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### Authors

Principe, Patricia

Wong, Lulu

Luke, Janiene

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# Amyloid associated alopecia: A case report and review of the literature

Patricia Principe<sup>1</sup> BS, Lulu Wong<sup>2</sup> MD, Janiene Luke<sup>3</sup> MD

Affiliations: <sup>1</sup>Loma Linda University School of Medicine, Loma Linda University, Loma Linda, California, USA, <sup>2</sup>Division of Dermatology, Harbor-UCLA Medical Center, Torrance, California, USA, <sup>3</sup>Department of Dermatology, Loma Linda University, Loma Linda, California, USA

Corresponding Author: Patricia Principe BS, Division of Dermatology, Loma Linda University School of Medicine, Email: [pprincipe@students.llu.edu](mailto:pprincipe@students.llu.edu)

## Abstract

Primary systemic amyloidosis is a condition marked by the extracellular deposition of amyloid proteins within various organ systems in the body. Although cutaneous involvement is well-described, scalp involvement in the form of alopecia is rarely reported. We report a case of amyloid associated alopecia confirmed by histologic analysis to highlight this rare scalp manifestation associated with systemic amyloidosis.

*Keywords: androgenetic alopecia, case report, scalp, systemic amyloidosis*

## Introduction

Primary systemic amyloidosis, also known as amyloid light chain (AL) amyloidosis, is the extracellular deposition of monoclonal immunoglobulins in multiple tissue organs across the body that may lead to organ dysfunction and death. Clinical manifestations are often vague and nonspecific and may include fatigue, peripheral edema, orthostatic hypotension, exertional dyspnea, and weight loss [1]. The cutaneous manifestations of systemic amyloidosis are most commonly reported as pinch purpura, ecchymoses, petechiae, and macroglossia [2]. Alopecia is a less frequently reported skin finding associated with AL amyloidosis and is often a presenting sign preceding its

diagnosis [3]. We report a patient with known systemic primary amyloidosis in remission and progressive AL amyloid associated alopecia. This case highlights an underrecognized skin finding of this systemic disorder and the importance of scalp biopsy in workup and management.

## Case Synopsis

A 65-year-old woman presented to the Loma Linda University dermatology clinic for evaluation of constant scalp tenderness accompanied by diffuse hair thinning that had been stable for 2 years. The patient's medical history was significant for discoid lupus erythematosus well controlled on hydroxychloroquine, thyroid disease, and primary systemic AL amyloidosis reportedly in remission. Prior treatments with topical clobetasol foam and intralesional triamcinolone injections failed to improve alopecia or scalp tenderness. Previous biopsies reported follicular miniaturization consistent with nonscarring hair loss suggestive of androgenetic alopecia.

Physical examination revealed diffuse, nonscarring hair loss at the frontotemporal and vertex scalp (**Figure 1**). Owing to persistent and progressive hair thinning, a repeat biopsy was performed on the left parietal scalp (**Figure 2**) revealing diminished hair follicle density with preservation of sebaceous glands and no significant perifollicular fibrosis or inflammation. The limited evidence of follicular

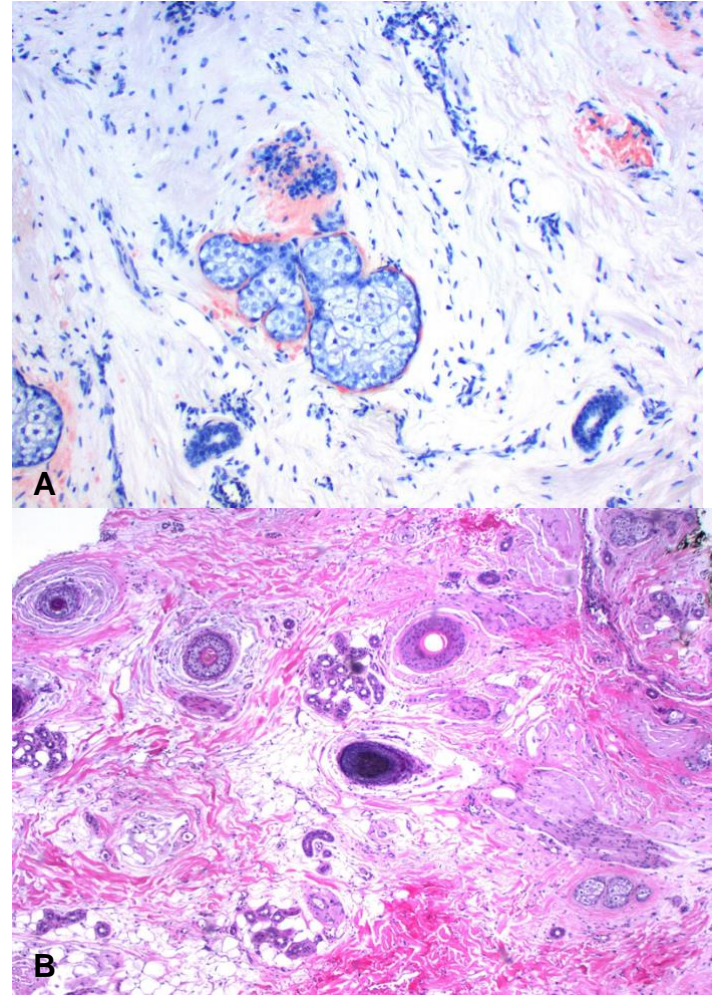
miniaturization and a normal number of telogen follicles argued against telogen effluvium and androgenetic alopecia. Perivascular, perifollicular, and interstitial deposition of eosinophilic, amorphous material was noted. Congo red stain revealed apple-green birefringence of deposits under polarized light, favoring a diagnosis of amyloid-associated alopecia. The patient was ultimately treated with intralesional kenalog, 2.5mg oral minoxidil daily, and quarterly platelet-rich plasma injections.

## Case Discussion

Amyloid light chain amyloidosis is a multisystemic disorder characterized by the deposition of misfolded immunoglobulin light chains forming aggregates in extracellular tissues. The inability to degrade these proteins results in tissue and organ dysfunction leading to a variety of nonspecific clinical symptoms.



**Figure 1. A)** Frontotemporal hair thinning, nonscarring. **B)** Right frontotemporal. **C)** Left frontotemporal. **D)** Frontal-middle.



**Figure 2. A)** Congo red. **B)** Hematoxylin and eosin stain. Both biopsies show similar features and are characterized by a diffuse loss of follicular structures. Sections show diminished number of hair follicles with no significant perifollicular fibrosis or inflammation. Sebaceous glands are preserved, and there is limited evidence of follicular miniaturization.

Although cutaneous manifestations are well described, scalp involvement is less commonly reported in the literature. To date, there are 17 other reports describing systemic amyloidosis-associated alopecia. Demographics reflect a predominance for female gender, older age, and White race ([Table 1](#)). Many of these reports describe alopecia as a presenting symptom preceding the diagnosis of amyloidosis ([Table 2](#)) [4]. On the contrary, we report a patient with progressive alopecia despite reported remission of underlying systemic amyloidosis. The histologic features of amyloid-associated alopecia involve deposition of eosinophilic,

amorphous material identified by Congo red staining surrounding hair follicles, upper dermis, and vessels. The pathogenesis for amyloid-induced alopecia remains unclear. Hunt et al proposed that mechanical compression of hair follicles by amyloid prohibits the progression of telogen follicles to the growth phase [5]. Additionally, amyloid invading blood vessels leading to vascular compromise has been suggested as a possible etiology.

Follicular miniaturization is a feature shared with androgenetic alopecia and the high ratio of telogen to anagen hairs can be seen in telogen effluvium. These nonspecific features contribute to the difficulty in recognizing amyloid associated hair loss in the absence of clinical suspicion. Miteva et al discuss the possibility of using dermoscopy to detect amyloid-associated alopecia, describing unique salmon-colored halos surrounding follicular ostia [6]. Future reports of dermoscopic findings may improve the detection of alopecia caused by amyloidosis.

## Conclusion

Amyloid induced alopecia is difficult to detect and often precedes the diagnosis of systemic amyloidosis. Scarce literature exists reporting clinical and histological findings. Early detection allowing appropriate management may be improved by careful dermoscopic and histopathologic examination.

## Potential conflicts of interest

The authors declare no conflicts of interest.

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**Table 1.** Demographics of patients reported with amyloid induced alopecia.

Age	Gender	Ethnicity	Type of amyloidosis	Reference
68	M	N/A	Primary systemic amyloidosis	Bedlow et al. [7]
68	F	White	Primary systemic AL amyloidosis	Bilal et al. [8]
81	F	N/A	Systemic AL amyloidosis	Bnaya et al. [9]
59	M	Caucasian	Amyloidosis	Cooley [10]
65	F	N/A	Systematized amyloidosis	Goltz.[11]
64	M	Asian	Primary systemic amyloidosis	Hsieh et al. [12]
59	F	Caucasian	Primary systemic amyloidosis	Hunt et al. [5]
63	F	N/A	Primary systemic amyloidosis	Lutz et al. [2]
50	F	Caucasian	Primary systemic AL amyloidosis	Magro et al. [4]
65	M	N/A	Primary systemic amyloidosis	Miteva et al. [6]
66	F	Caucasian	Primary systemic amyloidosis	Muller et al. [13]
65	F	African American	Primary systemic amyloidosis	Nia et al. [14]

66	F	Caucasian	Primary systemic AL amyloidosis	Renker et al. [15]
79	M	White	Primary systemic amyloidosis	Richey et al. [16]
48	F	N/A	Primary systemic amyloidosis	Samuelov et al. [17]
74	F	N/A	AL amyloidosis	Sutherland et al. [18]
65	F	N/A	Primary systemic amyloidosis	Wheeler et al. [19]

N/A, not available, AL, amyloid light chain, F, female, M, male

**Table 2.** Clinical features of amyloid-induced alopecia in patients with systemic amyloidosis.

Scalp exam	Scalp Biopsy findings	Systemic involvement	Other cutaneous findings	Preceded Dx	Underlying plasma cell dyscrasia	Treatment	Outcome	Reference/year published
Diffuse scalp alopecia	Ill-defined focal eosinophilic change in collagen fibers positive with Congo red. Numerous amorphous positive between collagen fibers on EM.	Nephrotic syndrome	Partial anonychia, macroglossia	yes	Plasma cell dyscrasia, not enough for multiple myeloma diagnosis	Continuous ambulatory peritoneal dialysis	N/A	Bedlow et al., 1998 [7]
complete hair loss of body, scalp, eyebrows, eyelashes, axillae, and genitalia	N/A	kidney failure requiring HD, heart failure	none	Yes	multiple myeloma	bortezomib and dexamethasone, switched to ixazomib due to lack of response	hair regrowth with chemotherapy initiation	Bilal et al., 2018 [8]

FT hair thinning, nonscarring	declined biopsy	joint pain, nephrotic syndrome	brittle nails, longitudinal ridging, onycholysis	yes	multiple myeloma	Bortezomib, cyclophosphamide, dexamethasone, daratumumab	unknown	Bnaya et al., 2023 [9]
Sparse scalp, axilla and pubic hair	N/A	Anorexia, inguinal node enlargement, generalized lymphadenopathy, splenomegaly, hepatomegaly,	Dry and flaky skin, boggy, brown and discolored eyelids with scarring and entropion	yes	Primary amyloidosis	Antiluetic, penicillin, ACTH	No improvement	Cooley, 1953 [10]
Sparse scalp hair and eyebrows	N/A	Elephantiasis, enlarged heart, anemia, itching,	Purpura, thickened skin, loss of fingernails, friable toenails, waxy skin with an ivory cast	yes	Multiple myeloma	urethane	Unaltered condition, no apparent change in skin lesions, sudden death ~45days after starting therapy	Goltz, 1952 [11]
rapid hair loss with whitening of hair on scalp, beard area, axillae, and genitalia	amyloid deposits around blood vessels and dermal papillae	hepatomegaly, cardiomegaly with atrial fibrillation, prostate hypertrophy	macroglossia	yes	primary systemic amyloidosis	DMSO	hair regrowth with repigmentation, cardiomegaly and hepatomegaly remained stable	Hsieh et al., 1987 [12]

diffuse scalp/body hair thinning, positive HPT	perifollicular and dermal amyloid deposits, persistent telogen follicles and lack of anagen restoration on serial biopsies	renal disease	pinched purpura, easy bruising	yes	primary systemic amyloidosis	melphalan, prednisone, colchicine, topical minoxidil	decreased shedding, no regrowth, death at 12 mo	Hunt et al., 1991 [5]
diffuse scalp thinning, sparse axillary/genital hair	marked alopecia with loss of sebaceous glands, atrophic and involuted follicular units/appendages, amorphous eosinophilic amyloid deposited around blood vessels and between dermal collagen bundles	bone marrow involvement	dystrophic fingernails and toenails, onychoschizia, brittleness, diffuse thickening of palms, macroglossia	yes	primary systemic amyloidosis	N/A	N/A	Lutz et al., 2002 [2]
coarse, brittle, grayed hair with broken hairs, diffuse hair loss on scalp, axillae, genitalia, and eyebrows	hair follicle miniaturization, eosinophilic amyloid deposits noted	bone marrow involvement	separation of nail plates from nail bed	yes	multiple myeloma	thalidomide and decadron, minoxidil topical	unknown	Magro et al., 2019 [4]
hair loss at vertex/FT scalp, upper trunk, lateral	preserved follicular architecture, intact sebaceous glands, atrophic follicular structures compressed by surrounding	N/A	nail ridging	Yes	multiple myeloma	N/A	N/A	Miteva et al., 2015 [6]



eyebrows	amyloid deposits representing persistent telogen follicles							
diffuse hair on scalp with sponginess to scalp throughout	Band-like amyloid deposit replacing much of upper/papillary dermis, thickened/amyloid infiltrated blood vessel walls, replacement of hair follicles with amyloid, epithelial cells and sebaceous lobules encased in amyloid. Patchy perivascular mixed infiltrate and dermal edema present.	gastrointestinal, cardiac conduction abnormality	blistering rash with subsequent atrophic scarring of distal upper extremities, under breasts, and buccal mucosa, periorbital ecchymoses, easy bruising, koilonychia of fingernails	yes	primary systemic amyloidosis	melphalan daily	no improvement	Muller et al., 1969 [13]
intense scalp itching, burning, and tenderness with diffuse nonerythematous scaling, patchy diffuse scalp alopecia sparing mid-lower	amyloid deposits within dermis, around hair follicles, and focally within small subcutaneous blood vessels	nephrotic syndrome, bone marrow involvement	none	yes	plasma cell dyscrasia	bortezomib, dexamethasone, cyclophosphamide	improvement in plasma cell dyscrasia, no improvement in alopecia	Nia et al., 2021 [14]

occiput. Negative HPT.								
hair thinning at vertex/FT scalp, axillary/genital hair loss	dense homogenous eosinophilic amyloid deposits, miniaturized hair follicles within broad sheath of amyloid	small fiber neuropathy, SICCA syndrome	atrophic nails, ridging, onychorrhexis, atrophic oral mucosa and tongue, scleroatrophic skin on hands	Yes	N/A (patient declined further workup)	skin moisturizers	stable at 18 mo FU	Renker et al., 2014 [15]
Diffuse hair loss with residual fine white hair on the scalp	N/A	Bilateral ankle swelling. Glomerular proteinuria. SICCA Syndrome	Severe dystrophy of nails on both hands. Both ankles were mildly edematous. Diffuse large and small patches of asymptomatic, nonpalpable petechiae and purpura. Dry oral mucosa	yes	Primary systemic amyloidosis	N/A	N/A	Richey et al., 1996 [16]
diffuse, non-scarring scalp alopecia, scalp diffusely	paucity of hair follicles with large amount of amyloid deposited around blood vessels/within dermis	arthralgia and tenosynovitis of hands, cardiac amyloidosis	none	yes	multiple myeloma	bortezomib, dexamethasone, cyclophosphamide	partial hematologic response, no improvement of scalp	Samuleov et al., 2013 [17]

thickened							alopecia	
diffuse scalp alopecia	Follicular miniaturization. Majority of follicles shifted into catagen/telogen phase. Amyloid deposits within deep dermis, subcutis, and surrounding follicular epithelium in mid dermis. Non scarring, non-inflammatory.	mild renal impairment with proteinuria	none	yes	plasma cell dyscrasia	melphalan	disease stable	Sutherland et al., 2019 [18]
generalized hair loss of scalp, eyelashes, eyebrows, extremities, axillae, and genitalia	extensive amorphous amyloid deposits around hair follicles	hepatomegaly, congestive heart failure, firm submandibular glands, bone marrow involvement	skin thickening on chin and neck, hemorrhagic macules on lips and pretibial purpura, absent fingernails, onycholysis of toenails, macroglossia, narrowed external auditory canals	yes	multiple myeloma	unknown	unknown	Wheeler et al., 1981 [19]

N/A, not available, Y, Yes, BM, bone marrow, SAA (secondary amyloid), serum amyloid A, AL, amyloid light chain, LA, lichen amyloidosis, DMSO, Dimethylsulfoxide, F, Female, M, Male, FT, frontotemporal, HPT, hair pulling test, EM, electron microscopy, ACTH, adrenocorticotrophic hormone.