical picture was interpreted as UAU secondary to axial spondyloarthritis (SpA) associated with colonic mucosal inflammation (asymptomatic UC?).

The patient started prednisone (PDN) 0.5 mg/kg/day and SC methotrexate 25 mg per week. PDN was tapered and finished after 3 months of treatment continuing only with MTX achieving remission of her UAU (anterior chamber cells grade 0) despite the fact that enthesitis required rescue with NSAIDs that responded favorably. At the end of the third month of treatment, she started with left hip pain secondary to avascular osteonecrosis (ON) with a good response to conservative therapy. After 1 year with MTX, and despite continuing in remission from the UAU she developed intolerance to the drug adding arthritis of the left knee and NSAID-refractory enthesitis. Although restarting corticosteroids was an option, the previous history of avascular ON limited its use and the activity of the disease despite MTX required progress in treatment strategy. She started ADA 40 mg SC every 15 days, achieving joint and enthesis remission with no relapse of her uveitis, but due to recurrent infections (1 episode of pharyngitis and 3 episodes of bacterial pneumonia without hospitalization requirement in a period of 10 months) it had to be withdrawn. Certolizumab pegol 200 mg SC every 15 days was started but not only she presented recurrent infections (3 episodes of pharyngitis and 1 episode of bacterial pneumonia without hospitalization requirement in a period of 6 months), the uveitis got worse (anterior chamber grade 1+) with reactivation of arthritis and enthesitis. Short courses of low-dose corticosteroids despite the history of avascular ON were necessary to achieve relative control of arthritis, enthesitis and uveitis in addition to dependence on topical corticosteroids. After this, we decided to change the mechanism of action of the drug. She was initiated on TOF extended-release 11 mg daily. After 4 weeks of treatment, uveitis, enthesitis and arthritis achieved remission. The patient was able to stop taking corticosteroids rescues at the end of the first month of treatment. After 1 year of follow-up, the patient did not present intolerance to the drug, ocular or extra-ocular relapse or infections.

Topical TOF three times a day reduced intraocular inflammation in an experimental autoimmune uveitis model.[7] It markedly suppressed the expression of many inflammatory chemokine and chemokine receptors in ocular tissues, and reduced infiltration of immune cells and subsequent tissue damage. Little evidence is currently available on the use of JAK inhibitors (JAKi) in the treatment of ocular inflammation. There is only some published case report of JAKi for Juvenile Idiopathic Arthritis (JIA) associated uveitis.[8–10] TOF is currently also under investigation with respect to uveitis in patients with polyarticular course of JIA in children and adolescent subjects (NCT02592434) but no results have been presented to date.

In the 2019 ACR-SAA-SPARTAN recommendations, TOF, currently not approved for axial SpA, is highlighted as a potential second-line option for patients with prominent peripheral arthritis and contraindications to a TNFi.[11] TOF is an approved treatment for ulcerative colitis.[12] This is why TOF was defined as a therapeutic option in our patient, instead of IL-17 inhibitors (secukinumab and ixekizumab) or IL-12/23 inhibitors (ustekinumab). Secukinumab and ixekizumab are not recommended in patients with IBD or recurrent uveitis.[11] Ustekinumab, demonstrated successful results in some case reports of noninfectious uveitis.[13,14] A phase 2 clinical trial evaluating

the efficacy and safety of ustekinumab for the treatment of Behçet disease is currently ongoing (NCT02648581).

New therapeutic options in patient with SpA associated uveitis with contraindication, adverse effect or insufficient response to MTX and/or ADA are necessary. Adequately designed studies are necessary in order to assert our clinical experience.

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Conflicts of interest

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