Primary localized cutaneous amyloidosis (PLCA) is characterized by deposition of keratinocyte-derived amyloid within the papillary dermis. PLCA often presents with intensely pruritic, waxy papules that coalesce into plaques on the extensor surfaces of the extremities. PLCA is most common in Asians and South Americans, and has been associated with atopic dermatitis (1–3).

PLCA poses a therapeutic challenge. Various treatment methods have been employed, but evidence in the form of randomized controlled trials is lacking. Topical therapies for PLCA include high potency steroids, calcipotriene, and menthol (4). Systemic therapies include acitretin, cyclophosphamide and cyclosporine. Additionally, the use of phototherapy and laser therapy has been reported (5). Despite the array of available treatments, PLCA often exhibits limited response, with frequent recurrence. Herein, we describe two cases of PLCA successfully treated with methotrexate (MTX).

CASE REPORTS

Case 1. A 57-year-old Chinese man presented with a 30-year history of pruritic papules and plaques on his forearms and shins. He rated his itch severity as 8 on a 10-point numeric rating scale (NRS). He failed to respond to multiple prior treatments including high potency corticosteroids with occlusion, combined topical ketamine 10% and amitriptyline 5%, and UV phototherapy. He experienced minimal relief of pruritus with doxepin 25 mg daily, gabapentin 1,200 mg daily, and use of compounded topical mometasone 0.075%, menthol 2% and pramoxine 2%. Dermatological exam revealed symmetrical, dome-shaped papules coalescing into plaques on his forearms and pretibial surfaces (Fig. 1). Histology revealed collections of homogeneous, eosinophilic material with artifactual cracks in the papillary dermis, with plump, stellate-shaped spindle cells. Clinical and histopathologic findings were diagnostic of PLCA. Due to the recalcitrant nature of this patient’s disease, treatment was commenced with methotrexate 15 mg weekly and folic acid. Within 4 weeks, the patient experienced resolution of plaques and papules (Fig. 1), and his pruritus severity decreased from 8 to 3. He tolerated the medication well and did not experience any adverse effects. After 4 months of use, the patient felt he no longer needed MTX and chose to discontinue it. He subsequently began to experience recurrence of pruritic papules on his forearms and shins. The patient was restarted on MTX and responded well.

Case 2. A 71-year-old Chinese man presented with a 30-year history of pruritic papules on his calves and shins. He rated his itch severity as 10/10. He failed to respond to numerous treatments including systemic antihistamines, high potency topical corticosteroids, intralesional triamcinolone, tacrolimus ointment, topical imiquimod and PUVA. Dermatological exam revealed extensive keratotic brown papules on bilateral shins and calves. Histology showed eosinophilic and amorphous amyloid deposits in the upper dermis that were enhanced by Congo Red staining and exhibited apple-green birefringence on polarised microscopy. The stratum corneum was hyperkeratotic and the epidermis showed mild acanthosis with hypergranulosis. These findings were consistent with the diagnosis of PLCA. He was started on methotrexate 10 mg weekly with folic acid. At a 2-month follow-up visit the patient reported complete resolution of
his itch and marked improvement in the appearance of the papules on his legs (Fig. 2).

DISCUSSION

The underlying pathophysiology of PLCA remains unclear. Severe pruritus is a hallmark finding, and skin manifestations are thought to arise as a reaction to chronic scratching. The origin of pruritus in this condition has not been fully elucidated. Recent studies have demonstrated decreased innervation within the epidermis and dermo-epidermal junction, as well as evidence of small fiber neuropathy in lesional skin of patients with PLCA (6). It has been postulated that pruritus may arise from hypersensitivity of the remaining nerve fibers (7). Additionally, increased cutaneous expression of the interleukin (IL)-31 receptor has been detected in PLCA skin samples. Increased IL-31 expression has also been detected in other pruritic conditions including atopic dermatitis, prurigo nodularis, and cutaneous T-cell lymphoma (8). While the mechanism underlying the effect of methotrexate on PLCA is unclear, MTX has well-established ability to reduce itch in each of the aforementioned conditions (9).

A recent systematic review of PLCA therapies analyzed numerous therapeutic approaches but did not include MTX (10). The review emphasized the need for an effective PLCA therapy, as the treatment options mentioned have little evidence of reproducible efficacy. Notably, in our patients MTX was effective not only in resolving the skin manifestations of PLCA, but also in reducing pruritus. Moreover, MTX provided relief in longstanding disease that persisted for decades and failed to respond to several other treatment attempts. Thus, we propose that methotrexate be considered as a treatment option in cases of refractory PLCA.

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