The use of dupilumab for the treatment of recalcitrant brachioradial pruritus

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INTRODUCTION

Acquired cutaneous brachioradial pruritus (BRP) is a neuropathic condition that presents with intense itching and burning along the dorsolateral forearm and significantly impacts patients' quality of life.[1,2] Although there are treatment options that may prove effective, there is limited literature regarding guidelines for BRP patients who are resistant to first-line therapies. Here, we describe a case of BRP that was refractory to numerous topical and systemic treatments and eventually showed remarkable improvement with dupilumab, a biologic agent that modulates cytokines involved in the type 2 helper T-cell response.[3] We also examine the pathophysiology of this condition and provide commentary on the use of dupilumab for the treatment of BRP.

CASE REPORT

A 53-year-old woman with a history of fibromyalgia and a bulging cervical disc presented with a four-month history of a pruritic rash on her right forearm. The patient described constant itching and a burning sensation throughout the day that was unresponsive to triamcinolone 0.1% cream. The patient's medical history was significant for scoliosis and a protruding disc in her cervical spine, as proven by magnetic resonance imaging. She denied any history of atopy or new antibiotics, medications, or new skin care products. Upon initial presentation, her physical examination was notable for a poorly demarcated eruption on the lateral arms, and diffusely on the upper back and shoulders bilaterally, with hyperpigmented, flattened, lichenified micropapules in the areas where the patient was scratching (Fig 1, *A*).

Abbreviation used:

BRP: brachioradial pruritus

A punch biopsy demonstrated lichenified papular dermatitis with minimal inflammation, consistent with secondary changes and not primary inflammatory dermatosis according to the reviewing pathologist (Fig 2, *A*). Elastin tissue stain showed clumped and thickened elastin fibers (Fig 2, *B*). Over a two-month period, a number of different therapies were administered without symptom resolution. Topical therapies included fluocinonide 0.05% cream, doxepin hydrochloride 5% cream, crisaborole 2% cream, clobetasol 0.05% ointment, and mupirocin 2% ointment. Systemic therapies were also attempted, including anti-histamines (hydroxyzine, cetirizine, fexofenadine) and neuropathic agents (gabapentin, pregabalin). Additionally, antibiotic treatments (cephalexin 500 mg, sulfamethoxazole/trimethoprim 800mg/160mg, and ozenoxacin cream) were administered due to upper extremity cellulitis.

Given the lack of therapeutic improvement, the patient was started on dupilumab with a 600 mg loading dose followed by 300 mg every 2 weeks, as well as a soak-and-smear regimen with pramoxine cream and clobetasol in a 3:1 ratio and amitriptyline 25-50 mg for additional relief. Following dupilumab initiation, the patient reported a 95% improvement of her pruritus within the first 3 months (Fig 1, *B*). She discontinued amitriptyline after one month due to excellent control of the pruritus, and she remained free of pruritus flares for the past 8 months without any

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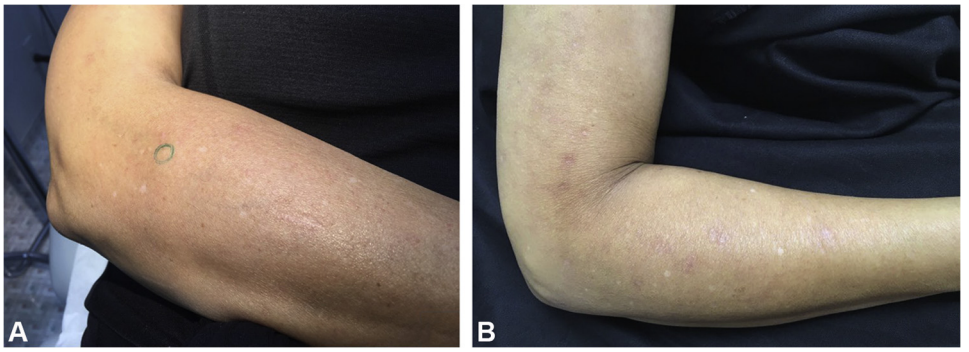

Fig 1. **A**, Our patient initially presented with widely scattered, flattened lichenified papules on the right mid-extensor forearm without primary lesions. **B**, The lichenified surface improved due to the resolution of the pruritus, and hypopigmented macules from chronic skin manipulation remain. However, she experienced significant resolution of her pruritus following dupilumab therapy for 12 weeks.

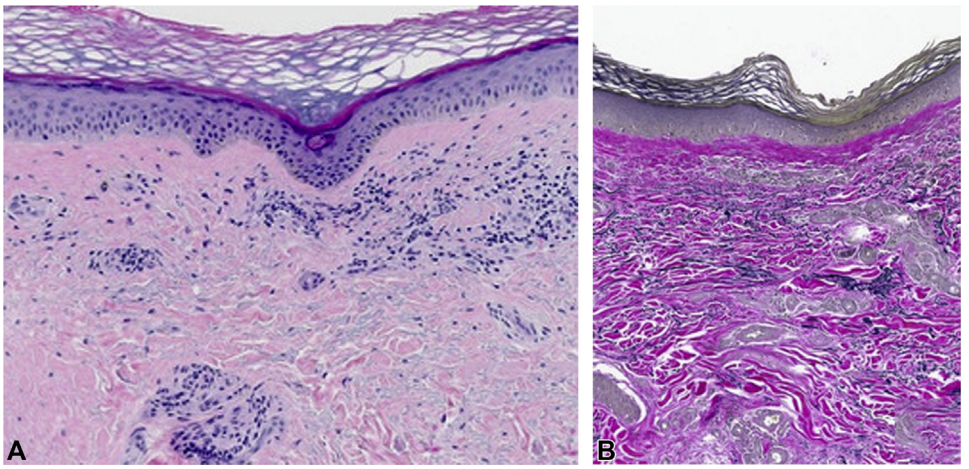

Fig 2. **A**, Punch biopsy demonstrating lichenified popular dermatitis with minimal inflammation. **B**, Elastin tissue stain showed clumped and thickened fibers.

supplemental oral therapy. Patch testing was deferred due to the neuropathic nature of her pruritus and the lack of primary dermatitis on both physical exam and biopsy.

DISCUSSION

BRP is a relatively uncommon neuropathic dysesthesia localized to the dorsolateral forearm and upper arm that is most commonly observed in middle-aged females.[1] The condition is characterized by constant unilateral or bilateral itching, tingling, stinging, or burning sensations that can extend proximally as far as the cervical region or upper thorax and significantly impacts quality of life.[2] While patients may present with secondary skin findings, including excoriations, lichenification, and/or prurigo nodules, no primary skin lesions are typically observed on physical exam.[4] Additionally, there are no pathognomonic histopathological findings representative of BRP, although actinic elastosis, as noted in our patient, and decreased density of dermal and epidermal nerve fibers are often appreciated on dermopathologic examination.[1]

The underlying pathogenesis of BRP is largely unknown. Leading theories suggest that cervical spinal nerve impingement due to degenerative changes (as seen in our patient) or spinal cord tumors and/or extensive ultraviolet radiation exposure may contribute to BRP development.[1,4,5] This cervical spinal nerve irritation causes normal stimuli to be interpreted as noxious, resulting in neuropathic itching that is distributed along the affected dermatomes.[6] Importantly, however, the diagnosis of BRP can be made in the absence of radiographic cervical spine abnormalities or extensive ultraviolet radiation history.[1]

Given the underlying mechanism of BRP, the key first-line treatment options are neuropathic agents that improve pruritic symptoms, including topical neuropathic agents (pramoxine, lidocaine, doxepin,

and capsaicin), oral neuropathic agents (amitriptyline, gabapentin, and pregabalin), and narrowband ultraviolet B therapy. However, it is possible that these first-line agents may not provide adequate relief from BRP, particularly if the patient presents with more generalized pruritus[7] or has an underlying atopic dermatitis.[3] In these situations, dupilumab may be a highly beneficial and effective alternative.

Dupilumab is an IL-4 receptor-α monoclonal antibody antagonist used for the treatment of moderate-to-severe atopic dermatitis that results in that significantly reduces itch severity.[8,9] It is thought that IL-4, IL-13, and IL-31, the key cytokines of Th2-mediated inflammation, act on peripheral sensory itch neurons. By binding to the IL-4 receptor, dupilumab inhibits the signaling of these cytokines and JAK1 signaling downstream, thereby impeding the inflammatory cascade that has been shown to drive chronic, non-specific pruritus.[9] Recent case reports have demonstrated the potential benefits of dupilumab in patients with pruritic conditions, such as refractory anogenital pruritus, uremic pruritus, prurigo nodularis, and chronic pruritus of unknown origin.[3,10] However, to our knowledge, this is the first study to suggest the efficacy of dupilumab in the treatment of BRP.

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Conflicts of interest

Dr Murase has participated in Advisory Boards for Genzyme/Sanofi, Eli Lilly, Dermira, and UCB, participated in Disease Statement management talks for Regeneron and UCB, and provided dermatologic consulting services for UpToDate. Dr Fullerton Stone has served as a consultant for Ortho Pharmaceuticals and Dermira.

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