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Case Report

Unilateral Isolated Primary Cutaneous Amyloidosis of the External Auditory Canal

Giuseppe Magliulo, Ludovica de Vincentiis, Annalisa Pace, Irene Claudia Visconti, Francesco Le Foche, Mara Riminucci, Alessandro Corsi

Department of Sense Organs, Sapienza University of Rome, Italy (GM, AP, ICV)
Department of Molecular Medicine, Sapienza University of Rome, Italy (LdV, MR, AC)
Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy (FLF)

ORCID iDs of the author: G.M. 0000-0003-3052-1969; L.d.V. 0000-0002-2812-2590; A.P. 0000-0002-0954-929X; I.C.V. 0000-0002-5831-1042; F.L.F. 0000-0002-1372-8725; M.R. 0000-0002-8643-9211; A.C. 0000-0001-6896-4509.

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Isolated primary cutaneous amyloidosis (PCA) of the external ear is extremely rare. We describe the case of a 65-year-old woman presenting with itching within the left external auditory canal (EAC). Otoscopy revealed a 3 mm whitish lesion involving the cartilaginous portion of the left EAC. The lesion was excised. Histological and immunohistochemical features were consistent with keratinic amyloidosis. A clinical workup was negative for systemic amyloidosis. As far as we know, only nine cases of PCA exclusively involving the EAC have been reported. The frequent occurrence of itching in these patients and the keratinic nature of the amyloid support the role of chronic stimulation/irritation in the pathogenesis of isolated amyloidosis the EAC.

KEYWORDS: External auditory canal, itching, amyloidosis, primary cutaneous amyloidosis, high molecular weight cytokeratins

INTRODUCTION

Primary cutaneous amyloidosis (PCA) refers to the deposition of amyloid either at the dermal–epidermal junction or within the dermis in otherwise normal skin and in the absence of any underlying systemic illness [1]. Three main clinico-pathological types have been distinguished. Lichen amyloidosis (LA) and macular amyloidosis (MA) commonly occur sporadically and can concur (biphasic amyloidosis) in the same patient [1]. Because LA and MA have been related to keratinocytes' degeneration and High Molecular Weight-Cytokeratins (HMW-CKs) have been demonstrated within the amyloid deposits, they are considered variants of the same disease and classified as keratin-type amyloidosis [1]. Conversely, nodular amyloidosis is due to the deposition of immunoglobulin light-chains, associated with plasma cell infiltration, and, sometimes, may progress to systemic disease [1, 2].

External ear skin involvement in PCA is uncommon and typically not associated with other concurrent skin lesions [2]. It presents with normochromic, yellowish-whitish or erythematous, usually pruritic, either unilateral or bilateral, variably sized papules mainly in the auricular concha [2]. Because isolated PCA of the external auditory canal (EAC) has been very rarely described [2-10], we report here a patient with unilateral localized PCA of the left EAC and review the pertinent literature.

CASE PRESENTATION

A 65-year-old female presented for itching within the left EAC. She denied any history of local trauma and was not under dialytic treatment. Her history was negative. Otoscopy revealed a smooth, firm, white papule, 3 mm in maximum dimension, in the cartilaginous portion of the left EAC. The examination of the right ear was negative. The lesion was excised through a microscopic transmeatal approach. Histologic examination revealed nodular deposits of an amorphous, eosinophilic, and homogenous material in the papillary dermis (Figures 1a and 1b). The deposits contained some clefts and were partially encircled by epidermal collarets. The overlying epidermis was thin and hyperkeratotic. Inflammatory cells and melanophages were absent. The deposits stained with Congo Red and, under polarized light, revealed the apple green birefringence characteristic of amyloid (Figure 1c). In addition,

Corresponding Address: Alessandro Corsi E-mail: alessandro.corsi@uniroma1.it
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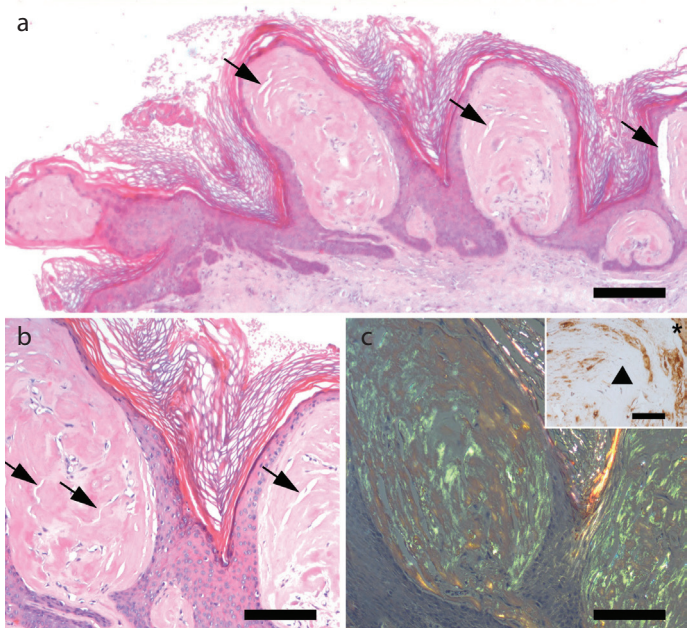

Figure 1. a-c. Low and high-power magnifications of the excissed sample are illustrated in a) and b) respectively. Deposits of amorphous, eosinophilic, and homogenous material are evident within the dermis. Clefts within the dermal deposits and at the dermal-epidermal junction are identified by arrows. The overlying epidermis is thin and shows hyperkeratosis. Polarized light view of a Congo Red stained section is shown in c. The deposits show the apple green birefringence characteristic of amyloid. The insert in C documents the presence of some immunoreactivity of the amyloid deposit (triangle) for CK34bE12. The basal portion of the epidermis, which immunostains for CK-34bE12, is identified by an asterisk. a) and b) haematoxylin and eosin. Bars: 200 µm in a, 100 µm in b and c and 50 µm in the insert.

immunohistochemical stains, performed as described previously [11, 12], revealed some immunoreactivity of the deposits for HMW-CKs (clone CK34bE12, RTU, Leica Biosystems, Newcastle, UK, insert in Figure 1c) but not for lambda (clone SHL53, RTU, Leica Biosystems) and kappa (clone CH15, RTU, Leica Biosystems) light chains. Because of the amyloid nature of the lesion, the patient underwent systemic examination, including full blood count, renal and liver function tests, serum immunoglobulin assays, and protein electrophoresis, which excluded other skin lesions and systemic diseases. Overall, the clinico-pathologic findings were consistent with the diagnosis of isolated (keratinic) PCA of the left EAC. A six-month follow-up showed a well-healed surgical site and no recurrences.

MAIN POINTS

- Unilateral localized cutaneous amyloidosis of the external auditory canal is rare.
- We describe a 65-year-old female presenting with itching in which histology and immunohistochemistry were consistent with keratinic amyloidosis.
- The immunohistochemical demonstration of HMW-CKs in the amyloid deposits could represent a simple and reproducible tool to establish their epidermal origin and to exclude an underlying associated condition such as plasma cell dyscrasia or chronic disease with secondary involvement of external ear.
- Taken together with the clinico-pathologic findings of previous reports, our case suggest that local chronic stimulation/irritation of the skin of the external auditory canal may be the cause of the amyloid deposition.

DISCUSSION

The term amyloidosis encompasses a spectrum of conditions sharing deposition in the extracellular spaces of insoluble polymerized protein fibrils in b-plated sheet configuration [1, 2, 13, 14]. Deposition may be either systemic or localized and occur sporadically as also in the context of hereditary disease [1, 13, 14]. Most common systemic variants of amyloidosis include: (1) AL- and AH-amyloidoses, typically occurring in hematological disorders like multiple myeloma, in which amyloid fibrils derives from immunoglobulin light and heavy chains; (2) AA-amyloidosis that is secondary to chronic inflammatory diseases such as rheumatoid arthritis and other connective tissue diseases; (3) Dialysis-related-amyloidosis in which the precursor protein is the b2-microglobulin; (4) ATTR-amyloidosis, in which the precursor protein is wild type (acquired ATTR-amyloidosis) or mutated (hereditary ATTR-amyloidosis) transthyretin. In all these variants, major organ dysfunction may occur, eventually with the lethal outcome if left untreated. In contrast, in localized amyloidosis, deposits occur in skin or internal organs [1, 2, 13] and surgical excision or radiotherapy are the treatment of choice whenever they cause a functional problem [13].

One of the most common variants of localized amyloidosis is PCA.[1] It may involve the skin of the external ear [2]. In the largest series of PCA of the external ear reported to date, 8 cases out of 17 involved the auricular concha, and only one was limited to the EAC[2]. To date, only 9 cases of PCA limited to the EAC have been reported [2–10]. The analysis of these cases demonstrates the similar prevalence of the lesion in males and females, the appearance in adult age (range 41-76 years), and no relevant discrepancy when considering unilateral and bilateral involvement. Chief complaints included itching, otorrhea, otalgia and hypoacusia, and, in one case [4], discomfort when wearing a hearing aid. Itching was also the major complaint in our case, in which, as in previously reported cases [6, 9, 10], the amyloid deposits showed some immunoreactivity for HMW-CKs, thus supporting their origin from degenerative changes of keratinocytes [1, 2]. Conversely, only in one of the previously reported cases the amyloid deposits showed immunoreactivity for the kappa light chain of the immunoglobulins [7]. The clinico-pathologic correlates of itching and HMW-CKs-positive amyloid deposits may support a vicious circle where itching and subsequent scratching induce degenerative changes of keratinocytes favoring further amyloid deposition, in turn leading to intensified itching. Obviously, whether scratching of intact skin or other mechanisms, including environmental and genetic factors [1], represent the trigger of the amyloid deposition is still an open issue.

The diagnosis of amyloidosis of the external ear may cause concern for physicians for raising the possibility of underlying systemic amyloidosis. The demonstration of HMW-CKs in the amyloid deposits could represent a simple and reproducible tool to establish their epidermal origin, thus excluding an underlying associated condition with secondary involvement of external ear [2]. As a consequence, it seems reasonable that physicians do not need to pursue extensive systemic clinical workup for these patients, except dermatologic ex-

amination since, even though rarely, amyloidosis of the external ear can concur with the involvement of other skin regions in the context of LA and MA [2, 15]. However, because of its rarity, further cases should be examined to exclude definitely a relationship between amyloidosis of the EAC, and more in general of the external ear, and systemic amyloidosis.

Finally, on the basis of the data from the literature, resection is the treatment of choice for isolated PCA of the EAC [3-5, 7, 9, 10]. In the cases in which follow-up was available [3, 9], recurrences have not been reported.

CONCLUSION

We describe a case of unilateral localized keratinic PCA of the EAC. The clinico-pathologic findings observed in our case, in combination with those described in the other few cases reported in the literature, support the absence of an association with systemic disease and a role of local chronic stimulation/irritation in its pathogenesis.

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