Dermatology Practical & Conceptual

Dermal Amyloid Deposits: A Possible Misleading Pathologic Finding

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Key words: amyloid deposits, drug eruption, systemic amyloidosis, cutaneous involvement

Citation: Giacalone S, Maronese CA, Genovese G, Cusini M, Marzano AV. Dermal Amyloid Deposits: A Possible Misleading Pathologic Finding. *Dermatol Pract Concept.* 2023;13(1):e2023009. DOI: https://doi.org/10.5826/dpc.1301a9

Accepted: May 9, 2022; **Published:** January 2023

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

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Introduction

Amyloid is a highly organized fibrillar substance resistant to macrophage degradation. It can originate from more than 27 misfolded proteins. Extracellular amyloid deposition may result from several pathophysiological processes: abnormal protein production, excessive presence of normal proteins or senescence. Recently, reclassification of amyloidosis based on protein type led to the identification of subgroups with different etiology (acquired or inherited), clinical manifestations, and prognosis [1]. Some forms are localized while others involve multiple organs. Dermal amyloid deposits can be detected in both cases. Cutaneous localized amyloidosis includes keratinic and nodular amyloidosis. In the first case the macular and lichenoid lesions correspond to subtle deposits limited to the upper dermis, in the second case plaque and nodules are secondary to deep dermal and subcutis deposits.

The spectrum of cutaneous involvement in systemic amyloidosis encompasses a wide variety of lesions that reflect localization and abundance of amyloid deposits. Generally, amyloid deposition affects dermal blood vessels, that easily rupture upon minimal trauma, with subsequent appearance of petechiae, purpura and ecchymoses, mostly located on body folds. Profuse infiltration of amyloid within the dermis and the subcutis can manifest also as papules, plaques, nodules, bullae, and even scleroderma-like lesions. Amyloid infiltration in or about sweat glands, sebaceous glands, and hair follicles can result in anhidrosis and alopecia [2]. Curiously, amyloid deposits have been demonstrated in all of the aforementioned sites, also in clinically uninvolved skin [3]. Here, we present a case of massive dermal amyloid deposit both in involved and uninvolved skin that mislead clinical diagnosis.

Case Presentation

A 53-year-old man presented with a pruritic, non-confluent, maculopapular eruption of one month duration, consisting of discrete 5-10 mm lesions, symmetrically distributed on his

trunk, arms and upper thighs (Figure 1). His medical history was significant for multiple myeloma and systemic amyloid light-chain (AL) amyloidosis with cardiac, gastric and bone marrow involvement. He had been treated with allogenic bone marrow transplantation followed by bortezomib, endoxaban and dexamethasone without any adverse cutaneous reaction. The patient received pomalidomide ten days before the onset of the rash and the drug was promptly discontinued. He complained of xerostomia and development of hematomas after mild trauma. Histological examination revealed presence of multiple hyaline deposits in the superficial dermis, with perivascular, peri-adnexal, and interstitial arrangement (Figure 2A). Congo-red staining positivity along with apple-green birefringence under polarized light was consistent with amyloid (Figure 2B). Immunohistochemical typing of amyloid revealed lambda light chain accumulation (Figure 2C).

A course with prednisone 25 mg daily tapered over three weeks quickly led to clinical resolution of the eruption. However, 3 days following pomalidomide reintroduction, sudden reappearance of the same monomorphous lesions was observed.

Two additional punch biopsies were performed, on lesional and non-lesional areas, respectively. The former showed diffuse vacuolar change in the basal layer of the epidermis with scattered necrotic keratinocytes and a band-like superficial inflammatory infiltration. Amyloid deposits were detected in both specimens. Finally, a diagnosis of lichenoid drug eruption in the setting of systemic AL amyloidosis with concomitant massive dermal amyloid deposits was made.

Conclusions

Globally, mucocutaneous lesions have been described in 30% of all cases of systemic amyloidosis, and in up to 50% those with AL type [4]. Although the dermatologist may have a crucial role in the prompt diagnosis of systemic amyloidosis [5], massive presence of cutaneous amyloid, as in our case, could mislead both the dermatologist and the pathologist involved in the diagnostic process, masking other concurrent disorders. Indeed, detection of amyloid deposits in normal-appearing skin has been widely demonstrated in literature: in the past, several studies proposed to perform biopsy on uninvolved skin to confirm systemic cases

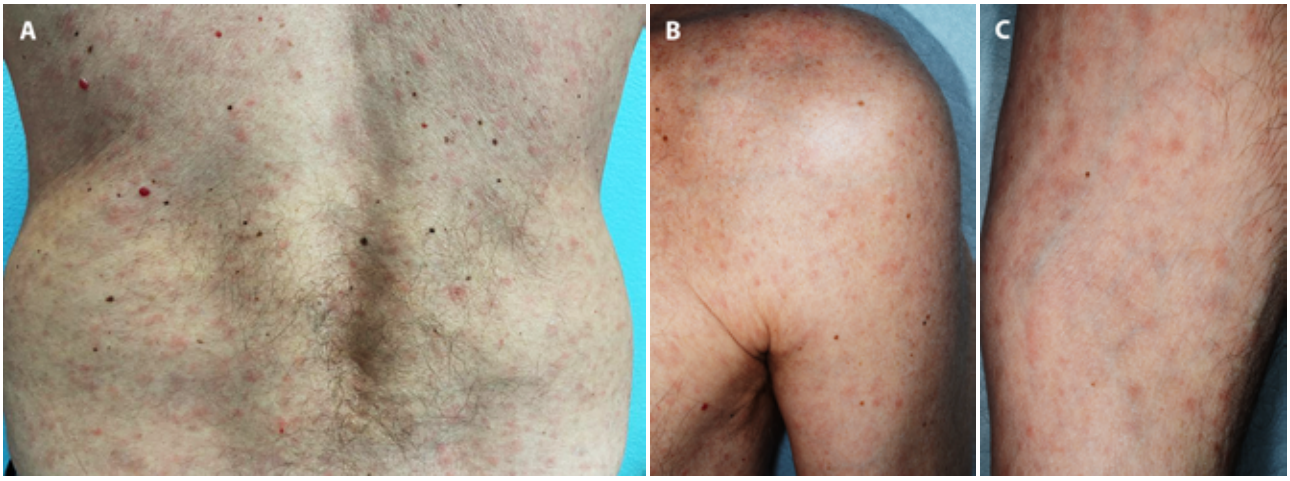

Figure 1. Non-confluent, maculopapular eruption of discrete 5-10 mm lesions on patient lower back (A), right arm (B) and right forearm (C).

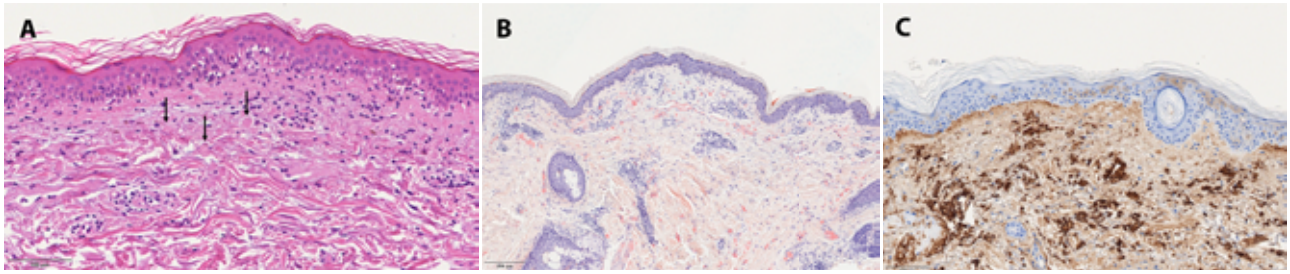

Figure 2. Histopathology showing diffuse vacuolar change in the basal layer of the epidermis with scattered necrotic keratinocytes and a band-like superficial inflammatory infiltration. (A) H&E x200 Notice dermal amyloid deposit (black arrows). (B) Congo red stain highlighting dermal perivascular, peri-adnexal, and interstitial infiltration of amyloid. (C) Immunohistochemical typing of amyloid revealing lambda light chain accumulation.

of amyloidosis [3]. However, even if type of dermatological findings depends on amyloid localization, the exact amount of deposit capable to trigger clinical modification has not yet been identified. In systemic amiloidosis, the presence of deposits in uninvolved sites enforces the idea that detection of amyloid in cutaneous lesions should not lead to hasty diagnostic conclusions. Although the possible cutaneous manifestations of systemic amyloidosis are protean, clinical confirmation bias should always be considered and avoided.

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