SKIN

BRIEF ARTICLE

Cutaneous Manifestations of Parry Romberg Syndrome and Complete Resolution with Upadacitinib

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ABSTRACT

Parry Romberg Syndrome (PRS) is a rare, slowly progressive degenerative disorder, marked by the progressive atrophy of facial muscles. Immunosuppressive medications for the treatment of PRS vary in efficacy, and surgical intervention is often utilized for optimal treatment outcomes. Here, we report a case of a 37-year-old female patient with PRS who demonstrated significant improvement after treatment with upadacitinib. The patient presented to the clinic with an indent on the forehead and pain around the area, consistent with Parry Romberg syndrome. Following the initiation of 15 mg upadacitinib daily, and a subsequent increase in dosage to 30 mg upadacitinib daily, the indentation on her forehead resolved. This case highlights the utility of Janus kinase inhibitors as an effective treatment for PRS.

INTRODUCTION

Parry Romberg Syndrome (PRS) is an uncommon, degenerative disorder, marked by the progressive atrophy of facial muscles.[1] The disease typically begins in early childhood and may progress for 2-10 years before stabilizing.[1] Cutaneous manifestations of PRS vary widely in severity, and atrophy may progress to involve underlying fat, muscle, and osseocartilaginous structures.[2] The prevalence of PRS is approximately 1 in 250,000 and its etiology is unclear. Potential etiologies include previous trauma, a genetic predisposition, infection, sympathetic nervous system dysfunction, or the manifestation of scleroderma and other autoimmune diseases.[3] The treatment of PRS is primarily focused on surgical reconstruction of the affected areas by autologous grafting, using synthetic tissue fillers, and performing free tissue transplantation.[4] Immunosuppressive medications including methotrexate, mycophenolate mofetil, cyclosporine, and cyclophosphamide have also been utilized, but with varying degrees of success and often requiring surgical intervention.[5] Although Janus kinase inhibitors (JAKi) are not indicated for PRS, they have been utilized to treat inflammatory skin conditions and connective tissue diseases.[6] In this article, we report significant improvement for a patient with PRS after treatment with upadacitinib.

CASE REPORT

A 37-year-old female with a history of PRS presented to the clinic with an indentation on the forehead and pain around the lesion which had developed over the past three years (**Figure 1A**). Previous dermatologists had treated her with botox, cyclobenzaprine, and a supraorbital nerve block, all without adequate treatment response. Due to the lack of efficacy from previous treatments and the extent of the forehead lesion, we initiated treatment with 15 mg of upadacitinib daily. At her 6-week follow-up, she experienced gradual improvement in the areas of lesion involvement, and she was advised to increase the upadacitinib dosage to 30 mg daily. After four months of treatment, the patient's forehead indention was completely resolved (**Figure 1B**).

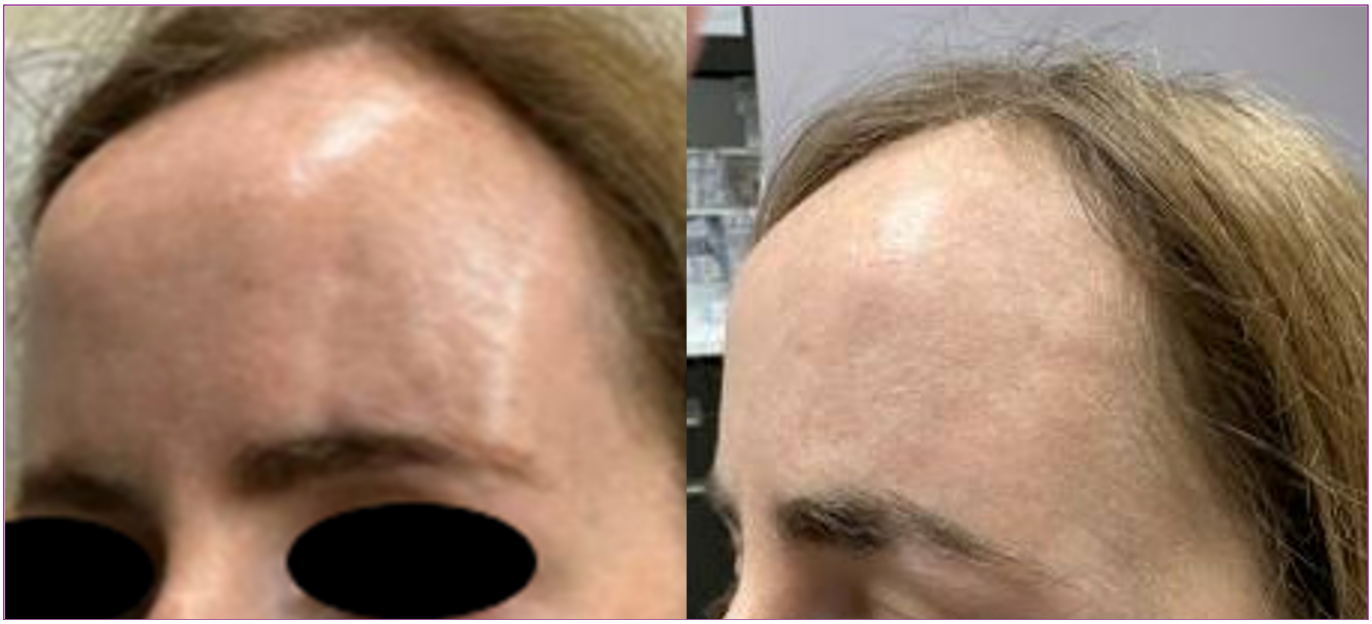

Figure 1. (A) Forehead lesion before initiation with upadacitinib 30 mg. (B) Resolved forehead lesion after initiation of upadacitinib 30 mg

DISCUSSION

JAKi are a class of therapeutics involved in the inhibition of the JAK/STAT signaling pathway.[7] Although there is limited literature demonstrating the use of JAKi for the treatment of PRS, they have been utilized for other connective tissue diseases including morphea and systemic sclerosis.[8] Notably, en coup de sabre and PRS share similar neurologic features and clinical presentations.[9] Furthermore, disease conversion of en coup de sabre to PRS has been previously reported, suggesting that these two diseases may exist on a continuum.[9] Mechanistically, JAK phosphorylates STAT proteins which initiates the transcription of profibrotic and proinflammatory genes.[8] JAK2 inhibitors have been shown to inhibit transforming growth factor (TGF)-β signaling, a cytokine involved in increased fibroblast proliferation and collagen deposition, in a dose dependent manner. Through this mechanism, sclerosis of the skin can be reduced as demonstrated in both in vitro and in vivo murine models.[8] Given that JAKi can be used for systemic sclerosis, this suggests that they may also be utilized for PRS due to its similarities with localized scleroderma. JAKi, including tofacitinib and ruxolitinib, have been previously used for the treatment of scleroderma and morphea.[8] A recent study

which utilized 1.5% ruxolitinib cream demonstrated remarkable resolution in a patient with suspected linear morphea presenting in an en coup de sabre configuration on her forehead.[10] Tofacitinib is an oral JAKi that targets the JAK1/JAK3 pathway, whereas ruxolitinib is a topical JAKi that inhibits the JAK1/JAK2 pathway. Upadacitinib is an oral JAKi targeting JAK1, which inhibits activation of IL-6, an essential pro-inflammatory interleukin.[11] Given the significant improvement of our patient on upadacitinib, and the favorable treatment outcomes associated with JAKi in the existing case reports, the JAK/STAT pathway may be a critical pathway for PRS disease progression. Ultimately, our case highlights that JAKi can be utilized for the treatment of PRS for reconstruction of the affected areas without requiring surgical intervention. Additional larger cohort studies are warranted to evaluate the efficacy of JAKi in treating PRS.

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