Psoriasis: Targets and Therapy

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CASE SERIES

Successful Treatment of Two Rare Pediatric Keratinization Disorders with Secukinumab: Epidermolytic Ichthyosis and PRP–GPP Overlap

Qianyue Xu[1–3], Jia Zhang[1–3]

[1]Dermatology Center, Xinhua Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, People's Republic of China; [2]Department of Dermatology, Xinhua Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, People's Republic of China; [3]Institute of Dermatology, Shanghai Jiaotong University School of Medicine, Shanghai, People's Republic of China

Correspondence: Jia Zhang, Dermatology Center, Xinhua Hospital, Shanghai Jiaotong University School of Medicine, 1665 Kongjiang Road, Shanghai, 200092, People's Republic of China, Email zhangjia@xinhuamed.com.cn

Abstract: Pediatric erythroderma can arise from either inherited keratin defects or cytokine-driven inflammation, yet evidence for biologic therapies in these settings is limited. We report two rare pediatric cases successfully treated with secukinumab, an IL17A–targeted monoclonal antibody: (i) a 2-year-old boy with genetically confirmed epidermolytic ichthyosis (EI, KRT10 mutation:c.467G>A, p. Arg156His) refractory to conventional care, who achieved >60% improvement in erythema and scaling one week after a single off-label 150 mg subcutaneous secukinumab dose, with remission maintained for 12 months on monthly dosing; and (ii) an 11-year-old girl with coexistent Type III (juvenile) pityriasis rubra pilaris and acute generalized pustular psoriasis (PRP–GPP overlap) unresponsive to acitretin and methotrexate, who attained complete remission for 12 months following standard secukinumab induction (300mg weekly ×5) and maintenance every four weeks. These cases extend the potential utility of IL17A blockade beyond psoriasis vulgaris to both structural keratinopathies and inflammatory pustular dermatoses in children. While limited by the nature of a two-patient case series, these findings warrant prospective studies to clarify optimal dosing and long-term safety of IL-17A blockade in pediatric dermatology.

Plain Language Summary: In this report, we describe (1) a two-year-old boy with a keratin 10 mutation causing epidermolytic ichthyosis, and (2) an eleven-year-old girl with a unique overlap of pityriasis rubra pilaris and generalized pustular psoriasis. Both children achieved rapid and sustained remission of their debilitating skin disease after off-label treatment with secukinumab, despite having failed conventional therapies. To the best of our knowledge, Case 1 is the first reported Chinese EI patient to respond to secukinumab, and Case 2 is the first case of concurrent GPP and PRP achieving remission with IL-17A blockade. The innovative aspect of our work lies in extending IL-17A blockade beyond its traditional use in psoriasis vulgaris to rare disorders of keratinization and autoinflammatory skin disease. We believe this demonstrates a novel therapeutic strategy and provides hope for patients with otherwise refractory pediatric dermatoses.

Keywords: epidermolytic ichthyosis, KRT10, pityriasis rubra pilaris, generalized pustular psoriasis, secukinumab, pediatric dermatology

Introduction

Pediatric erythroderma is an uncommon but urgent dermatological presentation that encompasses both inherited disorders of cornification and acquired inflammatory dermatoses. Epidermolytic ichthyosis (EI) is an autosomal-dominant keratinopathy caused by pathogenic variants in KRT1 or KRT10, characterised by neonatal blistering evolving into lifelong hyperkeratosis.[1,2] Conventional treatments, primarily based on topical keratolytics and systemic retinoids, offer only symptomatic relief and are often associated with significant side effects and limited efficacy, especially in severe cases. Generalized pustular psoriasis (GPP) and pityriasis rubra pilaris (PRP) are rare inflammatory diseases; their coexistence is extremely rare.[3] These conditions are often challenging to manage, with conventional systemic agents like retinoids

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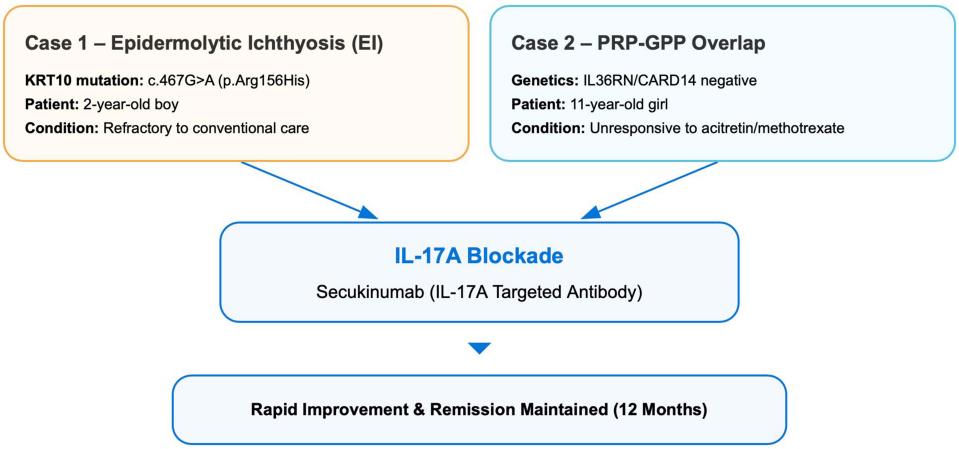
Graphical Abstract



and methotrexate providing variable responses. The former is often linked to IL-36 pathway dysregulation, whereas the latter involves aberrant Th17 signalling.[4–7]

Secukinumab, a fully human monoclonal antibody targeting IL-17A, is approved for plaque psoriasis in adolescents and adults. Its role in EI or in PRP–GPP overlap has not been fully explored. Recent immunologic studies indicate that Th17 cytokines (including IL-17A) may contribute to the pathogenesis of ichthyoses, providing a rationale for therapeutic IL-17A blockade in these conditions. We present two distinct cases highlighting the successful off-label use of secukinumab in these pediatric patients.

Case 1 – Epidermolytic Ichthyosis Responsive to Secukinumab

A 2-year-old boy was referred with lifelong generalized erythema, diffuse scaling, and intermittent acral blistering (Figure 1A). Previous therapies included daily emollients, topical corticosteroids, mupirocin for secondary infection, and three-monthly courses of intravenous immunoglobulin (15 g each), without durable benefit. Skin biopsy showed features of epidermolytic hyperkeratosis with suprabasal vacuolar degeneration and a mild superficial dermal lymphocytic infiltrate, consistent with EI (Figure 1B and C). Whole-exome sequencing confirmed a heterozygous KRT10 c.467G>A (p.Arg156His) mutation inherited from his father. The child suffered severe pruritus (7/10 on a visual analog scale), leading to fragmented sleep. This resulted in significant distress for both the child and his parents, impacting the entire family's quality of life and daily functioning.

After thorough parental counselling, he received a single 150 mg subcutaneous secukinumab injection (off-label). The patient's body weight was 15 kg. Although this dose is higher than the standard EMA recommendation for this weight (75 mg for <25 kg), the 150 mg dose was deemed appropriate by the clinical team given the extreme severity and refractory nature of the disease. This decision was informed by the urgent clinical need and existing reports of biologic use in severe pediatric dermatoses, including domestic case studies on infants (as detailed in the discussion). By day 7, erythema and scaling had improved by approximately 60% (Figure 1D), and pruritus was reduced to 1/10. Monthly 150 mg maintenance doses were given to sustain the response, maintaining near-complete remission of skin symptoms for 12 months. No adverse events or laboratory abnormalities were noted during treatment.

Case 2 – PRP–GPP Overlap Controlled with Secukinumab

An 11-year-old girl presented with a two-year history of widespread follicular keratotic papules and orange-red scaly plaques, complicated by the acute onset of fever and rapidly spreading sterile pustules. On examination, she was erythrodermic with >90% body surface area involvement, palmoplantar keratoderma, and numerous pustules on the

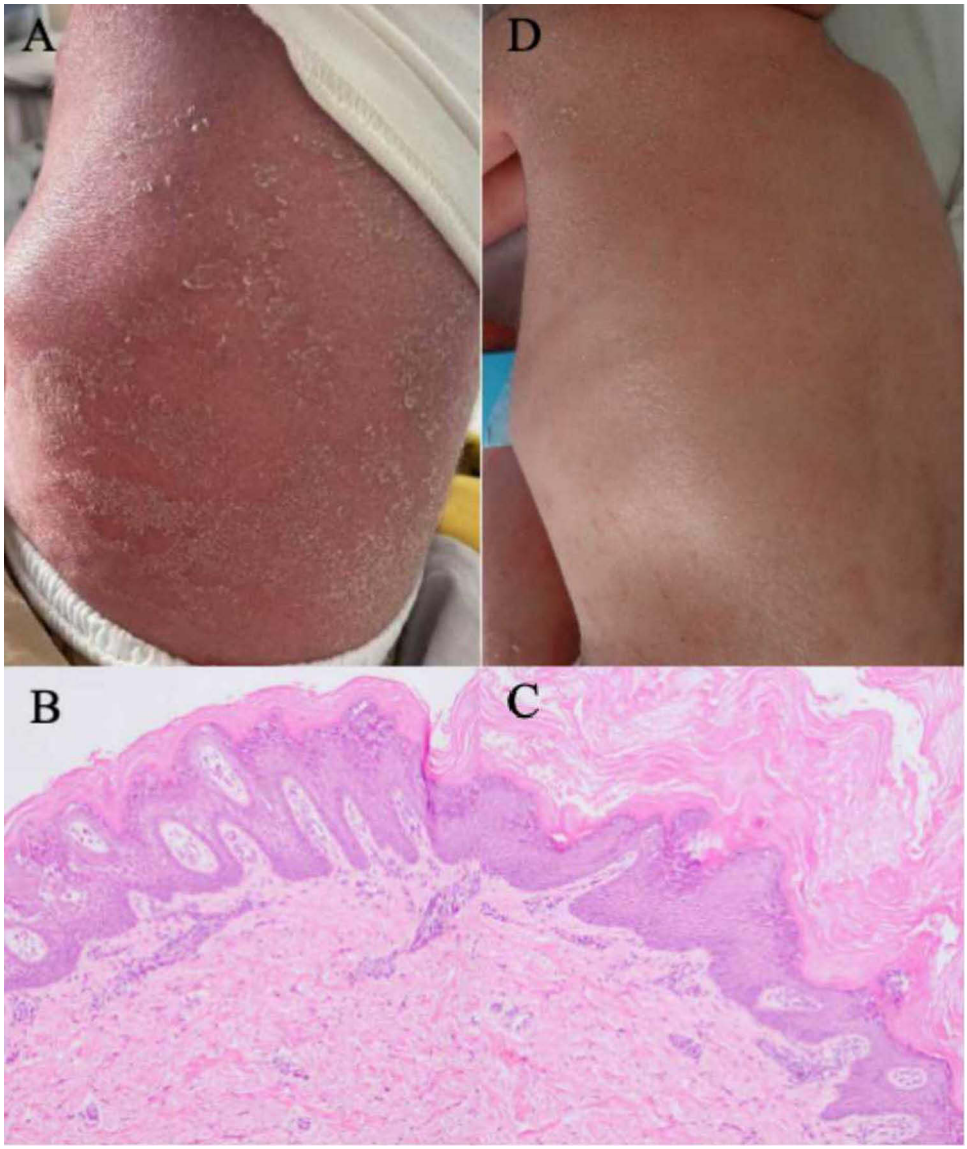


Figure 1 Clinical features of Case 1 (epidermolytic ichthyosis). (**A**) Diffuse erythema and thick scaling on the back at baseline, before secukinumab treatment. (**B** and **C**) Histopathology of lesional skin (H&E staining, ×200) shows compact hyperkeratosis, prominent vacuolar degeneration of the suprabasal keratinocytes, and mild perivascular lymphocytic infiltration in the superficial dermis. (**D**) Marked improvement in erythema and desquamation one week after initiation of secukinumab therapy (150 mg subcutaneous), with significant reduction in skin thickening.

limbs (Figure 2A). She had been previously diagnosed with Type III (classic juvenile) PRP and treated for one year with acitretin (20 mg daily) and methotrexate (5 mg weekly), which were later discontinued due to hyperuricemia and lack of adequate response. At admission, her C-reactive protein was 120 mg/L, although the white blood cell count remained normal. Dermoscopy of a representative plaque revealed yellow globules with dotted vessels (inset of Figure 2A). Histopathology demonstrated subcorneal neutrophilic pustules, psoriasiform epidermal hyperplasia with alternating ortho- and parakeratosis, consistent with pustular psoriasis. Targeted sequencing for IL36RN and CARD14 mutations returned negative results.

Off-label secukinumab 300 mg was initiated, given at weeks 0, 1, 2, 3, 4 (induction phase) and then every four weeks. The patient's body weight was 53 kg. The 300 mg dose was selected as this is in line with recommendations for severe psoriasis for patients weighing over 50 kg. The response was dramatic: pustules began resolving within four days (Figure 2B), and by week 4, the Psoriasis Area and Severity Index (PASI) had improved from 38 to 3 (a 92% reduction).

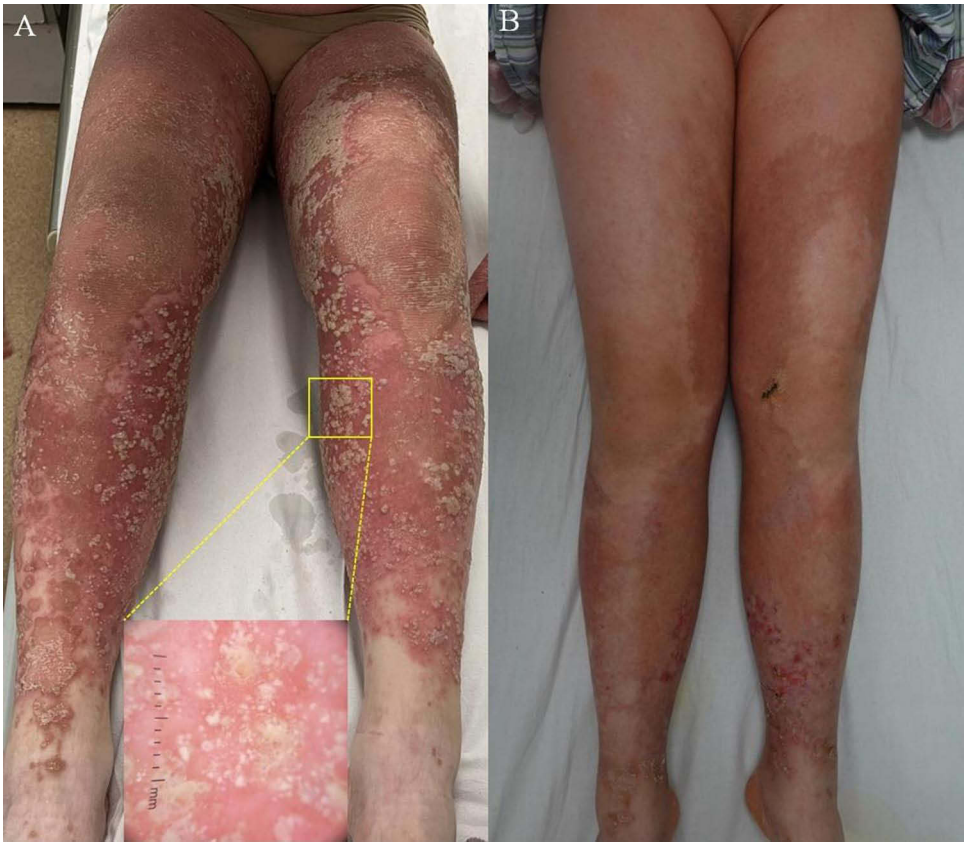


Figure 2 Clinical and dermoscopic features of Case 2 (PRP–GPP overlap). (**A**) Pre-treatment: widespread keratotic papules and plaques with Orange-red coloration and powdery scale, accompanied by palmoplantar keratoderma, generalized erythema, and numerous pustules on the limbs. Inset: dermoscopy revealing yellow globules with dotted vessels. (**B**) Four days after starting secukinumab (300 mg subcutaneous): almost complete resolution of pustules and a substantial reduction in erythema and scaling, with only post-inflammatory hyperpigmentation remaining.

The patient achieved complete skin clearance and defervescence, which persisted through 12 months of follow-up without relapse or significant adverse effects.

Discussion

To the best of our knowledge, Case 1 is the first reported Chinese EI patient to respond to secukinumab, and Case 2 is the first pediatric case of concurrent GPP and PRP achieving remission with IL-17A blockade. These cases underscore the heterogeneous mechanisms underlying pediatric erythroderma and illustrate the therapeutic promise of cytokine-targeted agents in rare dermatologic disorders. Notably, IL-17A–mediated inflammation appears to be a common pathogenic thread linking these otherwise disparate conditions (a structural keratin mutation disorder vs an autoinflammatory pustular dermatosis).

The IL-17A cytokine, produced primarily by Th17 cells, activates keratinocyte inflammatory cascades by binding to IL-17RA/IL-17RC heterodimers on keratinocytes. This leads to recruitment of the adaptor ACT1 and activation of NF-κB and MAPK pathways, promoting the expression of downstream proinflammatory mediators (eg, IL-6, CXCL1, CXCL8) and antimicrobial peptides (β-defensins). The result is epidermal hyperplasia, neutrophil chemotaxis, and sustained inflammation. This mechanism has been well documented in translational models of psoriasis and pustular dermatoses, including murine studies and transcriptomic analyses of lesional skin in GPP patients.[4]

In EI, IL-17A blockade represents a novel therapeutic strategy to interrupt the secondary inflammation triggered by epidermal barrier disruption. This innovative approach complements traditional keratolytic and retinoid therapies, often leading to significantly improved quality of life for patients. A recent case report described a 4-year-old boy with KRT1 gene mutation epidermolytic ichthyosis who experienced marked clinical improvement after three months of treatment

with Vunakizumab, China's first self-developed anti-IL-17A monoclonal, further supporting the role of the IL-17 pathway in ichthyosis management.[8] Similarly, another domestic report detailed the successful use of secukinumab 75 mg in a 16-month-old infant (6.5 kg) with SAM syndrome, a severe inherited dermatosis, underscoring the potential for IL-17A blockade in this very young population.[9]

For PRP–GPP overlap cases lacking IL36RN or CARD14 mutations, IL-17A likely emerges as a primary driver of inflammation. In our Case 2, blocking IL-17A produced a rapid therapeutic response, underscoring a mechanism-based advantage over conventional treatments. Specifically, pustular and erythrodermic symptoms resolved within days of secukinumab initiation—substantially faster than what is typically seen with traditional systemic agents such as methotrexate or acitretin, which often require weeks to achieve similar improvements. This swift response aligns with other reports in the literature: for example, Yu et al[10] documented a pediatric GPP patient who achieved rapid disease clearance on secukinumab monotherapy, highlighting IL-17A inhibition as a promising option even in severe pustular psoriasis without adjunctive systemic therapy.

Recent pediatric clinical data also reinforce secukinumab's efficacy and safety in psoriatic disease, supporting its integration into pediatric dermatological practice.[11] Furthermore, recent 4-year data from a Phase III trial by Kingo et al corroborates the long-term efficacy and safety of secukinumab in the pediatric population with plaque psoriasis, strengthening the case for its use in severe dermatological conditions.[12]

Secukinumab has demonstrated a favorable safety profile in children, consistent with adult psoriasis studies. This is supported by pediatric trial data (eg, the open-label IXORA-PEDS study) and post-marketing pharmacovigilance reports.[11] In our two cases, no significant infections, neutropenia, or organ toxicities occurred. Nevertheless, careful monitoring remains crucial, with attention to potential risks such as mucocutaneous Candida infections (related to IL-17A's role in mucosal immunity) and the need for up-to-date immunizations. Long-term considerations, including effects on growth, development, and immune responses, will require ongoing study.

While our report focuses on IL-17A inhibition, other biologic pathways are also being explored. For instance, IL-23 and TNF-α inhibitors have shown efficacy in psoriatic diseases, but their role in these specific rare keratinization disorders is less clear. Our findings suggest that for conditions with a strong Th17 signature, direct IL-17A blockade may offer a more targeted and rapid effect. We advocate for the establishment of prospective pediatric registries and clinical trials to optimize biologic dosing strategies, evaluate long-term safety, and identify predictive biomarkers of response in young patients.

Conclusion

While acknowledging the inherent limitations of a two-patient case series, our findings suggest that IL-17A blockade via secukinumab represents a significant therapeutic advancement for pediatric erythrodermic conditions that are resistant to conventional treatments. Our case series expands the indications of IL-17A inhibitors to include a congenital ichthyosis and a rare overlap autoinflammatory keratinization disease, illustrating that targeted biologic therapy can induce rapid and sustained remission in severe pediatric dermatologic diseases. Continued research and vigilant clinical monitoring will further clarify the long-term safety and optimal use of IL-17A inhibitors in children. Future studies should focus on long-term outcomes, age-specific dosing guidelines, and direct comparisons of IL-17A inhibitors with other biologics in pediatric populations to guide clinical decision-making.

Ethics Approval and Consent to Participate

This study protocol, including the publication of case details, was approved by the Institutional Review Board of Xinhua Hospital. Written informed consent to treatment was obtained from the patients' guardians.

Consent for Publication

Guardians provided written informed consent for the publication of anonymized clinical data and images.

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Disclosure

The authors declare no conflicts of interest regarding this publication.

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