Dermatology Practical & Conceptual

Upadacitinib for Treatment-Resistant Urticarial Vasculitis: A Case Study and Therapeutic Insight

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Introduction

Urticarial vasculitis (UV) is a rare entity characterized by recurrent episodes of wheal-like lesions and evidence of leukocytoclastic vasculitis on skin biopsy. Although its etiopathogenesis remains undefined, it seems to be driven by a type III immune reaction, and its treatment is often challenging [1].

Case Presentation

A 77-year-old woman presented for itchy urticarial lesions, widespread on the limbs and trunk, that had been present for about 15 years with a chronic relapsing course. She had a history of chronic urticaria, psoriatic arthritis, and mild psoriasis vulgaris that had been effectively treated over the years with corticosteroids, antihistamines, and cyclosporin, which was gradually tapered due to prolonged remission. After a SARS-CoV-2 infection, the patient reported a flare of oligoarthritis [Disease Activity in PSoriatic Arthitis (DAPSA) 28], which was treated with methotrexate, then discontinued due to gastrointestinal intolerance, and subsequently with adalimumab 40 mg every other week. After three months of treatment with adalimumab, a partial improvement in arthritis was observed (DAPSA 18), despite a severe worsening of urticarial skin lesions, whereby the patient came to our attention. On skin examination, diffuse pinkish and orange-colored wheals were present on the limbs and trunk, associated with ecchymotic hyperpigmentation (Figure 1A–C). No sign of psoriasis was present [Psoriasis Area and Severity

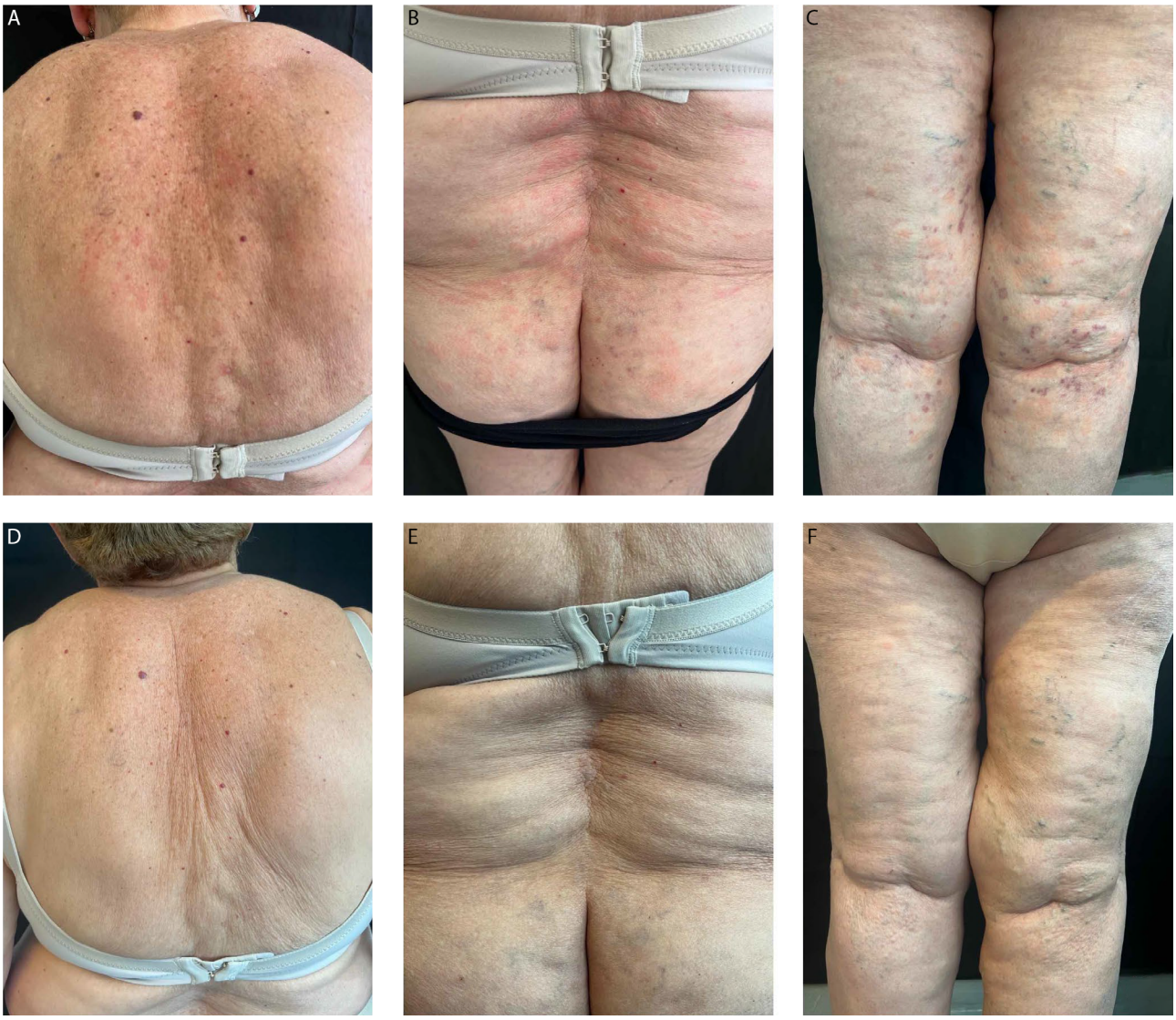

Figure 1. (A-C) Clinical appearance at presentation: wheal-like lesions widespread on the limbs and trunk associated with ecchymotic hyperpigmentation. (D-F) Complete remission of skin lesions after three months of treatment with upadacitinib.

Index (PASI) 0]. Upon considering the persistence of the lesions present longer than 24 hours, their color, and failure to disappear upon pressure, urticarial vasculitis was suspected, and a biopsy was performed, showing leukocytoclastic vasculitis. Blood examinations revealed increased C-reactive protein, normal C1q and complement levels as well as negative autoimmunity antibodies screening. Based on clinical and histopathologic data, a diagnosis of UV was made. Therapy with adalimumab was suspended and upadacitinib 15 mg daily was started. After one month, the patient reported partial improvement of cutaneous and articular symptoms, with clear worsening eight hours after taking medication. Therefore, we decided to increase the dosage of upadacitinib to 15 mg twice a day, resulting in complete remission of urticarial lesions and significant improvement in artrithis (DAPSA 5), at follow-up after three months (Figure 1D–F).

Conclusion

Upadacitinib is a selective JAK-1 inhibitor recently approved for the treatment of psoriatic arthritis and atopic dermatitis. Nevertheless, the drug targets multiple inflammatory cytokines involved in the pathogenesis of various inflammatory diseases [2]. With regard to JAKi, the literature reports a successful use of the pan-JAKi tofacitinib in one case of UV [3] and in one case of leukocytoclastic vasculitis [4]. However, evidence of the role of the JAK/STAT pathway in cutaneous vasculitis is increasingly growing. Several studies have reported the involvement of the JAK/STAT pathway in ANCA-associated vasculitis [5] as well as in leukocytoclastic vasculitis. Indeed, Ebata et al. recently demonstrated, by immunofluorescence, a significantly increased expression of phosphorylated JAK1/JAK2 in skin

samples of cutaneous leukocytoclastic vasculitis compared to healthy controls [6].

Our case provides evidence of the promising efficacy of upadacitinib for the treatment of refractory UV and also highlights the potential of this drug in cases featuring multiple concomitant immune-mediated comorbidities, quite frequent in clinical practice, thanks to its pleiotropism of action. Nevertheless, further investigations should be encouraged to determine the role of the JAK/STAT pathway in UV and the possible effective and safe use of JAKi in this condition.

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