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CASE REPORT

Upadacitinib for the Treatment of Systemic Immune Co-Morbidity in One Case: Alopecia Areata, Vitiligo, Ankylosing Spondylitis, and Allergic Rhinitis-Asthma – Multifaceted Control

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Background: Immune-mediated inflammatory diseases (IMIDs) often coexist, but treatment options for multi-system comorbidities are limited. This report evaluated the efficacy and safety of the selective JAK1 inhibitor upadacitinib (UPA) in a patient with refractory alopecia areata (AA), vitiligo, ankylosing spondylitis (AS), and allergic asthma-nasal syndrome comorbidity.

Case Presentation: A 52-year-old male patient, who had not responded to previous treatments including glucocorticoids, immunosuppressants, and biologics, received UPA (15 mg once daily) for 12 weeks. After treatment, all systemic symptoms significantly improved: the Severity of Alopecia Tool (SALT) score for AA decreased from 15 to 0.9, the vitiligo lesions re-colored and stabilized, spinal joint mobility increased, and the frequency of nasal and asthma attacks decreased. The serum total IgE level decreased from 295 ng/mL to 243 ng/mL.

Conclusion: UPA achieved rapid and simultaneous improvements in this patient with refractory multi-system immune comorbidity. A transient liver function abnormality (ALT 478.6 U/L, AST 167 U/L) occurred during treatment, which was considered related to concomitant medication and resolved spontaneously after close monitoring and maintenance of the original regimen. This case suggests that UPA is effective for such complex comorbidities and has controllable safety under monitoring, providing a clinical basis for the "targeting upstream common pathways" strategy.

Keywords: upadacitinib, JAK inhibitor, ankylosing spondylitis, vitiligo, alopecia areata, allergic rhinitis-asthma syndrome

Introduction

Immune-mediated inflammatory diseases (IMIDs) are a group of chronic disorders driven by abnormal immune responses, with diverse clinical manifestations, including ankylosing spondylitis (AS), atopic dermatitis (AD), allergic rhinitis/asthma, vitiligo, and alopecia areata (AA). Despite their varying phenotypes, multiple IMIDs share the key signaling pathway of JAK/STAT. For instance, IFN-γ mediates hair follicle and melanocyte damage in AA and vitiligo through this pathway;[1,2] the IL-17/IL-23 axis drives the Th17 inflammation in AS,[3] while IL-4/IL-13 dominates the Th2 response in allergic asthma.[4]

In recent years, small molecule JAK inhibitors have emerged as an important treatment option for IMID through targeting the aforementioned pathways. Although its long-term application requires attention to risks such as infection,[5] it shows potential value in addressing abnormal co-immunization. For instance, a case report indicated that oral abutinib could lead to simultaneous improvement in refractory AD and systemic vitiligo.[6] However, most existing evidence focuses on such dual comorbidities. When dealing with complex IMID comorbidities involving

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multiple systems such as the skin, joints, and respiratory tract, the characteristic of multiple system involvement makes comprehensive control of the condition a clinical challenge. For upadacitinib (UPA), a highly selective JAK1 inhibitor, the application in such complex situations has still witnessed a relatively limited number of successful cases and systematic evaluations.

This article presents a rare and complex case of a patient with concurrent AA, vitiligo, AS, and allergic rhinitis-asthma syndrome, who experienced simultaneous remission across multiple systems following treatment with UPA (15 mg once daily). This case contributes new insights into the mechanistic and clinical applications of JAK inhibitors for multi-system immune comorbidities.

Case Report

A 52-year-old male presented with multiple scalp hair loss patches and longstanding generalized dry skin with pruritus. Despite conventional treatments, including antihistamines, the pruritus was only partially alleviated. Over the past two years, there has been progressive patchy hair loss on the scalp, accompanied by persistent itching. In the past year, the extent of hair loss has fluctuated significantly, but has not been alleviated. At the same time, white patches gradually appeared on the sole of the foot. The patient had visited several hospitals multiple times and received various traditional treatment plans, but the condition relapsed, the hair loss area gradually expanded, seriously affecting the quality of life. Therefore, he came to our hospital for treatment.

The patient had a history of AS, allergic rhinitis and asthma. He had been taking amlodipine besylate for blood pressure control and febuxostat for uric acid reduction for a long time. His AS had been treated with non-steroidal anti-inflammatory drugs (celecoxib) and conventional synthetic disease-modifying antirheumatic drugs (sulfasalazine and methotrexate), but the treatment was ineffective. The allergic rhinitis-asthma was controlled with ICS/LABA. The symptoms of dry skin and itching were treated with moisturizers and antihistamines, but the effect was limited. AA and vitiligo had not received systemic treatment. There was no history of family genetic hair loss or other autoimmune diseases.

The physical examination revealed that the patient's skin was dry throughout the body, with lichenoid changes in the elbow pits and popliteal fossae. There were multiple patchy areas of alopecia on the head, with 15 on the Severity of Alopecia Tool (SALT), and no scar formationsee (see Figure 1). Skin biopsy showed active AA (see Figure 2). Clear borders of hypopigmented patches were observed on the dorsum of the feet (see Figure 3). Laboratory tests showed elevated serum total IgE (295 ng/mL). The comprehensive diagnosis was AA, vitiligo, AS, and allergic rhinitis-asthma syndrome with multiple-system immune comorbidity.

In the face of this series of refractory comorbidities that do not respond to conventional treatments, the multi-disciplinary team, after assessment, considered adopting a treatment plan targeting the JAK-STAT pathway. It should be noted that UPA has not yet been officially approved for the treatment of AA or vitiligo. Before the treatment, we had a detailed communication with the patient, clearly informing them of the nature of this drug as off-label use in this indication, the potential benefits and risks, as well as other approved or conventional treatment options. The patient fully understood and voluntarily signed the informed consent form. After screening for active infections and viral hepatitis before the treatment, the patient started taking UPA (15 mg once daily). During this period, complete blood cell counts, liver and kidney functions, and lipid levels were monitored regularly, and risk education was provided to the patient.

After 12 weeks of treatment, the patient's multiple systemic symptoms significantly improved: hair regrowth occurred in the alopecia area, the SALT score decreased from 15 to 0.9 (see Figure 1), pigmentation appeared in the vitiligo lesions and stabilized (see Figure 3), skin dryness and itching were relieved, and the quality of life improved. Spinal joint symptoms and allergic symptoms were significantly reduced. The serum total IgE level dropped to 243 ng/mL.It is worth noting that during the treatment period, there was a transient abnormality in liver function (ALT 478.6 U/L, AST 167 U/L, GGT 302 U/L), suggesting a mixed injury pattern. After ruling out other causes, it was considered related to the patient's long-term use of antihypertensive and uric acid-lowering drugs. With the maintenance of the original dosage and monitoring, the liver function indicators returned to normal in the later follow-up.

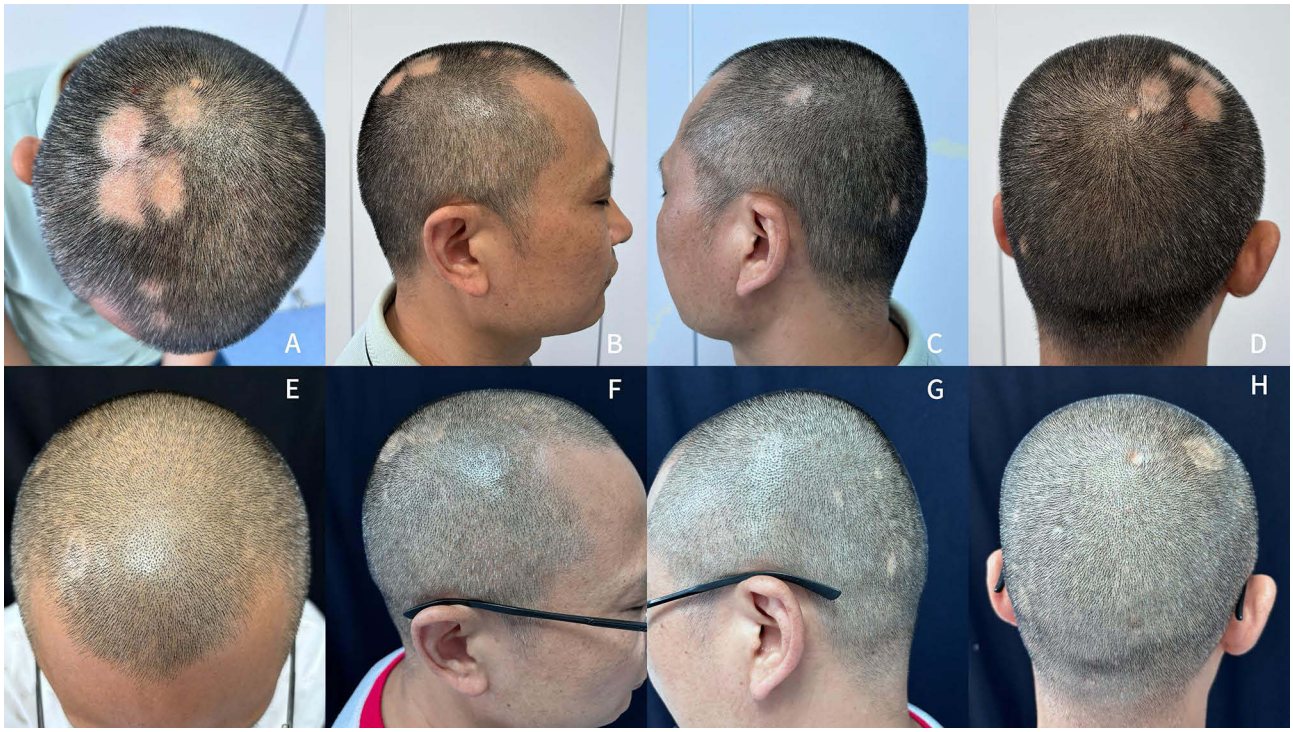

Figure 1 (**A–D**) Before treatment: Clear circular hair loss patches could be observed on the top of the head (**A**), right temporal side (**B**), left temporal side (**C**), and occipital region (**D**). (**E–H**) After 12 weeks of UPA treatment: Dense new hair growth could be seen in the corresponding areas, and significant improvement was observed in the original hair loss regions.

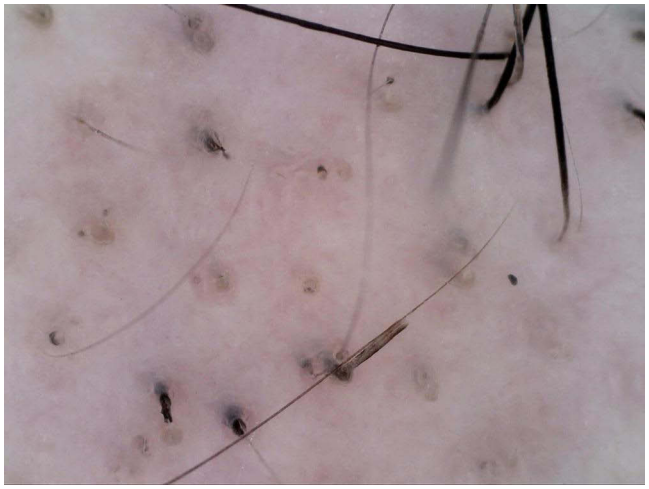

Figure 2 Dermoscopy (pre-treatment): The scalp shows multiple black dots, yellow dots, and exclamation-mark hairs, with no signs of scarring, consistent with active AA.

Discussion

Here, we report a case of an IMID patient who simultaneously suffered from AA, vitiligo, AS, and allergic rhinitis with asthma syndrome. Without adding or adjusting any other medications, after 12 weeks of treatment with UPA (15 once daily), the multiple systemic symptoms of the patient were simultaneously improved. It is notable that only AS was included in the approved indications of this drug, while symptoms of AA, vitiligo, etc. (off-label medications) were also effectively controlled, and no drug-related adverse events were reported during the treatment period. This case confirmed the efficacy of UPA for AA and vitiligo, suggesting that it may be a potential treatment option for complex immune comorbidities with poor responses to traditional treatments.

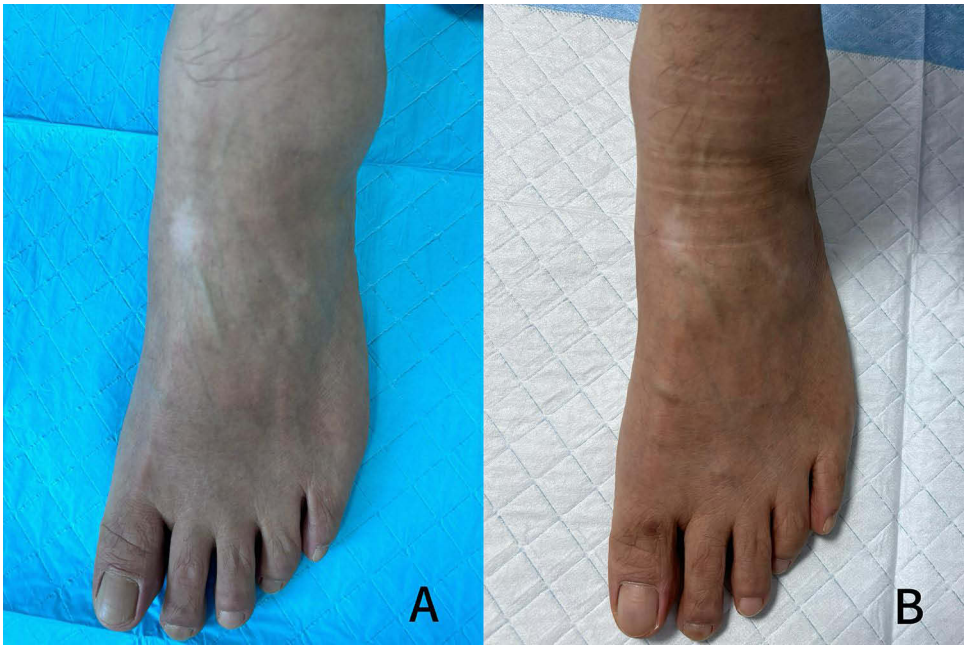

Figure 3 (**A**) Before treatment, a clearly demarcated depigmented patch could be observed on the right foot sole. (**B**) After 12 weeks of UPA treatment, a significant re-pigmentation occurred at the same site, with the border of the lesion becoming blurred and the area shrinking.

In terms of AA, the patient's SALT score decreased from 15 to 0.9, with an improvement rate of 93.3%. This is consistent with the efficacy trend of other JAK inhibitors in this disease, and it shows advantages in terms of onset speed and improvement degree. According to reports, after 36 weeks of treatment with baricitinib for patients with severe AA, the average improvement in SALT score was 61.6%, and the rate of achieving SALT≤20 gradually increased with the treatment time (26.5%, 38.1%, and 54.6% at 16 weeks, 24 weeks, and 36 weeks, respectively).[7] The study of ritlecitinib showed that all newly treated patients (22 individuals) with JAK inhibitors achieved SALT50 after 24 weeks of treatment, and 78% of them achieved SALT≤20.[8] In this context, this case observed significant clinical improvement within a shorter treatment period, suggesting that UPA may have the potential for rapid onset in patients with AA accompanied by complex comorbidities.

Notably, studies indicate that patients with AAhave a 2–3 times higher risk of developing atopic diseases, such as asthma and AD, compared to the general population.[9] Traditional treatments often show limited efficacy due to their single-target approach. This gap between clinical needs and treatment challenges underscores the importance of innovative strategies targeting co-morbidity mechanisms. Mechanistically, in this case, the four coexisting diseases were driven by different key cytokine axes, but their signal transduction was highly dependent on JAK1: AA and vitiligo mainly involve IFN-γ-mediated Th1 responses, AS involves the IL-23/IL-17 axis, and allergic diseases are dominated by IL-4/IL-13. Therefore, the synergistic inhibition of JAK1 by UPA may be the mechanism underlying its rapid and synchronous improvement of multiple systemic symptoms. This case provides a basis for the "targeting of common upstream pathways" strategy for treating complex comorbidities, suggesting that JAK1 inhibitors may have the potential to synergistically control multiple IMIDs, and their broad-spectrum and mechanism-oriented characteristics demonstrate the application prospects of precise intervention.

The monitoring results showed that during the 12-week treatment period, no infections, thromboembolic events, or dyslipidemia occurred in the patients, but a transient increase in liver enzymes was observed. This is consistent with the results of a real-world study conducted in 2024, which indicated that approximately 20% of patients using UPA might experience such abnormalities, and their occurrence was related to metabolic risk factors such as hypertension.[10] Moreover, a meta-analysis in 2025 also supported that UPA did not significantly increase the risk of severe liver diseases.[11] This suggests that for patients with multiple system IMID comorbidities who have poor response to traditional treatments and also have metabolic abnormalities, the short-term safety of using UPA under close monitoring is

controllable. Moreover, the oral administration of UPA is expected to improve patient compliance, which is an important clinical practice advantage for patients who need long-term management of multiple diseases.

Conclusion

This study observed through the treatment of a patient with complex multi-system immune co-morbidity that UPA achieved synchronous improvement of multiple system symptoms. This innovative "single-drug multi-effect" strategy is expected to control multiple clinical symptoms simultaneously through a single therapy, thereby simplifying the treatment plan and potentially enhancing the overall efficacy. This provides preliminary real-world evidence for the clinical management of such complex comorbidities. Although the study had good short-term tolerance, the risks in the context of combined metabolic abnormalities and multiple drug treatment need to be vigilant. However, this study also has several limitations: it is a single case report, and the results have limited extrapolation; the follow-up period is short, which affects the assessment of the persistence of efficacy and long-term safety; combined medication may also constitute confounding factors. Therefore, in the future, it is necessary to conduct prospective designs, with large samples, long-term follow-ups, and multi-center studies, to systematically verify the efficacy, safety, and risk-benefit ratio of this treatment strategy in a wider population, and further explore the clinical application of JAK inhibitors in "treating multiple diseases simultaneously", in order to optimize the clinical management of IMID comorbidities.

Abbreviations

SALT, Severity of Alopecia Tool; AS, ankylosing spondylitis; AD, atopic dermatitis; AA, alopecia areata; ALT, alanine transaminase; AST, aspartate transaminase; GGT, gamma-glutamyl transferase.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical Declaration

This study is a retrospective analysis. According to the policy of our hospital, no additional approval from the institutional ethics committee is required for publication of the case details.

Informed Consent

The patient provided written informed consent for the publication of this case report and the associated images.

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Disclosure

The authors report no conflicts of interest in this work.

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