CASE REPORT

Chromatic Curiosity: A Rare Case of Amyloidosis Cutis Dyschromica

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Abstract: Amyloidosis cutis dyschromica (ACD) is a rare form of primary cutaneous amyloidosis, first described by Morishima in 1970. Fewer than 100 cases have been documented in medical literature, with under 10 patients reported from the Philippines. It presents as widespread macular, reticular hyperpigmentation and hypopigmentation, often appearing before puberty and accompanied by focal subepidermal amyloid deposits. We report a case of ACD in a 35-year-old Filipino woman presenting with asymptomatic dyschromic skin lesions, with the primary aim of aiding dermatologists in recognizing this rare but benign condition.

Keywords: Amyloidosis cutis dyschromica, Cutaneous amyloidosis, Dyschromia, Hyperpigmentation, Hypopigmentation, GPNMB mutation

Introduction

Amyloidosis cutis dyschromica (ACD) is a rare form of primary cutaneous amyloidosis characterized by localized hyperpigmentation and hypopigmentation. First described by Japanese dermatologist, Morishima in 1970, fewer than 100 cases have been reported in the medical literature [1]. This condition presents with (i) widespread macular, speckled, and reticular hyperpigmentation interspersed with hypopigmented spots; (ii) minimal to absent pruritus; (iii) onset before puberty; and (iv) localized deposition of amyloid in the subepidermal region. [2]. In the Philippines, fewer than ten cases have been documented, with reports suggesting a higher prevalence in East and Southeast Asia [3]. Limited access to confirmatory histology and low clinical awareness may contribute to underdiagnosis. We present a case of ACD with prepubertal onset of dyschromia and a positive family history. This case report aims to help dermatologists recognize ACD as a rare but benign pigmentary disorder, supporting accurate diagnosis and appropriate counselling.

Case Presentation

A 35-year-old Filipino female domestic worker from Bukidnon, Philippines, born to non-consanguineous parents, presented with hypopigmented and hyperpigmented macules and patches on the trunk and extremities, which initially appeared on the arms at around 5 years of age. Over time, the lesions gradually increased in size and number but were not associated with symptoms such as pain, pruritus, or

photosensitivity. Although asymptomatic and not interfering with daily activities, the lesions were incidentally detected during routine pre-employment medical examinations for overseas deployment. The patient reported a prior consultation with a physician, during which a diagnosis of pityriasis versicolor was made. She was prescribed ketoconazole shampoo; however, no improvement was noted, and she was subsequently lost to follow-up.

The patient had no history of chronic sun exposure, as she mostly stayed indoors, and reported inconsistent use of sun protection. Her birth and developmental milestones were normal. She had no history of other cutaneous conditions or systemic illnesses. A history of similar skin lesions was noted in her maternal grandmother **(Figure 1)**, but no other family members were known to be affected.

Dermatological examination revealed multiple well-defined hypopigmented to depigmented patches and macules on a background of patchy hyperpigmentation over the trunk and upper and lower extremities **(Figure 2a to 2g)**. Dermoscopy showed white structureless areas with irregular borders, along with brown dots, and globules **(Figure 2h).** Systemic examination was unremarkable, and laboratory investigations including complete blood count, liver enzymes, serum chemistries, and chest radiograph were all within normal limits.

A 4-mm punch biopsy was taken from hypopigmented lesions on the back and arm. Histopathological examination with hematoxylin and eosin (H&E) staining revealed a basket-woven stratum corneum. The dermis showed amorphous eosinophilic globules, pigment-laden macrophages, dilated blood vessels, widened papillae, and a mild superficial lymphocytic infiltrate **(Figure 3a, 3b)**. Congo red staining demonstrated amyloid deposits in the papillary dermis **(Figure 3c)**, while direct immunofluorescence (DIF) revealed globular IgG deposits at the papillary dermis **(Figure 3d)**.

Based on the clinical, histopathologic, and immunofluorescence findings, a diagnosis of ACD was established. As the patient reported no symptoms or significant cosmetic concerns related to the dyspigmentation, she was managed conservatively. Supportive treatment with mild soap, emollients, and sunscreen was prescribed to maintain skin barrier integrity, prevent xerosis, and minimize further pigmentary alteration and UV-induced keratinocyte damage that could exacerbate dyschromia or trigger disease progression. Genetic testing was offered to further characterize the inheritance pattern; however, the patient declined additional investigations.

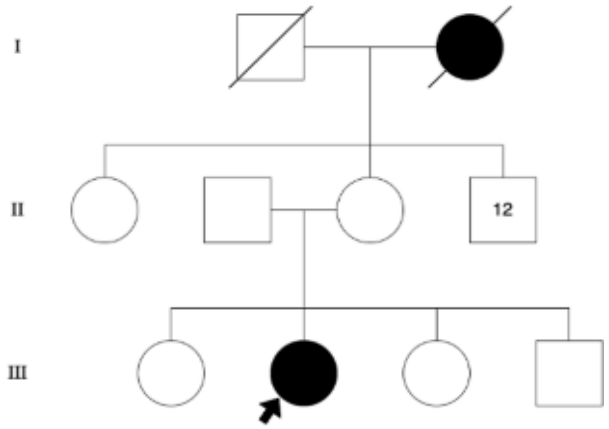

Figure 1. The pedigree for ACD includes a deceased, affected maternal grandmother in the first generation (I). In the second generation (II), the proband's mother is the second of 14 children, with the eldest daughter and 12 younger brothers all unaffected. In the third generation (III), the proband is the second daughter among four siblings, with her older sister, younger sister, and younger brother all unaffected.

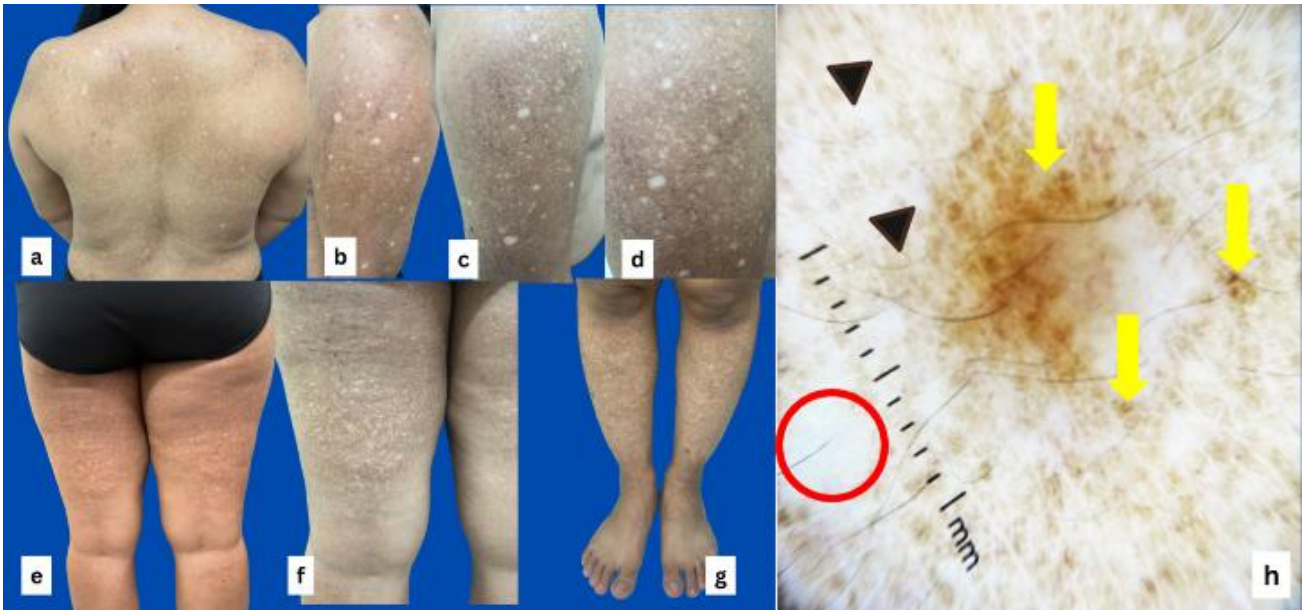

Figure 2. (a–g) Multiple well-defined hypopigmented to depigmented patches and macules on a background of patchy hyperpigmentation affecting the trunk, upper extremities, and lower extremities; **(h)** Dermoscopy reveals white patches with poorly defined margins (red circle), surrounded by small white spots (black arrowheads) and hyperpigmented blotches and patches (yellow arrows).

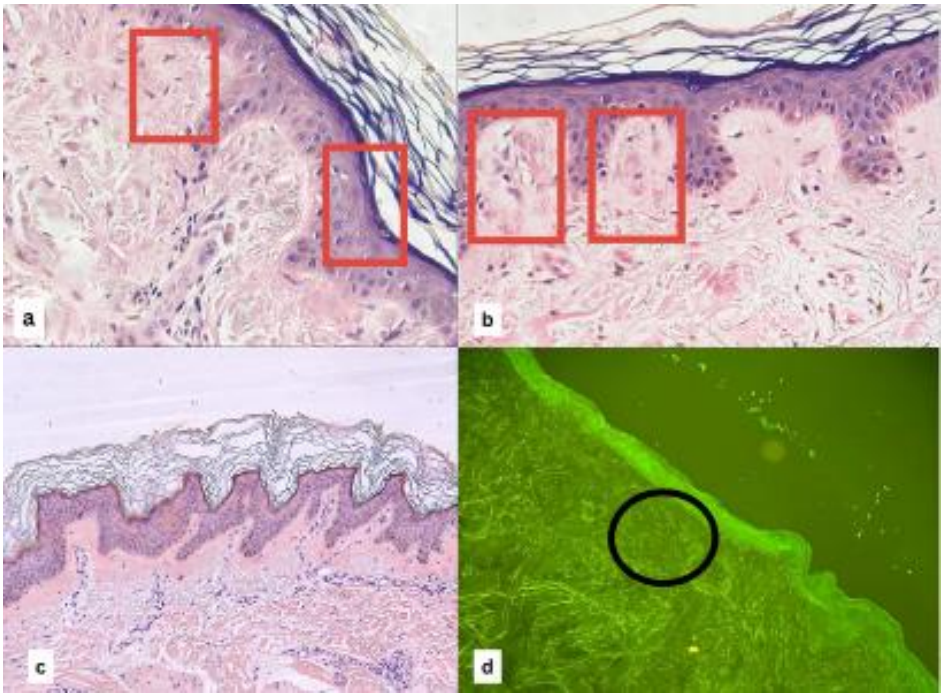

Figure 3. (a, b) Histopathologic examination shows basket-woven stratum corneum, amorphous eosinophilic globules (red box), pigment-laden macrophages, dilated blood vessels, widened papillae, and mild superficial inflammatory infiltrate of lymphocytes in the dermis of the arm and back, respectively; **(c)** Congo red staining demonstrates amyloid deposits in the papillary dermis; **(d)** Direct immunofluorescence reveals globular deposits of IgG in the papillary dermis.

Discussion

ACD affects men and women equally, often presenting prior to puberty, with a mean age of onset of 6 years and a mean age at diagnosis of 30 years [3]. Clinically, ACD manifests as slowly progressive dyschromia, typically sparing the palms, soles, and mucosal surfaces. Facial involvement is rare. Distinguishing features include dotted, reticular, or diffuse hyperpigmentation mixed with hypopigmented macules. The disease results from the deposition of amyloid derived from degenerate keratinocytes, although the exact mechanisms remain unclear. Diagnosis is confirmed through biopsy, which reveals amyloid deposits in the papillary dermis [4].

Among the characteristics of ACD described by Morishima, our patient exhibited all features, including macular, speckled, reticular hyperpigmentation with hypopigmented spots distributed extensively over the body, little or no pruritus, prepubertal onset, and focal subepidermal amyloid deposition confirmed by biopsy. On histopathological examination with H&E, ACD shows amyloid deposits in the papillary dermis as small, amorphous globules of eosinophilic material with Congo red staining demonstrates amyloid deposits in the papillary dermis; DIF reveals globular deposits of IgG in the papillary dermis.

All subtypes of primary cutaneous amyloidosis share amyloid deposition in the papillary dermis; therefore, Congo red and DIF remain valuable tools for confirming amyloid in suspected cases of ACD. In a study by Mehrotra et al. [5], Congo red staining demonstrated a sensitivity of 89.6% and specificity of 100%, while DIF showed a sensitivity of 91.7% and specificity of 100% in cutaneous amyloidosis.

ACD has been postulated to have a genetic component. The majority of cases are associated with autosomal recessive mutations in the GPNMB gene, which encodes glycoprotein non-metastatic melanoma protein B [6,7]. Semidominant mutations, in which some heterozygotes exhibit a milder phenotype, have also been reported [8].

In addition to genetic factors, sun exposure may contribute to ACD pathogenesis. This is because UVB- and UVC-induced keratinocyte damage takes longer to repair in ACD [4,9]. Damaged keratinocytes then undergo apoptosis which release cytokeratins which result in amyloid formation once phagocytosed [10]. However, the role of photosensitivity is debated, as sun-exposed areas often exhibit milder involvement [4]. In our patient, sun-exposed and sun protected areas are equally affected. Genetic testing was offered due to the known gene association, early onset, positive family history, and to assess potential transmission risk to offspring, but it was not performed as the patient declined.

ACD has no known complications, and no effective therapy has been established. Various topical agents and oral supplements have been tried with inconsistent outcomes. Reported treatment options include photoprotection, topical corticosteroids, keratolytics, dimethyl sulfoxide (DMSO), capsaicin, CO_2 laser, and systemic acitretin [2]. Sunscreen is recommended to minimize UV-induced keratinocyte DNA damage, while topical corticosteroids help reduce inflammation. Keratolytics, such as urea or salicylic acid, soften hyperpigmented or hypopigmented macules, flatten papules, and enhance the permeability of active agents. In addition, DMSO and capsaicin may be used to relieve minor pruritus, whereas CO_2 laser therapy reduces amyloid deposits through transepidermal elimination induced by fractional photothermolysis [11]. Among systemic therapies, oral acitretin has been shown to be effective in ACD by inducing apoptosis of damaged keratinocytes, thereby preventing amyloid formation [12].

Conclusion

ACD is a rare, progressive pigmentary disorder with characteristic early-onset dyschromia and subepidermal amyloid deposition. While benign and often asymptomatic, it remains underdiagnosed due to its rarity and clinical overlap with other pigmentary conditions. This case highlighted the importance of clinicopathologic correlation in diagnosing ACD and reinforces the need for awareness among dermatologists to ensure accurate identification, appropriate counseling, and avoidance of unnecessary interventions.

Acknowledgement

None

Potential Conflict of Interest

The authors declare no potential conflicts of interest.

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