Treatment of refractory psoriasis with dermatomyositis using upadacitinib

Sirs,
Psoriasis is a chronic inflammatory skin disease characterised by erythematous plaques with adherent scales, which are sometimes accompanied by pruritus. Traditional treatments include local or systemic steroids, retinoids, and immunosuppressants. Activation of the JAK-STAT pathway is an important mechanism in its pathogenesis (1).

Dermatomyositis is an autoimmune disease with skin features including Gottron’s papules, symmetrical purplish-red peri-orbital oedema, V-sign on the neck, and Shawl sign, and is characterised by muscle damage giving rise to muscle pain, swelling, tenderness, and weakness in the extremities. Traditional treatment involves systemic steroids and immunosuppressants. Its pathogenesis is mainly related to activation of interferon (IFN)-α, which binds to IFN receptors, which then activate signal transduction by phosphorylating JAK1, TYK2, and STAT1/3 intracellularly (2).

Upadacitinib is an inhibitor of Janus kinase 1 (JAK1) of high selectivity, with 593-, 1860-, and 2715-times greater selectivity for JAK1 than for JAK2, JAK3, and TYK2, respectively. It is used to treat moderate-to-severe atopic dermatitis (3). This article reports a case of refractory psoriasis with dermatomyositis demonstrating a positive response to oral upadacitinib and the treatment was well tolerated.

A 41-year-old woman with a 27-year history of psoriasis started experiencing weakness, dyspnoea, joint pain, and lower-extremity swelling 6 months earlier but did not receive treatment. She presented 4 months later with generalised erythema with adherent scales and pruritus without any obvious cause. After receiving seven injections of adalimumab, she developed symmetrical purplish-red peri-orbital oedema, a V-sign on the neck, and the Shawl sign. She also had large purplish-red skin lesions covering almost 60% of her body, muscle pain, swelling, tenderness, and weakness in the extremities (Figs. 1 a,b). She had muscle strength of level 4, ANA+ (1:1000), creatine phosphophatase kinase concentration of 291 U/L, creatine kinase isoenzyme concentration of 41 U/L, and lactate dehydrogenase concentration of 556 IU/L. Histopathology showed lattice-like keratosis, incomplete keratosis, incomplete granular layer, mild hyperplasia of the epidermis, and keratinized cell necrosis in the epidermis. Blood vessels in the dermal papillae were dilated, and perivascular eosinophilic and mononuclear cells infiltrated the entire thickness of the dermis (Figs. 2 a,b). Magnetic resonance imaging showed abnormal signals in the skin, muscles, and interstitial spaces of the thighs and calves bilaterally, indicating inflammatory exudates and soft-tissue swelling (Fig. 3).

We considered a diagnosis of psoriatic disease complicated with dermatomyositis. After discontinuing adalimumab, intramuscular betamethasone and oral steroids were ineffective. Therefore, the patient was prescribed oral upadacitinib at 15 mg/day. After one month of treatment, the sizes and coverage of the purplish-red skin lesions significantly reduced (Figs. 4 a,b). Her muscle strength improved. Her creatine phosphate kinase, creatine kinase isoenzyme, and lactate dehydrogenase concentrations were 112 U/L, 26 U/L, and 317 IU/L, respectively. Magnetic resonance imaging showed improvement of the inflammatory exudate and soft tissue swelling, and the patient remains under follow-up (Fig. 5).

Fig. 1. 1a. Purplish-red patches on the skin. 1b. Bilateral lower limb oedema. 2a, 2b. Histopathological images supporting the diagnosis of psoriasis after initial treatment and dermatomyositis. 3. Before treatment with Upadacitinib, MRI of the lower limbs showing extensive inflammation. 4a, 4b. The purplish-red patches have resolved, the inflammation has subsided, and the oedema has disappeared. 5. After one month of treatment with Upadacitinib, follow-up MRI of the lower limbs showing reduced inflammation.
The patient in this case had a complicated medical history with a poor response to traditional treatments, which seriously affected her quality of life. To alleviate the symptoms quickly, upadacitinib was chosen as an effective treatment method after obtaining the patient’s verbal consent.

Adalimumab is a biological agent commonly used in clinical practice to treat various skin- and immune-related diseases. Although some studies have shown that adalimumab can treat dermatomyositis (4), some data suggest that it can worsen this condition (5).

JAK1 and TYK2 are primarily involved in the development of psoriasis (6). In the past five years, 39 cases of dermatomyositis have shown improvement after treatment with non-selective JAK inhibitors (7). Since the JAK1-STAT pathway plays a critical role in psoriasis and dermatomyositis, upadacitinib, a highly selective JAK1 inhibitor, can effectively alleviate skin symptoms and improve muscle strength in patients with refractory psoriasis with dermatomyositis, while avoiding the adverse effects of non-selective inhibitors that can lead to JAK2 and JAK3 inhibition, adversely affecting erythropoiesis (8) and NK cells (9), respectively.

To date, we have found no reports of successful treatment of refractory psoriasis with dermatomyositis using upadacitinib. Since the JAK1-STAT pathway is widely activated in skin autoimmune diseases, upadacitinib may be an effective and safe option for treating refractory comitant skin autoimmune diseases with JAK1-STAT pathway activation.

References