Ultraviolet-A1 phototherapy in the treatment of primary diffuse cutaneous amyloidosis: an additional phototherapy regimen for cutaneous amyloidosis with review of treatment options

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Summary

Primary cutaneous amyloidosis (PCA) is a chronic pruritic skin disorder of unknown origin. We report on the case of a 48-year-old Indian woman with diffuse biphasic amyloidosis in which UVA1 phototherapy resulted in marked improvement of skin lesions and pruritus. UVA1 phototherapy was administered as monotherapy five times a week for 3 weeks with an exposure at a single dose of 130 J/cm² resulting in a cumulative UVA1 dose of 1950 J/cm². After treatment, the skin appeared less pigmented with flattened papules, and the histology revealed the disappearance of amyloid deposits and the presence of melanophages in the dermis. A comprehensive review of the literature on the treatment options for PCA showed no controlled trials available. However, case series indicated phototherapy (UVB, narrow band UVB, photochemotherapy) as the most successful treatment.

KEY WORDS: primary cutaneous amyloidosis; biphasic amyloidosis; ultraviolet A1 phototherapy.

Introduction

Primary cutaneous amyloidosis (PCA) is a rare, chronic pruritic skin disorder characterized histologically by the deposition of amyloid in the papillary dermis, without systemic organ involvement (1). The spectrum of clinical presentation of PCA includes macular hyperpigmented, nodular and papular (lichenoid) forms (2-4). Lichen amyloidosis is a form of primary localized cutaneous amyloidosis that is associated with pruritic skin-colored or hyperpigmented hyperkeratotic papules (5). In biphasic amyloidosis both macular and papular lesions are present (4, 6). Amyloidosis cutis dyschromica is an additional rare form of primary cutaneous amyloidosis (7, 8). Therapy of PCA is not standardized and many treatment modalities have been used with variable success. We describe the clinical case of an Indian woman with diffuse biphasic amyloidosis in which ultraviolet (UV) A1 phototherapy resulted in marked improvement of skin lesions and pruritus, with disappearance of amyloid deposits in the affected skin.

Case report

A 48-year-old Indian woman presented a ten-year history of multiple pruritic brownish macules and papules involving the arms, limbs and the upper back. She was affected by autoimmune thyroiditis since seven years and was taking tapazole. Examination revealed brownish macular lesions with reticular pattern surmounted by hyperkeratotic and hyperpigmented papules on the extensor aspects of the limbs and on the interscapular area (Figure 1). Widespread and symmetrically distributed papules coalescing into plaques were prominent on the arms, thighs and legs. Laboratory tests, including total cell blood count, liver and renal function, LDH, serum calcium and immunoglobulin, serum protein electrophoresis, and β2 microglobulin levels were in the normal range. Urine electrophoresis was negative for Bence-Jones proteins. Free T3 and free T4 were normal, whereas thyroid stimulating hormone (TSH) was reduced at 0.01 microU/mL (n.v., 0.25-5 microU/ml). Anti-tyreoglobulin and anti-tyreoperoxidase antibodies were elevated at 259 UI/mL (n.v., < 31 UI/mL) and at 541 UI/mL (n.v., <12 UI/mL), respectively. Antinuclear antibodies were negative. Laboratory test showed eosinophilia and the total IgE serum level was elevated at 136 KU/l (n.v., <10), whereas specific IgE against common allergens were absent. Chest X-ray and abdominal echo scan do not revealed abnormalities. Histological examination of a skin biopsy revealed mild epidermal acanthosis with mild orthokeratotic hyperkeratosis, and small eosinophilic, hyaline globular deposits in the papillary dermis admixed with melanophages, resembling the cytoid bodies of lichen planus (Figure 2). Crystal Vio-
let stains were positive, as well as immunohistochemical staining for cytokeratins 5 and 14. The patient had used repeatedly topical steroids and H1 antihistamines without benefit, and she was then treated with total body UVA1 phototherapy (cabin Sellamed System, Sellas, Gevelsberg, Germany) five times a week for 3 weeks with an exposure at a single dose of 130 J/cm². No other therapies were given with the exception of emollients. No treatment had been given for at least 6 weeks before the initiation of UVA1 photother-

Figure 1 - Hyperpigmented macules on the intra- and infra-scapular regions.

Figure 2 - Eosinophilic globular deposits of amyloid barely distinguishable from collagen are present in the papillary dermis admixed with melanophages (A). Amyloid deposits stain positively an antibody against cytokeratin 5 (B) and with Crystal Violet (C). Disappearance of amyloid deposits after UVA1 phototherapy, with the presence of numerous melanophages in the upper dermis (D).
apy. After 3 weeks the result was a cumulative and high UVA1 dose of 1950 J/cm². Irradiance was measured with a UVAmeter (Mutzhas, Munich, Germany) and found to be 80 mW/cm² at body surface. The skin appeared less pigmented and less infiltrated, the papules greatly improved, leaving slight pigmentation. The patient reported a consistent reduction of pruritus at the end of treatment, from 9 to 2 in a 0 to 10 visual analogue scale (VAS). A second biopsy revealed the absence or disappearance of amyloid deposits in the papillary dermis and the presence of numerous melanophages in the upper and mid dermis (Figure 1D).

Discussion

PCA is a rare skin disorder in Europe and North America but is common in South East Asia and in some South American countries (9). In one epidemiological study, Chinese women found to be predominantly affected and familial cases were not uncommon (9-11). Both sporadic and familial forms of lichen amyloidosis associated with either dominant or recessive mutations in IL-31RA and oncostatin M receptor mutations have been described. Familial cases with an autosomal dominant pattern of inheritance are more common in certain parts of the world, up to 10% in South America, Southeast Asia and the Middle East (10, 12). Other than genetic predisposition, prolonged friction, infections and other environmental factors may favor or trigger the development of PCA (1, 3).

Current evidence supports the hypothesis that in macular and papular PCA the amyloid derive from keratinocytes. Degenerated or apoptotic keratinocytes shed into the dermis are phagocytosed by histiocytes or fibroblasts and the aggregated keratin filaments are converted into amyloid. Amyloid fibrils may also be secreted by damaged or stimulated basal cells and produced at the dermo-epidermal interface (2, 12).

PCA is a chronic progressive skin disorder with disabling course and unsatisfactory treatment. A comprehensive review of treatment options for PCA showed no controlled trials available, and thus no evidence based therapy can be proposed. However, case series and case reports indicated phototherapy as the most successful treatment. Phototherapy, short-wavelength UVA, broad band and narrow band UBV have been employed with benefit in many patients (4, 9-13). Narrow band UBV phototherapy diminishes basal cell activity and reduces the production of amyloid (3), and it is effective to treat itch (5, 14), but the mechanisms involved in PCA improvement are unknown. Bath PUVA associated with oral acitretin have been used with satisfactory clinical results and itch reduction in two cases (5, 15). In PCA the combination therapy of narrow band UBV and tacrolimus ointment 0.1% have been used in one case with significant improvement of papules and hyperpigmentation and with remission of pruritus (4). In lichen amyloidosis, PUVA has been reported to be effective in alleviating itch and flattening of skin lesions. In a prospective left-right comparative study on 20 consecutive patients was found that there was more improvement in itch with PUVA compared to UBV, but UBV conferred an advantage for reducing roughness (9, 16). Narrow band UBV phototherapy become the most widely used treatment option being easier to use and highly effective in diminishing pruritus intensity. This treatment have been used in three patients with good results, and in two of those cases lichen amyloidosis was associated with atopic dermatitis (3, 5, 17). In our patient, we used UVA1 phototherapy, which is never been reported previously in the treatment of PCA. Long-wavelength UVA1 radiation has been used successfully and with good tolerability in a variety of inflammatory and neoplastic skin diseases (9, 11, 18).

During the last three decades, UVA1 phototherapy has emerged as a specific phototherapeutic modality with distinct modes of action and some well established indications. Atopic dermatitis, localized scleroderma and systemic lupus erythematosus seem to be the conditions with the best evidence regarding efficacy and safety of UVA1 phototherapy. Further indications for UVA1 include subacute prurigo, lichen sclerosus, dyshidrotic dermatitis, cutaneous T cell lymphoma, urticaria pigmentosa, and pityriasis rosea (19).

Other treatments attempted in PCA include systemic acyclovir and interferon-alpha (20). Topical, systemic and intralesional corticosteroid have been used but with limited success. Dermobrassion, curotherapy, oral and topical calcineurin inhibitors alone, cyclophosphamide, radiation and chemotherapy have also been used in general with limited efficacy (3-5, 9, 21, 22). Variable results have been obtained with antihistamines (hydroxyzine), topical and systemic retinoids such as etretinate, acitretin and isotretinoin, used especially in lichen amyloidosis (6, 9, 23). Topical dimethyl sulfoxide 50% solution in water was found to be beneficial in some cases with rapid and marked improvement of papules and pruritus (9), whereas partial and transient reduction of pruritus but no amyloid-dissolving properties have been reported by others (24).

Fractional CO₂ laser has been used to treat 25 patients affected by PCA with some benefit, using both superficial and deep modes of fractional laser (25). Two patients affected by lichen amyloidosis have been treated with CO₂ surgical laser with good response especially for the pruritus, after a failed treatment with topical corticosteroids in both cases (26). Amitriptyline was effective in controlling itch in two cases of lichen amyloidosis, supporting the hypothesis that small-fiber neuropathy may play a role in the pathogenesis of itch in PCA (1).

In summary, PCA may cause significant discomfort to patients and therapy effective on both pruritus and skin lesions is necessary. Current evidence indicated narrow band phototherapy the best treatment option. UVA1 phototherapy may represent an additional safe and effective therapeutic alternative.
References


