Skin Appendage Disorders

Novel Insights from Clinical Practice

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Nail Amyloidoma: Two Case Reports of a New Entity

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Established Facts

- Nail alterations such as brittleness, trachyonychia, longitudinal ridging, and distal onycholysis can occur in the context of systemic amyloidosis.
- Amyloidoma is defined as a localized tumoral deposit of amyloid in the absence of systemic amyloidosis. Currently, only one case of nail unit amyloidoma has been published.

Novel Insights

- Nail amyloidoma presents clinically as a firm nodule on the distal nail bed with associated onycholysis.
- Simple excision seems like an effective treatment. Long-term follow-up is currently recommended as immunoglobulin light chain amyloidoma may represent a localized plasma cell dyscrasia or a primary cutaneous marginal lymphoma.

Keywords
Amyloidosis · Amyloidoma · Localized amyloidosis · Nodular amyloidosis · Nail disorder

Abstract

Introduction: Amyloidosis is a group of diseases characterized by extracellular deposits of abnormal insoluble proteins in different tissues. Amyloidoma is a localized tumoral deposit of amyloid in the absence of systemic amyloidosis, and it has been described in different anatomic sites. We report two cases of amyloidoma in the nail unit and provide insights into this recently described entity. ***Case Presentation:*** Both cases presented as an asymptomatic, slowly growing nodule underneath the distal nail bed of a toe with associated onycholysis. Histopathology was characterized in both patients by the presence of deposits of Congo red-positive, homogeneous, amorphous, and eosinophilic material within the dermis and subcutaneous tissue admixed with aggregates of plasma cells. In both cases, an extensive workup excluded systemic amyloidosis. Treatment was based on local excision, and no local recurrence or progression to systemic amyloidosis was observed at 1 year of follow-up. ***Conclusion:*** These are the first reports of amyloidomas of the nail

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unit. The clinical and histopathological presentations parallel those of an amyloidoma affecting the skin. Local excision seems to be an efficient treatment modality, but long-term follow-up is warranted in order to exclude recurrence, an associated marginal B-cell lymphoma, or progression to systemic amyloid L amyloidosis.

Introduction/Literature Review

Amyloidosis encompasses a group of diseases characterized by extracellular deposits of abnormal insoluble proteins (amyloid) in different tissues. It can be either classified based on the amyloid chemical type or based on the affected tissues. Regarding amyloid type, amyloidosis can be subclassified into amyloid L (AL: immunoglobulin light chains), amyloid A (AA: serum amyloid-associated protein), amyloid K (AK: keratin-associated amyloid), and amyloid TTR (ATTR: transthyretin), among others [1, 2]. Based on the affected tissues, amyloidosis can be subclassified into systemic (generalized) forms, with involvement of several organs, and organ-limited (localized) forms, in which deposits are limited to a single organ. Amyloidosis affecting the skin can occur as a localized form, which can be primary (macular and lichen amyloidosis) or secondary (e.g., in association with a skin tumor), or as a cutaneous manifestation of systemic amyloidosis [1].

The term amyloidoma is defined as a localized tumoral deposit of AL or AA amyloid in the absence of systemic amyloidosis [3]. Amyloidomas have been described in widely varied anatomic sites besides the skin, including the genitourinary, respiratory, and gastrointestinal tracts, the breast, eye, bone, and tongue [4, 5]. Case reports with amyloidosis affecting the nail unit are sparse and usually limited to nail changes in the context of systemic amyloidosis [6–8]. Herein, we report two cases of AL amyloidoma in the nail unit and provide some insights of this recently described entity.

Case Report

Case 1

A 52-year-old Hispanic man with a clinical history of HIV infection with undetectable viral load and $CD4^+$ T-cell count of 800 cells/mm^3, hepatic cirrhosis due to chronic B and C hepatitis, and treated secondary syphilis presented with a painless subungual nodule of his first left toe evolving for 1 year. He denied any trauma or local symptoms. Physical examination showed an 8-mm yellowish hyperkeratotic firm nodule on the distal part of the nail bed, lifting up the plate (shown in Fig. 1a). X-rays of the second phalanx of the left great toe revealed a cutaneous mass on the dorsal aspect of the distal part of the toe without any relevant bone alterations. After plate avulsion for complete nail bed exposure, the nodule was fully excised. Histopathology of the nodule showed the deposition, throughout the whole dermis and subcutaneous tissue, of an amorphous acellular eosinophilic material, a moderate interstitial lymphocytic and plasma cell infiltrate, and focal calcification (shown in Fig. 1b). Congo red staining was positive on the amorphous material (shown in Fig. 1c). Positive apple-green birefringence under polarized light confirmed amyloid deposition. Immunohistochemistry on the amyloid deposits was negative for lambda or kappa immunoglobulin light chains, keratins, serum amyloid-associated protein (AA), and transthyretin. Immunohistochemistry showed predominance of lambda over kappa chains in the plasma cell infiltrate. An extensive workup, including a comprehensive metabolic panel, serum and urine protein electrophoresis and immunofixation, serum free immunoglobulin light chains, thoracoabdominopelvic computed tomography scan, and echocardiogram excluded systemic amyloidosis. A complete nail plate regrowth occurred 8 months after nail surgery. At 1 year of follow-up, there were no signs of local recurrence, amyloidomas elsewhere, or systemic amyloidosis.

Case 2

A 67-year-old Caucasian woman presented with a painless subungual nodule on her left third toe lasting for 1 year. Her medical history included stabilized rheumatoid arthritis with 13 years of evolution without need of specific treatment in the last 3 years, arterial hypertension, dyslipidemia, and osteoporosis. She denied any trauma on her toe or any local symptoms. Physical examination revealed a 10-mm pink smooth and firm nodule on the distal portion of the nail bed with associated distal onycholysis (shown in Fig. 2a). Ultrasound and X-rays showed a cutaneous and subcutaneous formation above the distal phalanx without any relevant underlying bone changes. The lesion was excised. Histopathology of the lesion revealed a homogeneous deposition of eosinophilic amorphous material in the dermis and subcutaneous tissue with few plasma cells (shown in Fig. 2b). Positivity for Congo red stain with green birefringence under polarized light confirmed the amyloid nature of the eosinophilic deposits. Immunohistochemistry on the amyloid deposits was negative for keratins, AA, and inconclusive for kappa and lambda chains. There was no monotypic expression of kappa or lambda chains on plasma cells. The same extensive workup as in case 1 was performed, and it ruled out systemic amyloidosis. A complete nail plate regrowth was observed after 10 months. Currently, at 1 year of follow-up, no signs of local recurrence or systemic amyloidosis have been detected.

Discussion

Along with a recently published article by Cheng et al. [9], the two previously presented cases are the first reports of amyloidomas of the nail unit. In both patients, deposition of amyloid occurred in the distal part of the nail bed, giving rise to a painless firm nodule slowly growing under

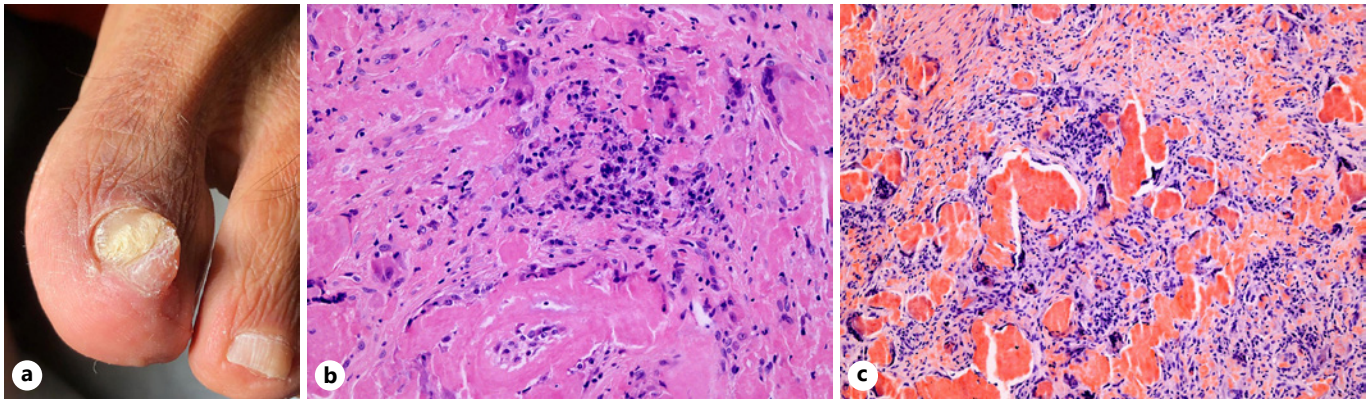

Fig. 1. a Hyperkeratotic nodule on the distal part of the nail bed, lifting up the plate. **b** Amorphous acellular eosinophilic material in the dermis and subcutaneous tissue and moderate interstitial lymphocytic and plasma cells infiltrate (H and E). **c** Amorphous material intensely stained with Congo red.

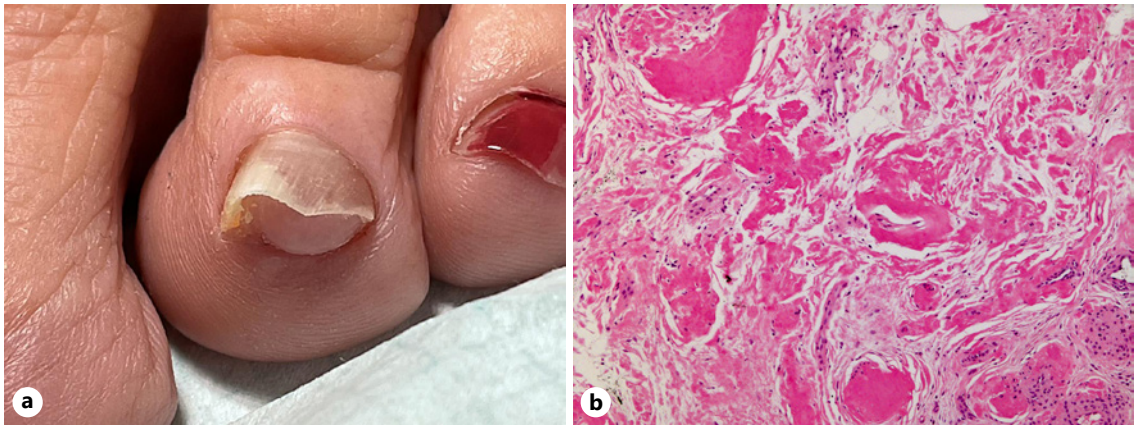

Fig. 2. a Smooth-surfaced nodule on the distal portion of the nail bed with associated onycholysis. **b** Homogeneous deposition of eosinophilic amorphous material in the dermis and subcutaneous tissue with few plasma cells (H and E).

the nail plate with consequent distal onycholysis. There was neither history of previous trauma or local symptoms nor obvious podiatric deformities that may generate microtrauma at those sites. Based on the presence of aggregates of plasma cells within the amyloid deposits, we rendered a diagnosis of AL amyloidoma in both patients. Systemic AL amyloidosis and multiple myeloma were excluded in both cases.

Nail changes in the context of systemic AL amyloidosis are uncommon, but they can be the first and unique sign of this systemic disease [6]. These include nail brittleness, trachyonychia, longitudinal ridging, onycholysis, subungual thickening, and subungual splinter hemorrhages, and the main clinical differential diagnosis is lichen planus [6, 10]. Nail biopsy may show amyloid deposits in the papillary dermis of the matrix, the nail bed, or nail folds [10, 11].

Nail changes in the context of a localized form of amyloidosis (amyloidoma) seem to be even rarer. The clinical presentation of a nail bed amyloidoma likely parallels that of an amyloidoma affecting the skin, in addition to the onycholysis caused by the nodule's growth. Cutaneous amyloidoma usually presents clinically as single or multiple pink to brown nodules or plaques affecting predominantly the skin of the face, extremities, and genitals [12–14]. It mainly occurs between the ages of 40 and 60, and there is no gender difference [12, 15]. It is found more frequently among Asians, South Americans, and Middle Easterners [12].

Histopathological features of the nodules of both of our patients were also similar to those observed in cutaneous amyloidomas. Histopathology of cutaneous amyloidoma shows a nodular deposit of eosinophilic material in the dermis and/or subcutaneous tissue staining with Congo red and showing apple-green birefringence under polarized light and corresponds to the amyloid deposits [16, 17]. Tissue architecture is usually preserved [18], but it can also be replaced by the tumoral deposits of amyloid [16]. A sparse perivascular infiltrate consisting of lymphocytes and plasma cells, which are usually monotypic, is also visible in cutaneous AL amyloidoma [3, 17–19]. Lesions are indistinguishable from cutaneous nodular deposits in systemic AL amyloidosis [16]. These features were also present in both of our cases, although monotypic expression of immunoglobulin light chains on plasma cells was absent in case 2.

AL amyloidoma is thought to be associated with a localized proliferation of monoclonal plasma cells, which presumably produce the AL [1, 17]. It may represent a localized "smoldering" type of extramedullary plasma cell neoplasm or a form of extranodal marginal zone lymphoma [3, 19, 20]. Exclusion of systemic amyloidosis, multiple myeloma, and other light chain-related diseases is mandatory [3, 19]. There is usually no systemic involvement in cutaneous AL amyloidoma, which remains a form of localized amyloidosis with an indolent course [17, 19]. Nonetheless, a minority of patients [4–15%] with AL amyloidoma may progress to systemic amyloidosis or other hematological dyscrasias [12, 17]. Therefore, long-term follow-up is recommended [14, 15, 17, 21]. There is also a well-documented association between cutaneous AL amyloidoma and autoimmune diseases, especially Sjögren syndrome and systemic sclerosis, but also primary biliary cirrhosis, systemic lupus erythematous, and rheumatoid arthritis [15–17, 20]. The continuous stimulation of the immune system in these conditions probably plays a role in the cutaneous plasma cell dysregulation associated with amyloidoma [14, 17]. Autoimmune diseases, especially rheumatoid arthritis, can also be associated with systemic amyloidosis rather than localized forms. In our case 2, however, despite the fact that our patient had rheumatoid arthritis, systemic amyloidosis was excluded.

In AA amyloidoma, the amyloid is derived from serum amyloid-associated protein, an acute phase reactant [18], and is associated with chronic inflammatory conditions, such as autoimmune diseases (especially rheumatoid arthritis) and chronic infections (e.g., tuberculosis), in addition to local trauma, infection, surgery, and peripheral vascular disease [16]. Although AA amyloidosis is generally regarded as a systemic amyloidosis, cases of skin AA amyloidomas without any systemic involvement have been reported and constitute proof that AA amyloidosis can occur locally [4], probably as a consequence of local chronic inflammation [16].

Based on case reports of cutaneous amyloidoma, treatment options may include surgical removal, debulking, dermabrasion, and ablative lasers, with variable results and recurrence rates [17, 21]. In case of partial excision, recurrence is common [21].

Conclusion

We described two rare cases of nail unit AL amyloidoma, which presented as an asymptomatic solitary nodule underneath the distal nail plate associated with onycholysis. The absence of systemic amyloidosis and the indolent clinical course were reassuring, and local excision appears to represent an efficient treatment modality. However, long-term follow-up is warranted in order to exclude recurrence, an associated marginal B-cell lymphoma, or progression to systemic AL amyloidosis.

Statement of Ethics

Written informed consent was obtained from patients for publication of these case reports and any accompanying images. This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

F.B. wrote the manuscript. U.S., A.K., and B.R. participated in the study design and final review.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Ueberdiek S, Kempf W, Kretschmer L, Peter Schön M, Mitteldorf C. AL-Amyloidoma of the skin: a rare manifestation of primary cutaneous marginal zone lymphoma. Am J Dermatopathol. 2019;41(7):518–21.
2 Magliulo G, Vincentiis L, Pace A, Visconti IC, Le Foche F, Riminucci M, et al. Unilateral isolated primary cutaneous amyloidosis of the external auditory canal. J Int Adv Otol. 2020;16(3):467–9.
3 Walsh NM, Lano IM, Green P, Gallant C, Pasternak S, Ly TY, et al. AL Amyloidoma of the skin/subcutis: cutaneous amyloidosis, plasma cell dyscrasia or a manifestation of primary cutaneous marginal zone lymphoma? Am J Surg Pathol. 2017;41(8):1069–76.
4 Kartal D, Canöz Ö, Balkanlı S, Çınar SL, Kesikoğlu A, Borlu M. Cutaneous amyloidoma: a rare case report. Ann Dermatol. 2016;28:643–5.
5 Sánchez López JD, Rodríguez Ruiz JA, Martínez-Sahuquillo Rico A. Isolated lingual nodular amyloidosis. Med Clin. 2020;154(10):424.
6 Litaiem N, Chabchoub I, Gara S, Slouma M, Hamdi MS, Zeglaoui F. Nail changes in systemic amyloidosis. Clin Case Rep. 2021;9(8):e04685.
7 Yang X, Liu D. Nail dystrophy as initial presentation of systemic amyloidosis. Australas J Dermatol. 2021;62(2):e310–1.
8 Jo G, Shin DY, Mun JH. Systemic amyloidosis-induced nail dystrophy. J Dtsch Dermatol Ges. 2019;17(10):1057–9.
9 Cheng YJ, Li Y, Lim KH, Oh CC. Dermatoscope of primary localized cutaneous nodular amyloidosis on hallux nail bed. JAAD Case Rep. 2022;27:46–8.
10 Rao RR, Yong WC, Wasko MC. Systemic light chain amyloidosis mimicking rheumatic disorders. Case Rep Med. 2016;2016:7649510.
11 Renker T, Haneke E, Röcken C, Borradori L. Systemic light-chain amyloidosis revealed by progressive nail involvement, diffuse alopecia and sicca syndrome: report of an unusual case with a review of the literature. Dermatology. 2014;228(2):97–102.
12 Wu X, Zhao Z. Primary localized cutaneous nodular amyloidosis presenting as lymphatic malformation: a case report. Open Life Sci. 2021;16(1):781–4.
13 Guillet C, Steinmann S, Maul JT, Kolm I. Primary localized cutaneous amyloidosis: a retrospective study of an uncommon skin disease in the largest tertiary care center in Switzerland. Dermatology. 2021;238(3):579–86.
14 Marano AL, Selim MA, Cardones AR, Burton CS. Nodular amyloidosis in a patient with systemic scleroderma. Dermatol Online J. 2018;24(9).
15 Dupont L, Martins Souza PR, Damiani L, Boff AL. Cutaneous nodular amyloidosis: a disfiguring aspect of the face. Am J Dermatopathol. 2019;41(12):945–7.
16 Billero VL, Jacobsen AA, Miteva MI, Wulkan AJ, Marasca C, Romanelli P. Nodular cutaneous amyloidoma of the extremity secondary to chronic granulomatous inflammation in setting of sarcoidosis. J Cutan Pathol. 2017;44(9):801–4.
17 Atzori L, Ferreli C, Matucci-Cerinic C, Pilloni L, Rongioletti F. Primary localized cutaneous nodular amyloidosis and limited cutaneous systemic sclerosis: additional cases with dermatoscopic and histopathological correlation of amyloid deposition. Dermatopathology. 2021;8(3):229–35.
18 Pasternak S, Wright BA, Walsh N. Soft tissue amyloidoma of the extremities: report of a case and review of the literature. Am J Dermatopathol. 2007;29(2):152–5.
19 Saggini A, Cerroni L, Lora V, Cota C. Biological significance of the association between cutaneous AL-amyloidoma and Sjögren syndrome. Am J Dermatopathol. 2020;42(7):553–5.
20 Caruana D, McCusker S, Harper C, Bilsland D. Curious facial plaque diagnosed as nodular primary localised cutaneous amyloidosis. BMJ Case Rep. 2019;12(5):e228163.
21 Reitboeck JG, Feldmann R, Loader D, Breier F, Steiner A. Primary cutaneous amyloidoma: a case report. Case Rep Dermatol. 2014;6(3):264–7.