

An alternative treatment model: The combination therapy of narrow band ultraviolet B phototherapy and tacrolimus ointment 0,1% in biphasic amyloidosis

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Abstract

Primary localized cutaneous amyloidosis (PLCA) is caused by the extracellular deposition of amyloid material in the skin without other cutaneous or systemic organ involvement. PLCA is classified into lichen, macular, and nodular amyloidosis. Macular amyloidosis and lichen amyloidosis are named as biphasic amyloidosis when they are concurrently seen in a patient. The treatment of this disease is insufficient, even if there are several alternatives for treatment. Here we present a case of biphasic amyloidosis that responded well to topical tacrolimus ointment 0,1% plus narrow band ultraviolet B (NB-UVB) treatment to be able to generate a new treatment alternative model. With this case presentation, by reviewing of the treatment modalities of this rarely observed case, will contribute to the solution of the disease.

Keywords: Amyloidosis, Lichen, Narrow band ultraviolet B.

Introduction

Primary localized cutaneous amyloidosis is composed of a group of diseases characterized by deposition of amyloid in skin without involvement with other cutaneous or systemic disorders.¹ Primary cutaneous amyloidosis can be grouped into three types: macular, lichen (papular), and nodular clinically. Concurrent appearance of lesions of macular and lichen amyloidosis (LA) is named as biphasic amyloidosis. The treatment of the disease is inadequate, even if there are several alternatives for treatment.² Presented here is a case of biphasic amyloidosis that responded well to topical tacrolimus ointment 0,1% plus narrow band UV-B treatment to be able to generate a new treatment alternative model. With this case presentation, by reviewing of the treatment modalities of this rarely observed case, contributing to the solution ways of the disease is targeted.

Case Report

A 26-year-old woman presented to the out-patient clinic of

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the dermatology clinic of Gaziosmanpasa University, Tokat, Turkey in October 2012, with hyperpigmentation and pruritic hyperkeratotic papules, mainly located on chest, back, face and both of the extensor aspects of extremities. The patient declined that these lesions initially occurred 7



Figure-1: The lesions on the limbs.



Figure-2: The lesions on the back before treatment.



Figure-3: The appearance of the back after treatment.

years ago and spread by time. Her medical history was negative for systemic diseases especially for conditions that are associated with pruritus. She did not have a family history of skin disorders. On dermatologic examination, brown-black rippled hyperpigmented patches on back, chest, extensor surface of arms and limbs were observed. (Figure-1). In addition to these, multiple hyperkeratotic firm, shiny, fine discrete violaceous to brownish lichenoid papules with the tendency to coalesce and form plaques were also seen especially on the back of the patient and also limbs (Figure-2). The laboratory examinations that consisted of full blood count, erythrocyte sedimentation rate, electrolytes, Hbs Ag, Anti-Hbs, Anti-HCV, HIV, hepatic, thyroid, and renal function tests, urinalysis and immunoglobulin E (IgE) level were within the normal

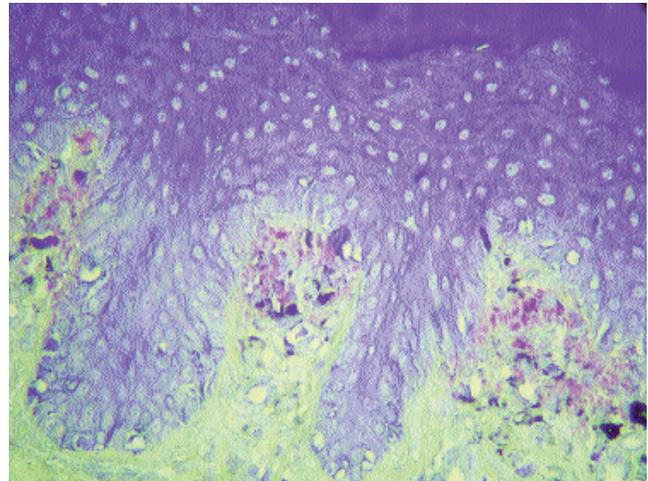


Figure-4: Amyloid deposits pink stained in a globular form in papillary dermis. Hyperkeratosis, acanthosis and melanophages stained in brown-black colour are seen (crystal violetx400).

range. Serum protein electrophoresis did not show a monoclonal spike. Thyroid ultrasonography, chest X-ray and abdominal ultrasonography did not reveal any systemic pathology. A punch biopsy was performed on the back of the patient. Hyperkeratosis, irregular acanthosis, superficial perivascular mononuclear cell infiltration and globular homogeneous eosinophilic deposits stained with crystal violet in the papillary dermis were detected by histopathological examination (Figure-3). The diagnosis of macular and lichenoid amyloidosis were established based on these histopathological and clinical findings.

The patient was treated with topical and/or systemic corticosteroids, topical moisturisers and systemic antihistamines before, however these drugs gave no satisfactory results. Topical tacrolimus ointment 0,1% and narrow band ultraviolet B (NBUVB) treatment simultaneously were started. The starting dose was 150 mJ/cm² and was increased by 20% for every treatment. Over a 8-week period, he received 20 treatment sessions (on average three treatments per week) reaching a total dose of 12.035J/cm². In the days that the patient did not receive phototherapy treatment, tacrolimus ointment 0,1% was applied two times a day. At the end of the 8 weeks, significant improvement was noted; remission of pruritus and flattening of the papules especially on the back and upper limbs were observed and also the amount of the cutaneous hyperpigmentation decreased (Figure-4). However, even if the results were encouraging, the patient gave up the narrow band ultraviolet B treatment since the patient moved to a city far from our center. So, we only recommended tacrolimus ointment 0,1% and topical

moisturisers till the next visit.

Discussion

The term biphasic amyloidosis is used when macular amyloidosis and lichen amyloidosis coexist.¹ Lichenoid form usually is observed as hemispheric papules forming plaques on the shin or other extensor surfaces of the extremities, however back involvement as pigmented macules in a reticulate pattern is generally viewed in macular amyloidosis.³ First of all the lesions shows unilateral pattern, later symmetrical distribution is observed.⁴ Our case was distinctive from the other cases since the location of lichen amyloidosis lesions were mainly located on the back as well as the extensor aspects of the extremities. In fact this posterior part of the trunk is usually involved as macular amyloidosis.

Chronic irritation of the skin has been postulated as an etiological factor.⁵ It is suggested that amyloid deposition in macular amyloidosis and lichen amyloidosis is primarily caused by epidermal keratinocyte degeneration, any relationship between systemic amyloidosis has not been detected.⁶

Even if there are several treatment alternatives for primary cutaneous amyloidosis, the results are unsatisfactory and since the disease runs a chronic course, therapeutic management remains challenging. Potent topical corticosteroids, topical calcineurin inhibitors, keratolytic agents, topical dimethyl sulfoxide (DMSO), intralesional corticosteroids, PUVA and UVB phototherapy, systemic retinoids, low-dose cyclophosphamide, cyclosporine have been used for medical management of LA.⁷ Electrodesiccation,⁸ dermabrasion,⁹ hydrocolloid dressings and pulsed-dye laser therapy^{1,10} are the other alternatives. There have been several reports about the successful usage of acitretin, especially found effective in treating pruritus and hyperkeratotic papules.^{11,12} Yüksek et al. demonstrated that tanscutaneous electrical nerve stimulation (TENS) therapy was quite effective treating pruritis in patients with macular amyloidosis.¹³ In an another study recently reported menthol was used effectively in the treatment of therapy resistant pruritus in lichen amyloidosis.¹⁴ There are not many reports about the usage of topical calcineurin inhibitors, however Cazares et al reported improvement in lichen amyloidosis using treatment with 0.1% topical tacrolimus ointment.¹⁵

Photochemotherapy was thought to be a potential complication of amyloid deposition, but these were not supported in subsequent studies.¹⁶ Jin et al. reported that both PUVA and UVB phototherapy are useful alternatives in the treatment of the disease by a comparative prospective study. Patients with lichen amyloidosis were

treated with UVB or topical PUVA on one limb and moderate to potent topical corticosteroids on the other limb. The patients reported that on the phototherapy-treated sides there was a certain improvement in itching and reducing skin roughness at 8 weeks.¹⁷ In an another report it was suggested that combined therapy with bath PUVA photochemotherapy and oral acitretin provides an efficacious and useful treatment method for lichen amyloidosis.¹⁸

NB-UVB phototherapy is especially effective in treating pruritus, suppressing keratinocyte proliferation, reducing inflammation and causing apoptosis of keratinocytes and infiltrated T-cells. This therapy causes reduction in basal cell activity and causes reduction in amyloid production.¹⁹ Oiso et al. reported a case of an adult man with LA associated with atopic dermatitis which was successfully treated with NB-UVB phototherapy, topical corticosteroids and an oral antihistamine.²⁰

Parsi et al. reported in a study that NB-UVB phototherapy over a 5-month period resulted in a marked improvement of pruritus and clearing of the amyloid deposits.¹⁶ As a result of these findings in these cases, we thought that this form of combination; both tacrolimus and NB-UVB treatment concurrently will be an alternative model that was never previously tried. Topical tacrolimus ointment 0,1% and NB-UVB treatment concurrently were started and in a period of eight weeks. At the end of the 8 weeks, marked relief of pruritus and decreasing in hyperpigmentation and flattening of skin papules were observed principally on the back and upper extremities. However, the patient gave up the NB-UVB because of the social reasons and was advised continuing with tacrolimus ointment 0,1% and topical moisturisers and called the next visit.

Conclusion

These findings, concluded that the combination therapy of narrow band ultraviolet B treatment and tacrolimus ointment 0,1% seems to bring hope and since this therapy is practical and has tolerable side-effects, it should be experienced by clinicians more widely. By the help of larger controlled studies we will be able to better establish the efficacy of this new modality of treatment.

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