Successful use of upadacitinib in a 14-year-old patient with juvenile idiopathic arthritis-associated uveitis and hidradenitis suppurativa

Sirs,

Janus Kinase inhibitors (JAKi), small molecules orally administered, showed potential alternatives for children with autoimmune disorders (1). Upadacitinib, a second-generation selective JAKi targeting JAK1, JAK2, JAK3 and TYK2, approved in Europe for adult patients with rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis, atopic dermatitis and ulcerative colitis, is off-label for juvenile idiopathic arthritis (JIA), and paediatric non-infectious uveitis. Nonetheless, in the last few years, it has been used with promising results in other inflammatory disorders, particularly inflammatory bowel diseases (IBD) (2). Here, we present the case of a JIA patient with uveitis, cutaneous vasculitis and hidradenitis suppurativa (HS), successfully treated with upadacitinib.

At 1 year old, she was diagnosed with polyarticular JIA, antinuclear antibody (ANA) positive, and experienced her first episode of anterior uveitis after 6 months from the disease onset. She received methotrexate (15 mg/m^2 weekly, subcutaneously), but, due to the failure to achieve articular and ocular remission, subcutaneous adalimumab 20 mg every two weeks was rapidly added, leading to persistent ocular and articular remission (Fig. 1). After a long period of clinical remission, at 8 years old, adalimumab was slowly tapered and then discontinued in 10 months along with methotrexate. After 4 months from drug withdrawal, arthritis and anterior uveitis flared again, thus immunosuppressive treatment was reintroduced. At 11 years old, she developed diffuse psoriasis on her scalp, retro-auricular folds, and palmoplantar region, which was initially treated with topical steroid therapy. In the suspect of adalimumab-induced paradoxical psoriasis and due to the worsening of the cutaneous disease along with the long articular and ocular remission, adalimumab was tapered. However, during the tapering, the patient developed painful abscesses in the suprapubic region and at the inguinal folds and she was diagnosed with HS that was initially treated with antibiotic (oral clindamycin). After about 3 months, she developed a cutaneous vasculitis on her lower limbs and a skin biopsy was performed, revealing a leukocytoclastic vasculitis characterised by perivascular chronic inflammatory infiltrates and perivascular deposits of immunoglobulin (Ig) M and C1q. She was treated with oral steroid therapy and, due to the exacerbation of the skin lesions during steroid tapering, immunomodulant treatment with azathioprine was started (150 mg/day)

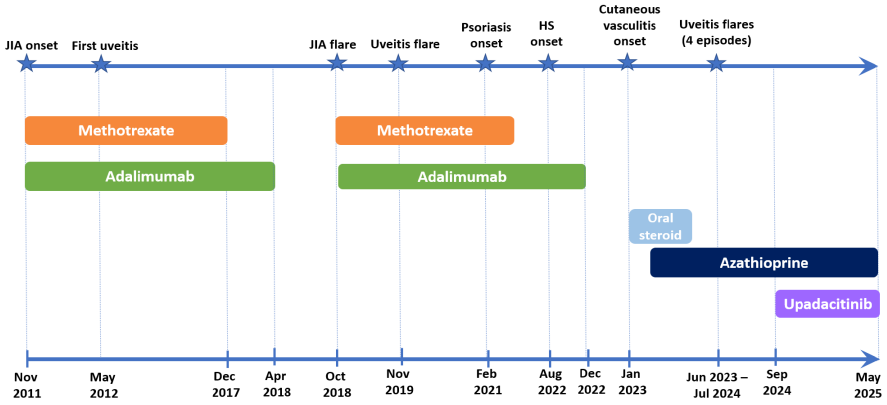

Fig. 1. Timeline of disease course and treatments.

with a rapid improvement. However, the HS was not completely controlled, especially at the inguinal folds. At 13 years old, after about 4 years since the last uveitis episode, a flare of anterior uveitis occurred, which was treated with topical steroid drops. Over the following 12 months, she developed 3 additional ocular relapses and a worsening of the HS. Upadacitinib was started at a dosage of 15 mg/day, and a rapid improvement of the skin lesions and no new episodes of uveitis occurred. At last available follow-up at 8 months since starting upadacitinib (Fig. 1), she is still in complete clinical remission on medication, with no adverse event and/or side effects.

Upadacitinib data in children with autoimmune disorders is still limited, and no data are available for treating chronic uveitis. Indeed, at the moment the results of an open-label Phase 1 trial published in 2024 (3), conducted on 57 children aged 2 to 18 years with pJIA, showed that upadacitinib was efficacious and well tolerated. Notably, no patients had a history of uveitis. However, a case report of an adult patient with JIA-associated uveitis (JIA-U) (4) was successfully treated with upadacitinib. Additional data are available regarding the use of JAKi in the management of paediatric non-infectious uveitis, but none with upadacitinib that was used only in adult patients with uveitis (4-8). Considering that each JAKi acts by a different profile of selectivity, efficacy and safety might be different among the different specific drugs in different clinical settings.

Intriguingly, our patient showed a complex picture of the disease, which also included skin involvement in terms of vasculitis and HS; upadacitinib resulted able to manage all these different aspects of the disease. Based on the literature data, upadacitinib has been shown to be effective in treating atopic dermatitis in children (9) and a phase 2, randomised, placebo-controlled study (10), conducted in adult HS described the successful use of this drug.

Nonetheless as a single case report, upadacitinib might be considered a promising treatment approach in children with refractory JIA-U and HS. To the best of our knowledge, this is the first case of the use of upadacitinib in a paediatric patient with JIA-U and HS. Further observations are needed to confirm this preliminary observation.

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