SKIN

BRIEF ARTICLE

Clinical Improvement of Necrobiosis Lipoidica Diabeticorum with Opzelura (Ruxolitinib) Cream: A Case Report

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ABSTRACT

Necrobiosis lipoidica (NL) is an idiopathic granulomatous, inflammatory skin disorder, traditionally linked to diabetes mellitus but often occurs independently of glucose metabolism abnormalities. Proposed pathogenic mechanisms include microangiopathy, collagen devitalization, metabolic changes, trauma, and immune dysregulation. Management of NL is limited by data on treatment efficacy but includes high-potency topical steroids, intralesional steroids, topical immunomodulators, psoralen-ultraviolet A photochemotherapy, hydroxychloroquine, or TNF-alpha inhibitors, pentoxifylline, topical aminolevulinic acid photodynamic therapy (ALA-PDT), and more recently Janus kinase (JAK) inhibitors. This case discusses a 66-year-old female with type 2 diabetes that presents with necrobiosis lipiodica diabeticorum (NLD) who was refractory to high-potency topical corticosteroid but showed improvement after use of Opzelura cream.

INTRODUCTION

Necrobiosis lipoidica (NL) is an uncommon, idiopathic granulomatous condition characterized by distinct red to yellow plaques, typically appearing on the lower legs.[1] More specifically, necrobiosis lipoidica diabeticorum (NLD) is used to refer to NL often seen in women and associated with diabetes, though it is a rare complication seen in 0.3% of diabetics. The precise etiology of NL remains uncertain, although potential factors include vascular pathology involving microangiopathy or deposition of immune complexes. Anomalies in collagen and compromised neutrophil migration have also been suggested.[2]

Managing NL poses challenges, with limited data on treatment efficacy available. High-potency topical steroids are commonly prescribed initially as first-line treatment. For cases resistant to conventional therapy, treatment options include intralesional steroids, topical immunomodulators, topical psoralen-ultraviolet A photochemotherapy, hydroxychloroquine, or tumor necrosis factor-alpha inhibitors. Pentoxifylline, known for its ability to improve blood flow and reduce inflammation, has shown promise in resolving NL.[3] Topical aminolevulinic acid (ALA) with photodynamic therapy (PDT) has also shown improvement in ulcer healing in NLD, possibly due to immunomodulatory activity, anti-inflammatory effect, and keratinocytes photoactivation.[4]

More recently, Janus kinase (JAK) inhibitors have emerged as a potential therapeutic avenue for granulomatous disorders, such as granuloma annulare, and ruxolitinib or tofacitinib for NL specifically.[5-9] This report details a case of NL showing significant improvement with the application of topical 1.5% Ruxolitinib cream (Opzelura, Incyte Corp). Specifically, Ruxolitinib is a selective JAK inhibitor targeting JAK1 and JAK2, which are involved in the inflammatory pathways contributing to necrobiosis lipoidica.

CASE REPORT

A 66-year-old female with history of type 2 diabetes mellitus presented with a one-year history of worsening, nonpainful, nonpruritic, bilateral lower extremity hyperpigmentation. On examination, multiple shiny, red, brown, tan-colored, firm patches were visualized on bilateral lower extremities (**Figure 1**). A punch biopsy was performed on the left anterior lower extremity, showing necrobiosis lipiodica diabeticorum (NLD). Once sutures of the biopsy site were removed, treatment with twice-daily application of both betamethasone diproprionate augmented 0.05% cream and tacrolimus 0.1% ointment were initiated. The patient was instructed to use the steroid cream for two weeks on, one week off to avoid adverse side effects. The patient declined kenalog injections and pentoxyfylline treatment throughout the duration of her visits. At three-month follow-up, there was minimal to no improvement of NLD, so hydroquinone 6% pads at bedtime were added for post-inflammatory hyperpigmentation.

At the next two-month follow-up, she was started on a stronger topical steroid with halobetasol propionate 0.05% cream and instructed to continue tacrolimus 0.1% ointment, applying both twice daily with continuation of hydroquinone 6% pads at bedtime. In the following six to eight months, she showed minimal to no improvement of NLD so hydroquinone pads were increased from 6 to 8%.

At the subsequent three-month follow-up (**Figure 2**), halobetasol and tacrolimus were discontinued due to lack of efficacy, and she was started on Opzelura 1.5% cream twice daily in addition to continuing hydroquinone 8% pads at bedtime. There was a delay in treatment as she was not able to start the Opzelura cream until two months after she was given the prescription. Once she initiated use of the Opzelura cream, there was minimal improvement after one month of use but significant improvement after four months. The most recent results were seven months after Opzelura cream use (**Figure 3**).

DISCUSSION

Necrobiosis lipoidica is a rare inflammatory cutaneous disorder with unknown etiology and various treatment options and efficacies have not been extensively researched. Left untreated, NL can be uncomfortable or painful, at risk of ulceration and subsequent infection, cosmetically undesirable, and rarely can lead to squamous cell carcinoma.[10] There is no standardized treatment for NL, especially in refractory cases, due to its rarity, though options that have proven to be successful include high-potency topical steroids, intralesional steroids, topical immunomodulators, psoralen-ultraviolet A photochemotherapy, hydroxychloroquine, or TNF-alpha inhibitors, pentoxifylline, topical aminolevulinic acid photodynamic therapy (ALA-PDT), and more recently JAK inhibitors. The clinical improvement observed in this patient's necrobiosis lipoidica (NL) upon treatment with Opzelura (ruxolitinib) cream

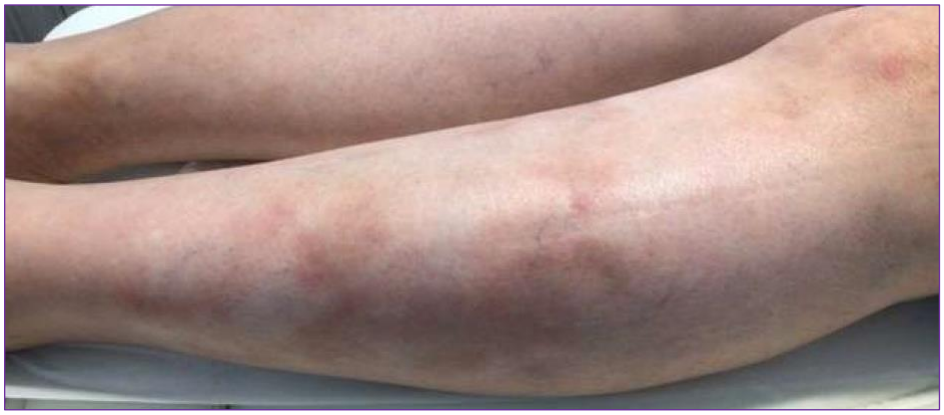

Figure 1. Baseline (10/5/2021)

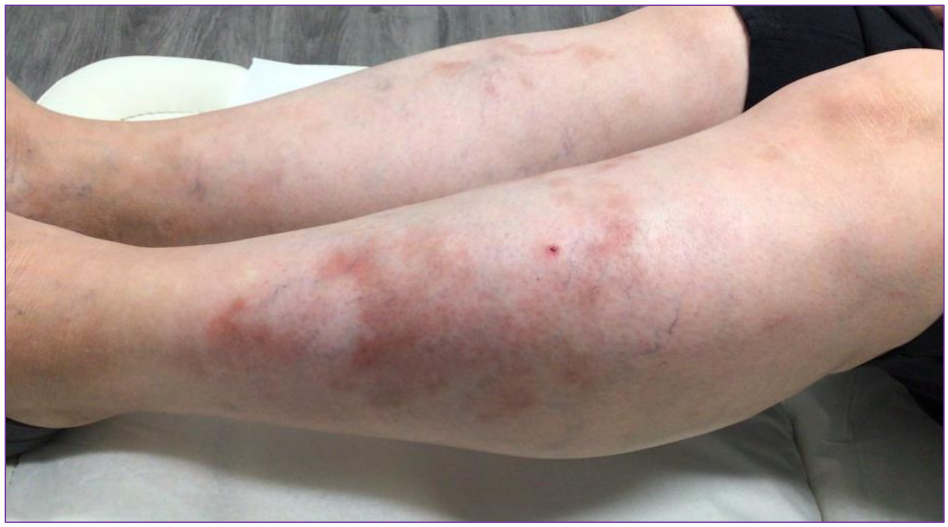

Figure 1. After 11 months of using halobetasol and 16 months of tacrolimus 0.1% ointment (3/20/23)

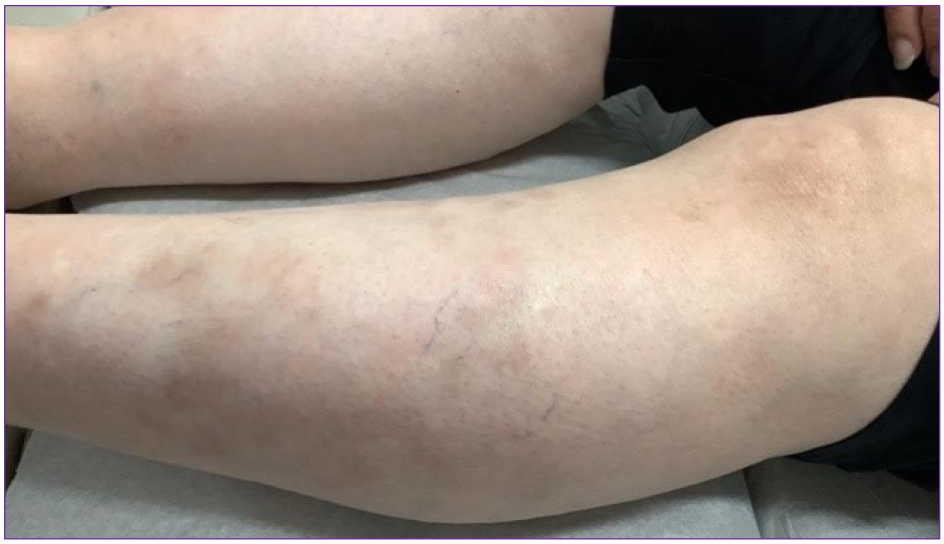

Figure 2. After using eight months of Opzelura cream daily and a total of 15 months of hydroquinone 8% pads (2/6/24)

contributes to the literature supporting the effectiveness of JAK inhibitors in managing granulomatous disorders. The pathophysiology involves cytokines recruiting and activating macrophages through JAK-signal transducer and activator of transcription (STAT) signaling.[11] Evidence suggests that JAK-STAT signaling may be chronically activated at a low level in NL.[7] Thus JAK inhibition can potentially dampen immune cell activation and T-cell-mediated inflammation.[11] Previous case reports have also highlighted positive outcomes in NL following treatment with JAK inhibitors.[5-8]

However, Opzelura cream has yet to be FDA approved as a monotherapy or an adjuvant treatment for granulomatous disorders, such as NL. Further research with larger, high-powered studies or increased randomized controlled trials to compare the relative efficacy of existing treatment options for NL may provide insight to the benefit of broadening the clinical spectrum for use of Opzelura cream, especially if it has already been FDA-approved for other conditions, such as myeloproliferative disorders and autoimmune diseases, such as vitiligo and rheumatoid arthritis.[12]

Our patient is continuing treatment with Opzelura cream presently with good results. A key takeaway after confirmed NL via biopsy may be to closely monitor for improvement or lack thereof on first-line treatment with topical corticosteroids and then promptly considering trying different treatments, such as Opzelura cream or other modalities. In conclusion, treatment of necrobiosis lipoidica is important to alleviate symptoms, prevent complications, and address cosmetic concerns. Further research is necessary to improve our understanding of the condition, develop more effective treatments, and enhance patient care and outcomes.

Conflict of Interest Disclosures: None

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