Treatment of lichen sclerosus and hypertrophic scars with dupilumab

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INTRODUCTION

Lichen sclerosus (LS) is an inflammatory dermatosis characterized by chronic pruritus that often leads to scarring and disfigurement and predominantly affects women.[1] The most common area of involvement is the anogenital region, but 20% of the patients develop extragenital LS.[1] The pathogenesis of LS is currently unknown. Recent work implicates T helper (Th)1 involvement with a cascade of proinflammatory cytokines (interferon gamma, CXCR3, CXCL9, CXCL10, CXCL11, CCR5, CCL4, and CCL5).[2] However, the significant pruritus of LS is not easily explained by these implicated pathways. The mainstay therapy for LS involves potent topical corticosteroids with a taper after resolution of symptoms.[3] Topical calcineurin inhibitors to prevent atrophy from long-term topical corticosteroids are also used. LS can be difficult to treat and frequently recurs. The use of dupilumab through inhibition of interleukin (IL)-4/IL-13 signaling to treat pruritus in patients without atopic dermatitis is becoming more common and has not been previously described for the treatment of LS. In addition, recent evidence suggests targeting IL-4/IL-13 may benefit keloids.[4-6] Here we present a patient with extragenital LS and symptomatic hypertrophic scars that improved with dupilumab.

Abbreviations used:

IL: interleukin
LS: lichen sclerosus
Th: T helper

CASE REPORT

An 80-year-old woman presented to our dermatology clinic with a 1-year history of a pruritic rash that started on her chest and spread to both her arms and legs. She had failed to improve with topical corticosteroids. On physical examination, her arms had confluent lichenified plaques in the antecubital fossae (Fig 1, *A*). Her chest had a hyperpigmented plaque centrally, surrounded by pink-brown firm papulonodules (Fig 2, *A*). Laboratory work was performed, and antinuclear antibody serology, serum protein electrophoresis, urine protein electrophoresis, immunofixation electrophoresis, anti-Scl-70, and polymyositis/dermatomyositis autoantibody panel (Jo1, PL-7, PL-12, SRP, Mi-2, MDA-5, EJ, Ku, OJ, transcription intermediary factor 1-gamma, and NXP-2 autoantibodies) were all negative. A skin biopsy of her right arm showed hyperkeratosis and homogenization of the papillary dermis with flattening of the rete ridge pattern and focal basal vacuolar change, consistent with LS with lichenification (Fig 3, *A*). A skin biopsy of a firm papule from her chest revealed epidermal acanthosis with whorled fibroplasia in the dermis, increased number of interstitial fibroblasts, and a perivascular lymphohistiocytic inflammatory cell infiltrate, consistent with hypertrophic scar (Fig 3, *B*).

The patient was initially treated for 3 months with halobetasol ointment twice daily and mycophenolate mofetil 1000 mg twice daily without improvement. Next, she was treated for 6 months with betamethasone ointment, phototherapy, and methotrexate 15 mg weekly without benefit. Given

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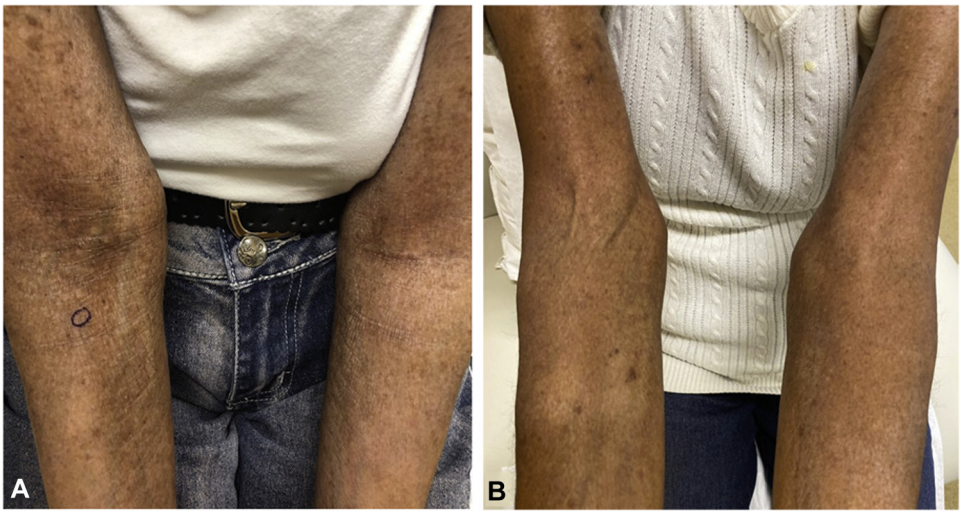

Fig 1. Lichen sclerosus (LS) improvement after 10 months of dupilumab therapy. **A,** Before treatment. **B,** After treatment.

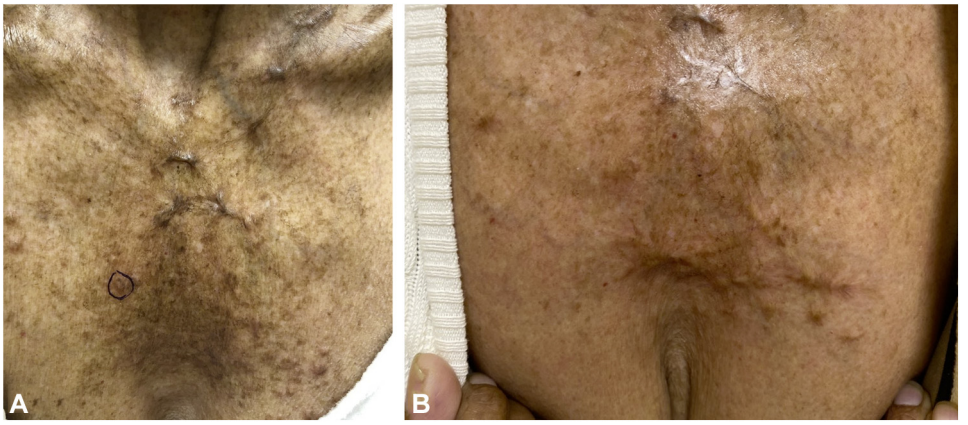

Fig 2. Improvement of hypertrophic scars and lichenified rash on chest after 10 months of dupilumab therapy. **A,** Before treatment. **B,** After treatment.

significant itch with lichenification, she was treated with dupilumab 300 mg every 14 days after an initial 600-mg loading dose. Within 3 months of starting dupilumab, the itch from her LS and hypertrophic scars was reduced. After 10 months of therapy with dupilumab, LS had resolved (Fig 1, *B*), and the hypertrophic scars (Fig 2, *B*) were reduced in size and asymptomatic.

DISCUSSION

This case suggests dupilumab as a potentially effective therapy for extragenital LS, especially for associated pruritus and lichenification. The response of extragenital LS to dupilumab may suggest underlying IL-4/IL-13 signaling in the pathogenesis of LS. While previous work has demonstrated a Th1 role in vulvar LS,[2] more research is needed to elucidate the potential involvement of Th2 and IL-4/IL-13 cytokines in the development of genital and extragenital LS. Furthermore, this case suggests that dupilumab may also be effective to treat the symptoms and clinical appearance of hypertrophic scars. In our case, dupilumab was more successful at alleviating itch than reducing the size of the hypertrophic scars. Recently, keloids were shown to respond, in part, to dupilumab therapy.[4] Moreover, keloids show expression of Th2 cytokines IL-4/IL-13 in addition to IL-22.[5,6] This unique case underscores targeting itch as a symptom with cytokine blockade and resultant disease resolution for dermatoses that are not considered Th2-mediated. Clinical trials are currently underway investigating the use of dupilumab for keloids (NCT04988022), but little is known about cytokine involvement in hypertrophic scars. Further research is needed to evaluate dupilumab as a potential therapy for LS.

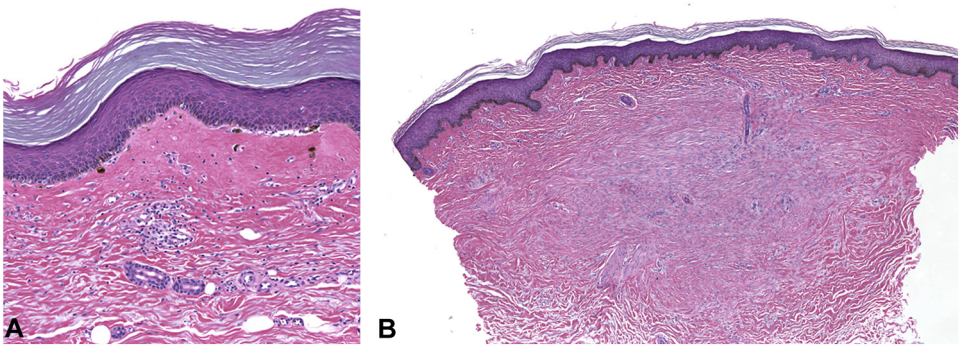

Fig 3. Histopathology of lichen sclerosus (LS) (**A**) and hypertrophic scars (**B**).

Conflicts of interest

Dr Vesely's spouse is an employee of Regeneron Pharmaceuticals, the maker of dupilumab. Dr Damsky is a consultant for Pfizer, Eli Lilly, and TWi Biotechnology, has received research funding from Pfizer, and receives licensing fees from EMD/Millipore/Sigma. Dr Peterson has no conflicts of interest to declare.

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