Intermediate Uveitis in an HLA-B27-Positive Patient Treated with Upadacitinib

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Intermediate Uveitis in an HLA-B27-Positive Patient Treated with Upadacitinib

Intermediäre Uveitis bei einem HLA-B27-positiven Patienten, der mit Upadacitinib behandelt wurde

Background

Janus activated kinases (JAKs) are a family of intracellular tyrosine kinases that function as intracellular mediators of multiple cytokines and growth factors involved in the pathogenesis of inflammation and immune-mediated diseases. Many JAK inhibitors (JAKinibs) have been developed over recent years and they have emerged as a new therapeutic class for immune-mediated inflammatory diseases. Tofacitinib (Xeljanz, an anti JAK1-JAK3 agent) and baricitinib (Omlumiant, an anti JAK1-JAK2 agent) are first-generation JAKinibs. Upadacitinib (Rinvoq) is a specific, newer Janus kinase (JAK-1) inhibitor recently approved for the treatment of inflammatory disorders such as rheumatoid arthritis, ankylosing spondylitis, atopic dermatitis, and psoriatic arthritis [1–4]. However, few data are available on the use of these recent therapies in the management of ocular inflammation.

History and Signs

A 33-year-old HLA B27-positive woman was referred for persistent bilateral anterior uveitis and macular edema, unresponsive to a treatment of oral steroids and adalimumab 40 mg every other week. HLA B27 was tested when she was 20 in the presence of right sacroiliitis (spondyloarthropathy). At the initial visit, best-corrected acuity (BCVA) was 1.0 in the right eye (RE) and 0.63 in the left eye (LE). Fundus examination revealed the presence of a bilateral intermediate uveitis, associated with a peripheral retinal vasoproliferative tumor (▶ **Fig. 1**). Optical coherence tomography (OCT) confirmed the persistence of macular edema in both eyes (▶ **Fig. 2a**). One month later, she developed a paradoxical tumor necrosis factor (TNF) inhibitor-induced psoriasis, secondary to adalimumab.

Due to recent the onset of skin lesions, which appeared 6 months after the introduction of adalimumab therapy, the patient was referred to a rheumatologist who could detect during rheumatologic examination the presence bilateral knee synovitis. The skin lesions were compatible with the diagnosis of parapsoriasis induced by anti-TNF therapy.

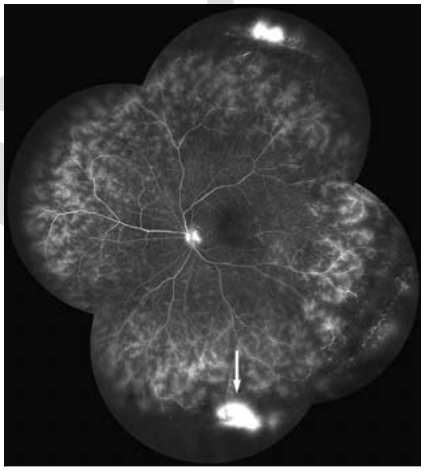
Therapy and Outcome

Because of the treatment failure of uveitis and the onset of parapsoriasis, systemic adalimumab was switched to upadacitinib (Rinvoq) 15 mg/day and oral prednisone 20 mg/day with progressive tapering of corticosteroids. Upadacitinib was chosen due to its recent approval for the treatment of inflammatory disorders such as ankylosing spondylitis and because of a decrease in the incidence of uveitis in patients treated with JAKinhibs. One month later, BCVA had improved from 1.0 to 1.25 (RE) and from 0.63 to 1.25 (LE). The central foveal thickness, initially 297 µm in the RE and 410 µm in the LE, had decreased to 281 µm and 294 µm, respectively (▶ **Fig. 2b**), despite the steroid tapering from 20 mg to 5 mg/day. Six months after adalimumab had been discontinued, the psoriatic lesions had resolved. At the last follow-up, 8 months after starting treatment with upadacitinib, the patient did not present recurrent intraocular inflammation or macular edema despite cancellation of corticosteroid therapy.

Discussion

We report the successful treatment of a patient with HLA-B27-positive spondyloarthropathy, whose noninfectious intermediate uveitis and macular edema had been refractory to adalimumab 40 mg every other week and who had developed parapsoriasis. She was switched to upadacitinib 15 mg/day, and her ocular inflammation showed significant clinical improvement 4 weeks later, with a disappearance of her cutaneous lesions after 6 months.

Uveitis is a frequently occurring extra-articular manifestation of spondyloarthropathies, which tends to express as a recurrent anterior uveitis, but can be associated with posterior uveitis in up to 20 % of cases [5]. The presence of a vasoproliferative tumor in patients with an intermediate uveitis reveals a long ongoing inflammatory process and justifies the use of immunosuppressive therapies to control inflammation [6]. Specific therapy of vasoproliferative tumors is determined by the size of the lesion (tumor height). In small lesions, laser photocoagulation is performed, cryocoagulation is used in lesions less than 1.5 mm, and ruthenium radioactive plates are used in larger lesions. A sys-



▶ **Fig. 1** Panoramic fluorescein angiography (LE) reveals severe peripheral leakage and papillitis. The hyperfluorescent inferior mass (white arrow) corresponds to a peripheral vasoproliferative tumor (H = 1.13 mm on B-scan ultrasonography), a classic complication of chronic intermediate uveitis.

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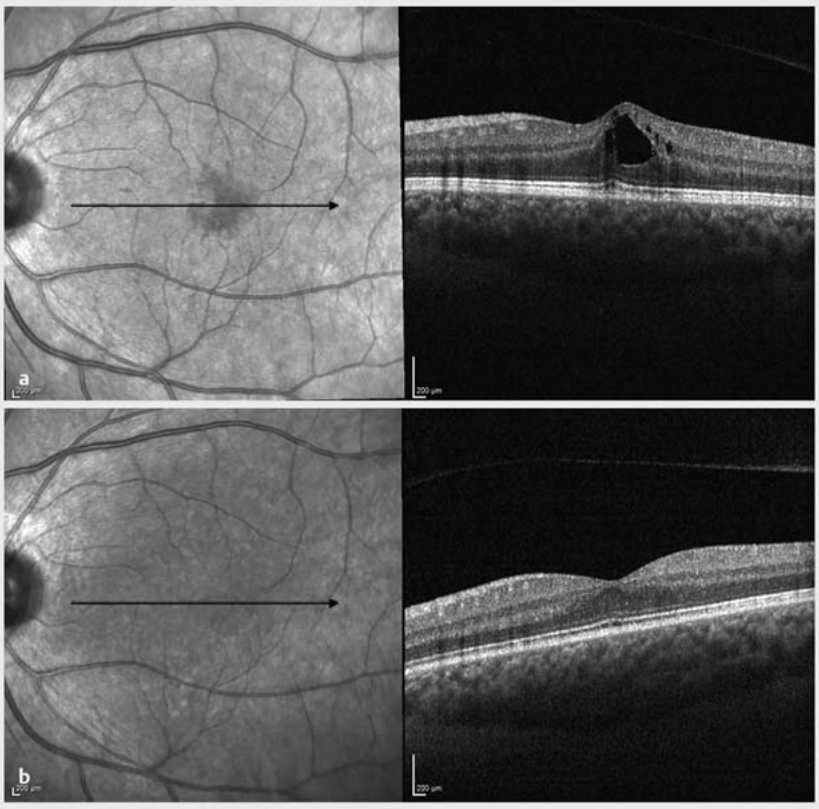

▶ **Fig. 2** B-scan optical coherence tomography (OCT) before (**a**) and 1 month after starting treatment with upadacitinib (**b**).

temic treatment is usually warranted for cases with intermediate, posterior, or pan uveitis. However, when conventional disease-modifying antirheumatic drugs (cDMARDs) and biologic disease-modifying antirheumatic drugs (bDMARDs), such as anti-TNF-α, are not efficacious or not tolerated, the management of noninfectious uveitis can be challenging.

Data in the literature on the specific use of upadacitinib in ocular inflammation are lacking. However, a few studies and case reports show encouraging results for other JAKinibs. In an experimental autoimmune uveitis (EAU) model, a systemic treatment with tofacitinib, a first-generation JAKinhib, was found to inhibit the development of EAU and reduce the level of secreted IFN-γ [7]. An adult patient with severe juvenile idiopathic arthritis-associated anterior uveitis was successfully treated with tofacitinib, with a resolution of his macular edema after 1 year of treatment [8]. Another study reports good results in treating two patients with tofacitinib, one with scleritis and another with anterior and intermediate uveitis, refractory to multiple steroid-sparing therapies [9]. A recent study documents four cases where JAKinhibs proved to be efficacious in juvenile idiopathic arthritis and/or its associated uveitis, which had been uncontrolled and refractory to different conventional and biologic DMARDs [10]. One patient was treated with tofacitinib and the three others with baricitinib, and they experienced an improvement of their uveitis.

Upadacitinib may provide a new therapeutic alternative for patients with intermediate or posterior uveitis associated with spondyloarthropathies, particularly when they are not adequately responding or do not tolerate the conventional or biologic DMARDs. They could also be useful in patients that have contraindications to TNF inhibitors, such as congestive heart failure or a concomitant demyelinating disease. Further studies are needed to determine the indications, safety, and efficacy of upadacitinib and other JAKinibs in ocular inflammatory diseases. Ongoing studies are comparing the efficacy of baricitinib versus adalimumab in juvenile idiopathic arthritis-related uveitis (www.clinicaltrials.gov).

Conflict of Interest

The authors declare that they have no conflict of interest.

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