Scalp biopsy identifies systemic amyloidosis presenting as isolated telogen effluvium: A case report

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Abstract
AL amyloidosis is a complication of B-cell dyscrasias and multiple myeloma, manifest as deposition of antibody fragments in many different organs, including the skin. We describe a rare case of this systemic disease which presented with isolated scalp alopecia. Further investigation led to the diagnosis of an occult plasma-cell dyscrasia, showing the benefit of including systemic amyloidosis in the differential diagnosis of alopecia. The biopsy finding of cutaneous amyloidosis should prompt further workup to exclude an underlying pathology.

Keywords
Amyloidosis, alopecia, occult plasma cell dyscrasia, case report

Introduction
AL amyloidosis (also known as primary amyloidosis) is a well-recognized complication of B-cell dyscrasias and multiple myeloma. It results from the deposition of modified fragments of the light-chain portion of antibodies, and most commonly affects the liver, kidneys, heart, gastrointestinal tract, peripheral nerves, and skin.

Case report
A 74-year-old otherwise healthy woman presented with diffuse alopecia of the scalp. Two biopsies were taken for investigation of suspected telogen effluvium or diffuse alopecia areata. No clinical features of amyloidosis, such as macroglossia, purpura, infiltrative skin lesions or nail changes, were observed.

The skin biopsies showed no inflammation or evidence of a scarring alopecia. A large proportion of follicles were shifted into catagen and telogen phase in both biopsies. The residual fibrous stelae within the deep dermis and subcutis showed a remarkable appearance, with an empty center and a peripheral zone containing eosinophilic periodic acid Schiff (PAS)-positive and diastase-resistant (Figures 1 and 2), Congo-red-positive (Figure 3), apple-green-birefringent material characteristic of amyloid. Similar amyloid deposits were also evident to a lesser extent surrounding follicular epithelium within the mid-dermis. There was no discernible amyloid deposition within dermal blood vessels, surrounding sweat apparatus or adipocytes, or within the dermal interstitium.

Further special staining was carried out on one of the biopsies, with PAS with diastase (PASD) staining showing no fungal organisms or dermoepidermal basement-membrane-zone thickening. Alcian blue staining showed no dermal mucin accumulation and was negative within the amyloid deposits. Verhoeff staining showed no scarring that might suggest a scarring alopecia.

Within one biopsy, 14 of 37 (38%) hairs were vellus or vellus-like. Of the non-miniaturized hairs, 16 of 23 (70%) were in catagen or telogen phase. The other biopsy was more irregularly shaped and subsequently obliquely sectioned, allowing visualization of only 14 hairs, 5 of which (36%) were vellus or vellus-like; of the 9 remaining hairs, 2 were in catagen or telogen phase (22%).

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As such, the biopsies were assessed to show a shift toward catagen and telogen hair follicles, consistent with the early phase of telogen effluvium. There was also moderate hair miniaturization consistent with pre-existing senile alopecia or androgenetic hair loss.

Perifollicular deposition of amyloid prompted further workup of the patient for systemic forms of amyloidosis. Plasma protein electrophoresis and immunofixation showed a 1.4 g/L monoclonal band in the mid-to-late gamma region. Additional minor bands were noted in the beta-gamma region of both the alpha heavy chain and lambda light-chain classes and migrated with slightly different mobility, suggesting that they were not the same paraprotein. Urine protein electrophoresis showed moderate proteinuria in a glomerular pattern, without excretion of the monoclonal protein in the urine.

Based on these findings, the patient was diagnosed with lambda AL amyloidosis. A bone-marrow biopsy performed 6 months after presentation showed a plasma-cell dyscrasia with lambda light-chain restriction and 8% plasma cells in the bone marrow. She subsequently received treatment with melphalan, and her disease is stable. At time of publication, she has no known involvement of the lymph nodes, oropharynx, liver, spleen, and cardiovascular system, and only mild renal impairment and proteinuria.

Discussion

Amyloidosis is the extracellular deposit of amyloid fibrils that can occur in various tissues of the body. It can be divided into AL (primary) amyloidosis, AA (secondary) amyloidosis, and multiple other less frequent types, including localized cutaneous amyloidosis. AL amyloidosis is the form of amyloidosis that characteristically occurs in patients with B-cell or plasma-cell dyscrasias or multiple myeloma. Components of the circulating immunoglobulins produced by the abnormal cells fold into insoluble fibrils and deposit extracellularly in tissues. It can affect multiple organs, with common features including macroglossia; cardiac, renal, hepatic, and gastrointestinal involvement; peripheral neuropathy; and cutaneous manifestations. Common skin lesions include smooth, waxy, yellow-brown papules or plaques, particularly on the face; “pinch” purpura easily induced by minimal trauma; and nail changes.

Histopathologically, hematoxylin-and-eosin stained amyloid is seen as pale pink, extracellular, hyaline material. Most of these deposits occur in vascular or perivascular locations,
but they can occur in the papillary and reticular dermis, within sweat glands and, less commonly, around the pilosebaceous units. With the Congo red stain, amyloid deposits are pink-to-red under standard illumination and show apple-green birefringence under polarized microscopy. Amyloid also stains positively and is diastase-resistant with PAS.

Our patient was diagnosed with AL amyloidosis after investigation of a seemingly benign and common complaint of alopecia. Many patients of her demographic present with androgenetic alopecia and senile alopecia under the influence of genetics, hormones, and aging. Although cutaneous manifestations of AL amyloidosis are likely to present early within the course of plasma-cell dyscrasias, alopecia is rare.1

Very few cases have been reported in the English literature to have had clinically prominent alopecia as the presenting complaint, with only 4 such cases known to the authors,2–5 and even fewer of those were isolated cutaneous lesions. The only other case in English literature of isolated alopecia as the presenting complaint was that of an elderly woman with 6 years of diffuse hair loss, with an additional year with nail brittleness and diffuse palmar thickening prior to diagnosis of AL amyloidosis.2 Other cases reported with investigation for and diagnosis of AL amyloidosis due to initial presentation of alopecia also had pinch purpura,3 palmar skin atrophy and sicca syndrome,4 small papules and blisters on the dorsal hands,5 and nail changes.4,5 Of those with reported follow-up, one developed macroglossia and significant renal disease within 12 months of onset of her alopecia, and died soon after despite treatment,3 while another had no further progression after 18 months of follow-up and only required skin moisturizers.4

In summary, we report an unusual case of AL amyloidosis secondary to an occult plasma-cell dyscrasia, presenting to medical care with isolated cutaneous involvement manifest as diffuse alopecia, but subsequently requiring melphalan therapy to prevent progression of renal and bone-marrow involvement. This case adds to the clinical and histopathological spectrum of AL amyloidosis. In particular, the predominant accumulation of amyloid in a perifollicular distribution and within the stelae of telogen hairs, without involvement of other histologic components of the dermis or subcutis, is unique. The report also highlights an additional, previously unrecognized benefit of the use of scalp biopsy for identification of the mechanisms behind alopecias.

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Informed consent
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