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CASE REPORT

Successful Treatment of Pediatric Atopic Prurigo Nodularis with Dupilumab

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Purpose: This study aims to evaluate the efficacy and safety of Dupilumab in treating pediatric atopic prurigo nodularis (PN).

Patient and Methods: We present a case of an 11-year-old child with refractory prurigo nodularis for 9 months, accompanied by concurrent allergic rhinitis for 2 years. Conventional therapies and Janus kinase 1 (JAK1) inhibitors had not provided satisfactory results. At presentation, the child presented with a Peak Pruritus Numerical Rating Scale (PP-NRS) score of 9 on a scale of 10, the Investigator's Global Assessment (IGA) score of 3 out of 3, and the Children's Dermatology Life Quality Index (CDLQI) score of 12 out of 30.Dupilumab was administered subcutaneously, starting with an initial dose of 600 mg, followed by 300 mg every three weeks for four months. Subsequently, the injection interval was extended to once every four weeks for an additional two months.

Results: Two weeks after initiating dupilumab treatment, the patient showed initial symptom relief, as evidenced by a reduction in PP-NRS, IGA, and CDLQI scores to 7, 2, and 6, respectively. By the fourth week, the patient experienced significant improvement in pruritus and skin lesions. Specifically, the PP-NRS, IGA, and CDLQI scores decreased by 7 points, 2 points, and 10 points, respectively. The patient discontinued medication after six months of treatment, and no recurrence was observed during the subsequent six-month follow-up period.

Conclusion: Dupilumab appears to be an effective therapy for refractory prurigo nodularis with atopic features.

Keywords: prurigo nodularis, pediatric dermatology, biologics, interleukins, dupilumab

Introduction

Prurigo nodularis (PN) is a chronic inflammatory skin condition characterized primarily by intensely pruritic papular lesions. The pathogenesis of PN is associated with various inflammatory cytokines, including interleukin-4 (IL-4), interleukin-13 (IL-13), and interleukin-31 (IL-31), as well as the JAK-STAT signaling pathway.[1,2] Clinically, PN is often associated with Th2-driven inflammatory diseases, especially atopic dermatitis (AD). Chronic scratching secondary to long-standing AD can lead to the development of nodular lesions resembling those seen in PN. Research on pediatric PN remains limited, with an estimated prevalence of approximately 21.6 per 100,000.[3] In contrast, atopic dermatitis (AD) exhibits a high global prevalence, affecting an estimated 20% of children worldwide.[4] However, a recent meta-analysis has revealed a bidirectional relationship between these two conditions, indicating that patients with either condition are at an increased risk of developing the other.[5]

While reports have highlighted the excellent therapeutic outcomes of dupilumab and JAK1 inhibitors in managing refractory PN in adults,[6–8] viable treatment options for refractory PN in children remain limited. This article describes a specific case in which a child with atopic PN was successfully treated with dupilumab.

Case Report

An 11-year-old girl presented with pruritic erythema, papules, nodules, and excoriations on her trunk and limbs for 9 months, and had a 2-year history of allergic rhinitis. Her PP-NRS, IGA and CDLQI scores were 9, 3 and 12, respectively, with a notable elevation in total IgE levels (Figure 1). A skin biopsy from the lower leg revealed epidermal hyperkeratosis

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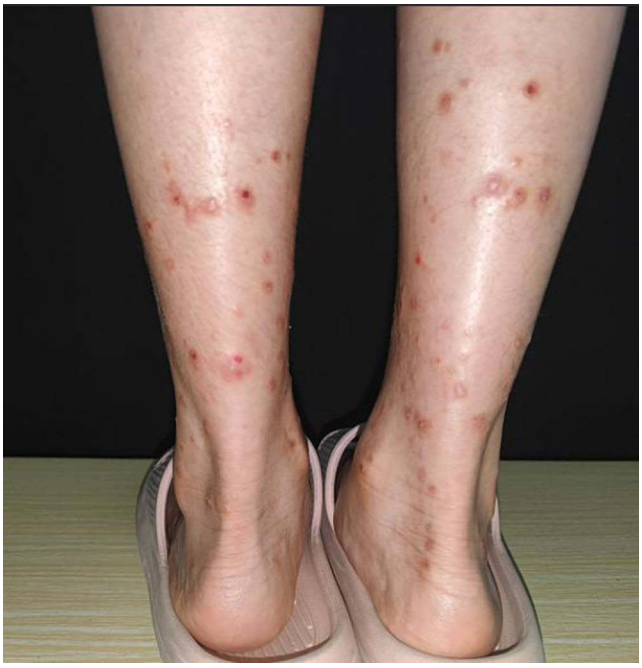

Figure 1 At week 0, extensive prurigo nodules and excoriations emerged on the lower limbs.

with parakeratosis, acanthosis, and perivascular infiltration of inflammatory cells in the superficial dermis. Based on these findings, a diagnosis of prurigo nodularis was made. She had previously been treated with upadacitinib, abrocitinib, antihistamines, and other medications. Initially, these treatments provided partial relief, but the response subsequently waned, and symptoms recurred upon dose reduction. Consequently, she received a loading dose of dupilumab at 600 mg (15 mg/kg), followed by subcutaneous injections of 300 mg (7 mg/kg) every 3 weeks. By the second week of treatment, the patient's PP-NRS score decreased from 9 to 7, the IGA score from 3 to 2, and the CDLQI score from 12 to 6, indicating an early positive response. After 4 weeks of treatment, significant improvement was observed in her symptoms and lesions. The PP-NRS, IGA, and CDLQI scores improved by 77.78%, 66.67%, and 83.33%, respectively (Figure 2). At week 16, due to financial constraints, the injection interval was extended to every 4 weeks. After 24 weeks, the biologic treatment was discontinued, and no adverse events were reported. During the 6-month follow-up period, the patient's condition remained stable, with no recurrence observed.

Discussion

Currently, research on pediatric PN remains relatively limited. This condition not only adversely affects the physical health of affected children but also increases their likelihood of developing anxiety, attention deficit hyperactivity disorder, and other dermatological conditions, such as atopic dermatitis (AD).[3] The interaction between keratinocytes, immune/inflammatory cells, and nerve fibers can initiate scratching behavior, thereby driving the progression of PN.[2] In patients with AD, cutaneous barrier dysfunction, immune dysregulation, and pruritus create a vicious cycle. Chronic scratching leads to the release of proinflammatory cytokines (such as IL-31, TSLP) from keratinocytes, which recruit immune cells to amplify the inflammatory response and ultimately promote PN development.[9,10] Therefore, blocking immune-inflammatory pathways and interrupting the pruritus-scratch cycle are therapeutic priorities for these patients. Interrupting these mechanisms is crucial for managing AD patients with PN. Regarding treatment modalities, dupilumab blocks IL-4/IL-13 signaling to comprehensively control Th2/Th22 inflammation, reduce the release of pruritogenic cytokines such as IL-31, and improve skin barrier function, thereby disrupting the "immuno-neural" interaction-driven pathological cycle. In contrast, JAK inhibitors (upadacitinib, abrocitinib) primarily suppress Th2/Th22 inflammation and provide rapid relief from acute pruritus, but do not effectively address chronic Th17/Th1 inflammation or neural

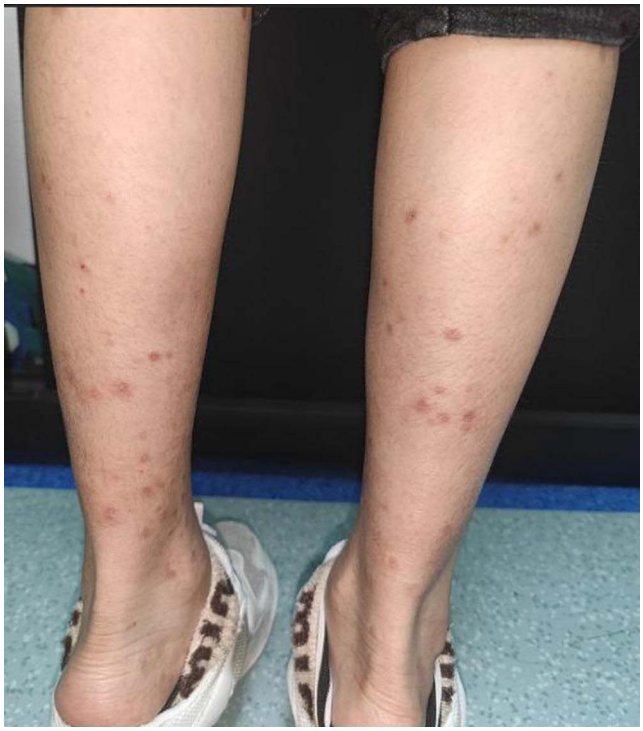

Figure 2 After 4 weeks of dupilumab treatment, the prurigo nodules on the lower extremities decreased in size and number.

remodeling processes. Antihistamines, on the other hand, only inhibit acute pruritus by blocking histamine H1 receptors and are ineffective against non-histamine-mediated pruritus pathways (for example, IL-31/TSLP).[11–17]

Due to the side effects of existing therapies and the high rate of recurrence, treating pediatric PN remains a significant challenge. Previously, only Lin Chia-Jen et al and Tahel Fachler et al each reported a single case of pediatric PN without atopic tendencies, in which significant symptom improvement was observed following dupilumab treatment. However, data regarding the use of dupilumab for pediatric PN with comorbid atopic conditions remain limited.[18,19] A recent multicenter study in China demonstrated the efficacy of dupilumab in treating PN irrespective of atopic status, including two patients aged 6–11 years with atopic features who had previously undergone systemic treatment with antihistamines or traditional Chinese medicine.[20]

In our case report, an 11-year-old child with PN complicated by rhinitis initially achieved a partial response to systemic therapies (antihistamines, JAK inhibitors); however, the efficacy declined, and recurrence was closely linked to disease progression. Early treatment provided transient symptom control by blocking histamine pathways and Th2/Th22 inflammation. However, in the chronic phase, the inflammatory pattern shifted toward Th17/Th1 dominance, with a compensatory elevation of non-histaminergic mediators (such as IL-17, IL-22). This was further compounded by chronic scratching-induced neural fiber remodeling and neuropeptide (for example, substance P)-mediated inflammatory cascades, ultimately leading to treatment failure.[2,13,14,21] Subsequent treatment with dupilumab resulted in a significant reduction in pruritus and lesion severity by week 4, along with notable improvements in quality of life. Following six months of treatment, dupilumab was discontinued; during the six-month follow-up period, neither recurrence nor adverse events were reported.

Although common adverse events associated with dupilumab in AD and PN include nasopharyngitis and conjunctivitis,[22] clinicians should remain vigilant for potential serious atypical reactions.[23] While these results suggest that dupilumab may offer favorable efficacy and safety in treating pediatric atopic PN, it is important to acknowledge the small sample size. Therefore, future large-scale, multi-center studies enrolling more children are necessary to validate the long-term effectiveness of dupilumab in this population.

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Meanwhile, unlike nemolizumab, which targets IL-31, dupilumab and nemolizumab exhibit different mechanisms of action. The absence of head-to-head comparative studies currently limits our ability to elucidate their relative efficacy in refractory cases. Omalizumab, which targets IgE, has only case studies supporting its efficacy in atopic PN patients, with the overall evidence for its efficacy far less robust than that for dupilumab.For patients who do not respond adequately to dupilumab, nemolizumab may be considered as an alternative treatment option, and clinical case series have demonstrated its positive effects of nemolizumab in alleviating pruritus and improving skin lesions in PN patients. Furthermore, emerging innovative therapies, such as small-molecule drugs, mu-opioid receptor antagonists, and nalbuphine (a μ-antagonist/κ-agonist), while still in the research phase, have shown potential and are expected to provide new treatment options for PN.[24] Currently, while there are reports on the use of dupilumab in pediatric PN, most are based on small sample sizes or case reports. Therefore, larger-scale, long-term follow-up controlled trials are urgently needed to clarify the role of dupilumab in the treatment of pediatric PN.

Conclusion

In conclusion, dupilumab, by targeting the IL-4/IL-13 pathway, provides an effective treatment option for patients with refractory PN, with multiple studies confirming its ability to significantly relieve pruritus.

Consent Statement

The patient's parents provided informed consent for the publication of case details and images. Institutional approval is not necessary for this case study.

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Disclosure

The authors declare no conflicts of interest in this work.

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