SKIN

BRIEF ARTICLE

A Rare Case of Superficial CD34+ Fibroblastic Tumor: A Case Report

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ABSTRACT

Introduction Pexidartinib, an oral tyrosine kinase inhibitor targeting the CSF-1R pathway, is FDA-approved for treatment of tenosynovial giant cell tumor (TGCT). We describe a patient with recurrent pigmented villonodular synovitis (PVNS) who developed cutaneous lupus erythematosus (CLE) during long-term pexidartinib therapy. This is an adverse event not previously reported in the literature, and this report focuses on the successful management of CLE while continuing pexidartinib therapy for underlying TGCT

Case Report A 63-year-old woman presented to dermatology with a photosensitive rash involving the scalp, face, upper chest, and arms three years into treatment. Initial skin biopsy demonstrated dense lichenoid dermatitis with dermal mucin, and labs revealed a positive dsDNA antibody with negative ANA and ENA panel. Although these findings may be seen in idiopathic CLE, the clinical context and temporal association raised concern for a drug-associated process. The rash persisted despite moderate potency topical steroids, leading to a formal diagnosis of CLE. Her cutaneous symptoms responded to intensified topical therapy including clobetasol 0.05% solution, tacrolimus 0.1% ointment, and intralesional triamcinolone injections. Four years after initiation of pexidartinib, hydroxychloroquine 200 mg twice daily was prescribed due to worsening joint pain and rising ANA titers. After one year of hydroxychloroquine therapy, her CLE showed near-complete resolution.

Discussion This case highlights that CLE, while potentially drug-associated, does not always necessitate cessation of essential systemic therapy. With appropriate dermatologic co-management, including topical corticosteroids and systemic immunomodulators, patients may experience major improvement without compromising oncologic care.

INTRODUCTION

Cutaneous lupus erythematosus (CLE) is a chronic autoimmune dermatosis with varied clinical presentations and multifactorial etiology.[1] It is characterized by photosensitivity, inflammatory plaques, and histopathologic features including interface dermatitis and dermal mucin deposition.[2] CLE can present independently or as a cutaneous manifestation of systemic lupus erythematosus, and its etiology includes both idiopathic and drug-induced forms.[3] A wide

range of medications have been implicated in drug-induced CLE, including antihypertensives, antiepileptics, chemotherapeutics, and biologic agents.[4-5] Proposed mechanisms involve medication-triggered immune dysregulation in genetically predisposed individuals, often leading to lupus-specific autoantibody production and characteristic cutaneous findings.[6]

Pexidartinib is an oral small molecule tyrosine kinase inhibitor that selectively targets the colony-stimulating factor 1 receptor (CSF-1R) pathway.[7] It is FDA-approved for the treatment of tenosynovial giant cell tumor (TGCT), a rare neoplasm characterized by overproduction of CSF-1 and infiltration of macrophages into synovial tissue.[8-9] By inhibiting CSF-1R, pexidartinib reduces the recruitment and survival of tumor-associated macrophages, leading to clinical improvement in patients with otherwise refractory disease.[9-10] However, CSF-1R also plays a broader role in regulating macrophage polarization and immune homeostasis. Disruption of this axis may promote aberrant immune responses in peripheral tissues, including the skin.[11-13]

While dermatologic adverse events such as rash, pruritus, and hair color changes have been reported during pexidartinib therapy, the development of CLE has not previously been described.[7-8,14] The latency of autoimmune dermatologic manifestations and their variable serologic profiles can complicate timely recognition and management. Here, we describe a case of CLE arising during long-term pexidartinib use, highlighting an approach to maintaining oncologic treatment while achieving dermatologic control through collaborative care.

CASE REPORT

A 63-year-old woman with recurrent pigmented villonodular synovitis (PVNS) of the right knee was enrolled in a clinical trial evaluating the CSF-1R inhibitor pexidartinib (Turalio). Following prior surgical interventions with limited success, she experienced significant functional improvement on pexidartinib 800 mg twice daily, reporting decreased pain and enhanced mobility. However, three years into pexidartinib therapy, she developed a progressive, pruritic, and photosensitive rash. Lesions initially appeared on the bilateral ears and subsequently spread to the bilateral cheeks, chest, upper back, arms, and scalp (**Figure 1A-G**). The patient denied systemic symptoms including fever, fatigue, arthralgia, myalgias, and oral ulcers at this time.

Physical examination revealed erythematous scaling plaques in a photo-distributed pattern. Also present were follicular papules and “carpet-tacking” features localized to the conchal bowls, along with involvement of the scalp and trunk. A 4 mm punch biopsy of the chest revealed lichenoid interface dermatitis with a superficial and deep perivascular lymphocytic infiltrate and prominent dermal mucin deposition, findings consistent with cutaneous lupus erythematosus (CLE) (**Figure 2**). Direct immunofluorescence was not performed.

Initial laboratory evaluation revealed a positive anti-dsDNA antibody (titer 24 IU/mL; reference >10 positive) with negative ANA, SSA, SSB, Smith, and RNP antibodies. Given the chronicity, distribution, and histopathologic findings, a clinical diagnosis of CLE was made. The patient was reluctant to discontinue pexidartinib treatment due to

its continued efficacy in controlling her recurrent PVNS.

Initial management included topical alclometasone 0.05% cream to the face, fluocinonide 0.05% cream to the trunk and extremities, and clobetasol 0.05% solution for the scalp. Tacrolimus 0.1% ointment was later introduced to minimize steroid-induced atrophy, particularly on the face. Persistent plaques on the scalp were treated with intralesional triamcinolone injections. These interventions yielded partial symptom control, with the patient experiencing intermittent flares.

Four years into pexidartinib therapy, the patient developed new-onset arthralgia affecting the small joints of the hands and reported morning stiffness. Repeat labs revealed a weakly positive ANA (1:40) while dsDNA and other ENAs normalized. Due to concern for evolving systemic autoimmunity, hydroxychloroquine 200 mg twice daily was initiated five months after she developed arthralgia.

Over the following months, the patient reported improved joint pain and near-complete resolution of cutaneous lesions (**Figure 3A-D**). After one year of hydroxychloroquine therapy, her CLE was clinically quiescent, with only mild erythema noted on the vertex scalp. Topical therapies were gradually de-escalated. She remained on pexidartinib without interruption

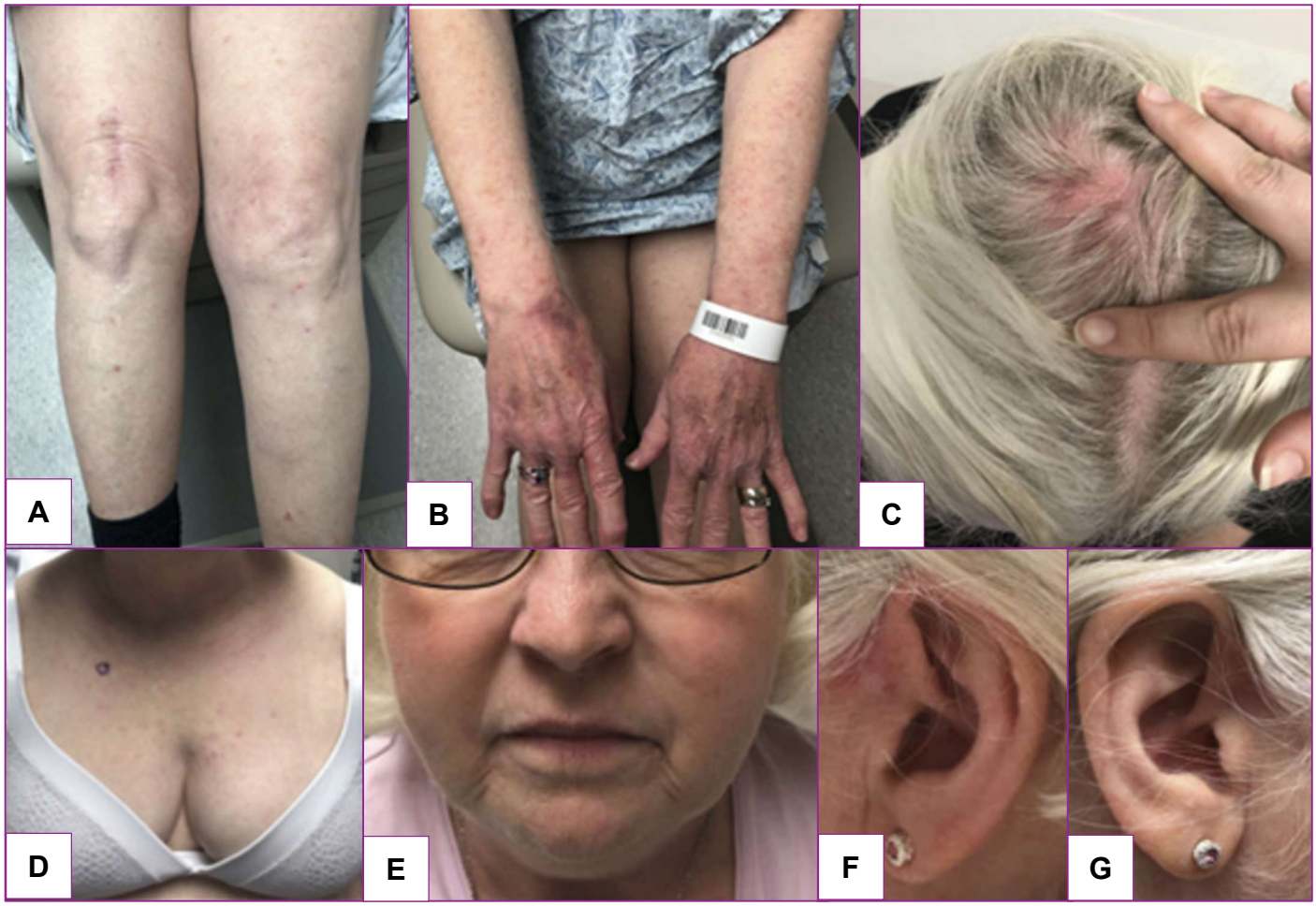

Figure 1A-G. CLE lesions on the scalp, ears, and chest prior to initiation of hydroxychloroquine

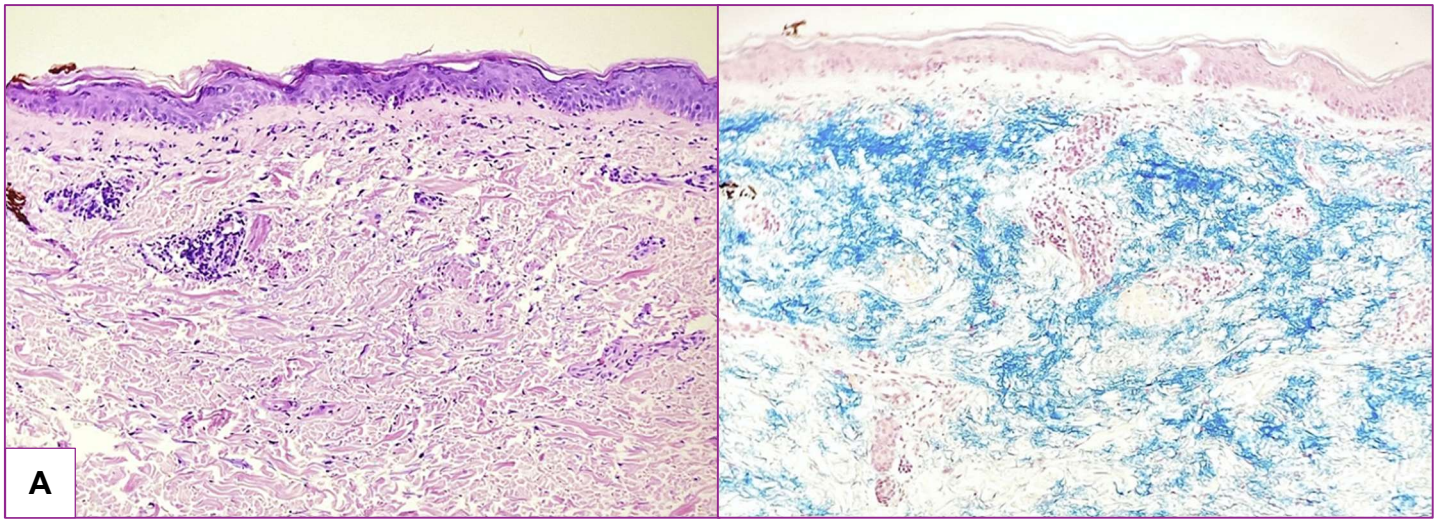

Figure 2(A). H&E-stained slide showing vacuolar interface dermatitis with scant lymphocytic infiltrate and scattered dyskeratotic keratinocytes. There is peri-adnexal scant inflammatory infiltrate composed of lymphocytes and scattered plasma cells (40x). **(B)** Colloidal iron stain shows significant dermal mucin deposition (20x).

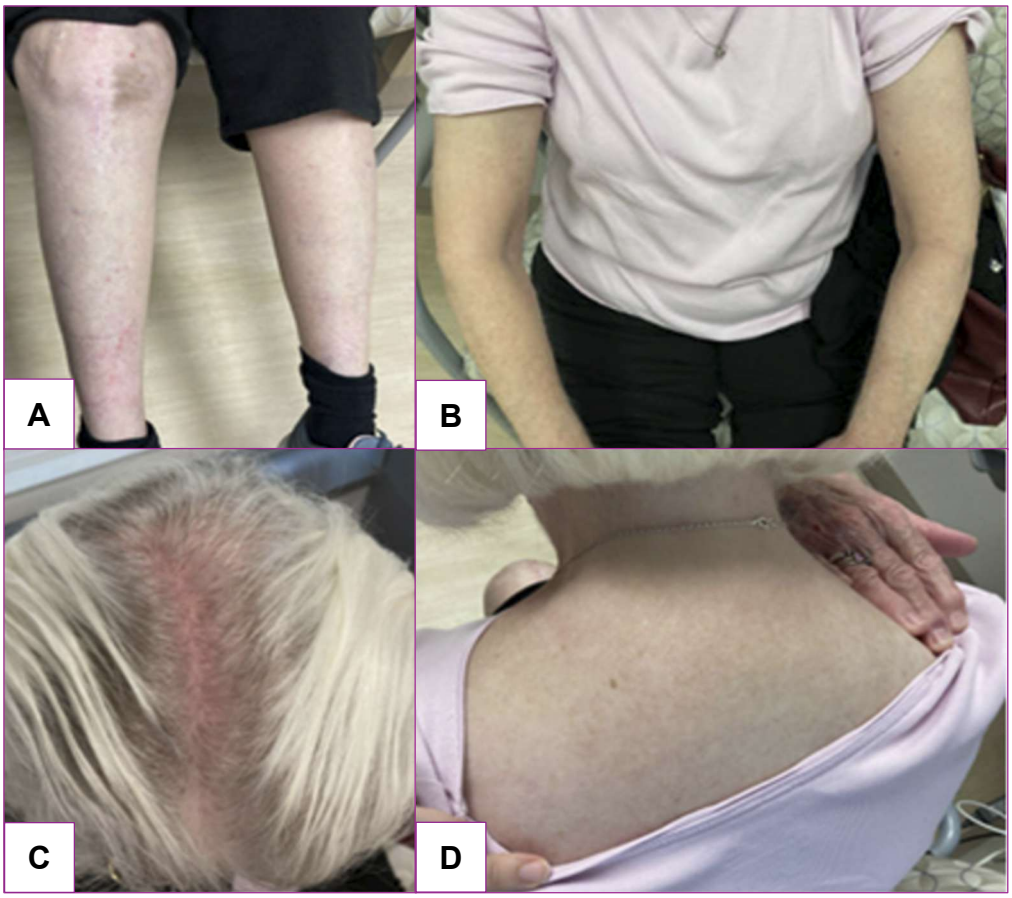

Figure 3A-D. Resolution of CLE lesions following initiation of hydroxychloroquine therapy

throughout the course of her dermatologic management.

DISCUSSION

Although drug-induced CLE has been described with multiple agents, this is the first reported association with the CSF-1R inhibitor pexidartinib. The latency of symptom onset (three years post-initiation) and serologic profile (initial dsDNA+ but ANA−) challenges traditional diagnostic frameworks and raises the possibility of pexidartinib-induced immune dysregulation.[5] CSF-1R inhibitors may alter macrophage activity and immune homeostasis, which may contribute to CLE pathogenesis in predisposed individuals.[6-7]

The patient's clinical course underscores that development of drug-induced CLE does not always necessitate discontinuation of the causative agent. CLE-associated symptoms may be adequately controlled with a combination of topical corticosteroids, topical calcineurin inhibitors, intralesional steroids, and oral hydroxychloroquine. In this case oral hydroxychloroquine was associated with dramatic clinical improvement, supporting its role in refractory CLE.[8]

This case highlights the need for dermatologist and oncologist awareness of emerging drug-induced CLE phenotypes and reinforces the value of dermatologic co-management to maintain oncologic therapeutic continuity.

Conflict of Interest Disclosures: Dr. Anne Marano is a consultant for Immunovant and a principal investigator for Biogen and Bristol Myers Squibb. All remaining authors report no conflicts of interest. No funding sources were utilized for this work.

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