

Onychodystrophy associated with dupilumab therapy for atopic dermatitis



Amanda E. Zubek, MD, PhD, and Matthew D. Vesely, MD, PhD
New Haven, Connecticut

Key words: atopic dermatitis; dupilumab; eczematous nails; nail dystrophy; onychodystrophy.

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory disorder affecting the skin and is characterized by a type 2 inflammation, including type 2 helper CD4⁺ T cells, interleukin 4 (IL-4), IL-5, and IL-13.¹ Dupilumab is a monoclonal antibody that blocks IL-4 and IL-13 signaling by binding to the IL-4 receptor alpha subunit that is shared by both IL-4 and IL-13 receptors. Treatment of AD by dupilumab has been shown to be efficacious, with long-term benefit.² Unique dupilumab-associated side effects in patients with AD have been reported, including conjunctivitis² and head and neck dermatitis³ caused by unknown mechanisms.

Nail changes associated with AD are underappreciated despite a similar incidence of nail involvement in other inflammatory disorders, such as lichen planus.^{4,5} It is estimated that about 11% of patients with AD have some nail changes that are likely related to a corresponding inflammation of the nail bed or matrix.^{4,5} There is a paucity of studies that focus on the therapy of eczematous nail changes or nail-specific side effects in response to AD treatment.

CASE REPORT

A woman in her 60s with a history of severe AD for more than 40 years was started on dupilumab therapy. Prior to starting dupilumab, she had extensive involvement of eczematous plaques on the head, neck, chest, back, legs, and arms, including the hands. There was mild nail involvement, with chronic paronychia of the bilateral thumbnails. Three months after starting dupilumab, she reported

Abbreviations used:

AD: atopic dermatitis
IL: interleukin

dramatic improvement of her eczematous plaques in addition to new severe nail changes.

On physical examination of the bilateral thumbnails, there was hyperkeratosis of the nail bed and hyponychium, scaling of the lateral nail folds and eponychium with loss of adhesion of the cuticle to the nail plate, and bilateral distal and lateral onycholysis. The remaining fingernails and toenails had no changes. On the right thumbnail, koilonychia, onychorrhexis, and irregular longitudinal nail plate fracturing were observed. The left nail plate exhibited multiple horizontal depressions consistent with Beau's lines, a proximal median longitudinal groove, and a mid-nail transverse split (Fig 1, A). Fungal culture from the nail plate and periungual skin was negative. Based on discussions in a private group chat on a social media platform composed of patients with AD who were taking dupilumab, she reported that other patients also had similar nail findings. Despite the nail changes, she continued therapy with 300 mg of dupilumab every 14 days, given the improvement of her AD. Three months later, her nails had dramatically improved, with residual longitudinal ridging, improving distal nail dystrophy, and less prominent horizontal ridging (Fig 1, B). At her follow-up visit 15 months since starting dupilumab for AD, her nails had significant improvement, with very mild changes, including

From the Department of Dermatology, Yale School of Medicine, New Haven.

Funding sources: Dr Vesely is supported by the Dermatology Foundation, Melanoma Research Alliance, and the National Center for Advancing Translational Sciences (KL2 TR001862).

Conflicts of interest: The spouse of Dr Vesely is an employee of Regeneron Pharmaceuticals. Dr Zubek has no conflicts of interest to declare.

IRB approval status: Not applicable.

Correspondence to: Matthew D. Vesely, MD, PhD, Department of Dermatology, Yale School of Medicine, 333 Cedar St, PO Box

208059, New Haven, CT 06520. E-mail: matthew.vesely@yale.edu.

JAAD Case Reports 2021;7:20-2.
2352-5126

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<https://doi.org/10.1016/j.jidcr.2020.10.024>



Fig 1. Nail changes in a patient with AD treated with dupilumab. Three months after starting the dupilumab therapy, the patient presented with hyperkeratosis of the nail bed and hyponychium, scaling of the lateral nail folds and eponychium with loss of adhesion of the cuticle to the nail plate, and bilateral distal and lateral onycholysis. **A**, On the right thumb, koilonychia, onychorrhexis, and irregular longitudinal nail plate fracturing were observed, while the left nail exhibited multiple horizontal depressions (Beau's lines), a median longitudinal groove, and a mid-nail transverse split. **B**, After 6 months of the continued dupilumab therapy, both the thumbnails improved and showed longitudinal ridging, improving distal nail dystrophy, and less prominent horizontal ridging. **C**, After 15 months of the continued dupilumab therapy, nail regrowth, with evidence of chronic paronychia and mild transverse ridges, mild longitudinal ridging, and nail pits were observed. AD, Atopic dermatitis.

chronic paronychia with transverse ridges, longitudinal ridging, and nail pits (Fig 1, C).

DISCUSSION

Many inflammatory diseases of the skin, including psoriasis, lichen planus, vitiligo, and alopecia areata, have associated nail changes. The reported nail abnormalities in AD include those involving the nail matrix, such as transverse grooves, nail pitting, trachyonychia, leukonychia, onychoschizia, onychomadesis, and melanonychia secondary to melanocytic activation.^{4,5} Additionally, nail dystrophy affecting the nail bed, including onycholysis, koilonychia, and brachyonychia, has also been reported.^{4,5} Regional eczematous changes of the skin around the nails may contribute to nonspecific inflammation of the nail matrix, which interrupts nail matrix formation. Thus, periungual inflammation may contribute to nail dystrophy in addition to the isolated inflammation of the nail unit.

Among the thousands of patients treated with dupilumab in clinical trials, there are no reports of any associated nail changes, although a case of dupilumab-associated resolution of median canaliform dystrophy of Heller has been reported.⁶ Future real-world phase IV studies may reveal a small subset

of AD patients with nail dystrophy that is affected by dupilumab intervention as both a potential cause of the nail dystrophy and therapy for the nail changes associated with AD. It is difficult to determine from our single patient whether dupilumab therapy resulted in a tissue-specific adverse event or whether dupilumab altered the local cytokine milieu, leading to a transient upregulation of type 1 helper cytokines, resulting in psoriasiform nail changes. We hypothesize that dupilumab therapeutically reduced the nail unit inflammation, resulting in acute nail changes that eventually resolved with the continued dupilumab therapy, allowing the nail to grow out normally. Thus, in this 1 patient, dupilumab may have both initiated the nail changes due to a transient alteration of the local cytokine milieu and treated the nail changes by reducing the nail unit inflammation over time. Dupilumab may be a biologic therapy that treats eczematous nails, just as biologics can be used to treat nail psoriasis. It is important to include a broad differential diagnosis when examining an AD patient with nail changes, including, but not limited to, trauma, local nail infections, and systemic infections associated with the nail changes, which were not evident in our patient. More work is needed to characterize the nail changes in AD patients and

determine whether the nail changes are due to type 2 inflammation and whether therapeutic intervention in AD results in improved nail outcomes.

We would like to thank the patient for sharing her experience.

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