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Amyloidosis cutis dyschromica: report of 3 cases

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Abstract

Amyloidosis cutis dyschromica (ACD) is a rare pigmentary disorder with about 50 cases having been reported in the English literature. Only one case of ACD has been reported from Iran. We present three patients who presented with generalized hyper- and hypopigmented patches, sparing face, hands, and feet in all three cases. The presence of amorphous eosinophilic deposits in the papillary dermis confirmed the diagnosis of ACD; the deposits were stained by crystal violet in the histopathological examination of the lesions. In all three cases, similar lesions were present in some of the family members. ACD should be considered in the differential diagnosis of diffuse hyperpigmentation studded with hypopigmentation, especially when beginning in childhood.

Keywords: amyloidosis cutis dyschromica, Iran

Introduction

Primary cutaneous amyloidosis is the deposition of amyloid in the skin with no systemic involvement. Amyloidosis cutis dyschromica (ACD) is a rare subtype of primary cutaneous amyloidosis, which is characterized by dyspigmentation including diffuse asymptomatic or mildly pruritic hyperpigmentation and macular hypopigmentation. Histology examination shows papillary dermal amyloid deposition in pathologic examination [1]. About 50 cases have been reported; however, the rising number of reported cases in recent years [1-5] may indicate that ACD is an under-recognized or under-reported disease. About three-fourths of the reported cases are familial and the others are sporadic. Most of the reported cases (63%) are from Asia or South-East Asia [1]. Searching PubMed and Google Scholar, we found only one case of ACD reported from Iran [2]. Herein, we report three cases of familial ACD from Iran, one of whom is Afghani.

Case Synopsis:

Case 1

The first case was a 20-year-old Afghani woman who presented to our dermatology clinic with

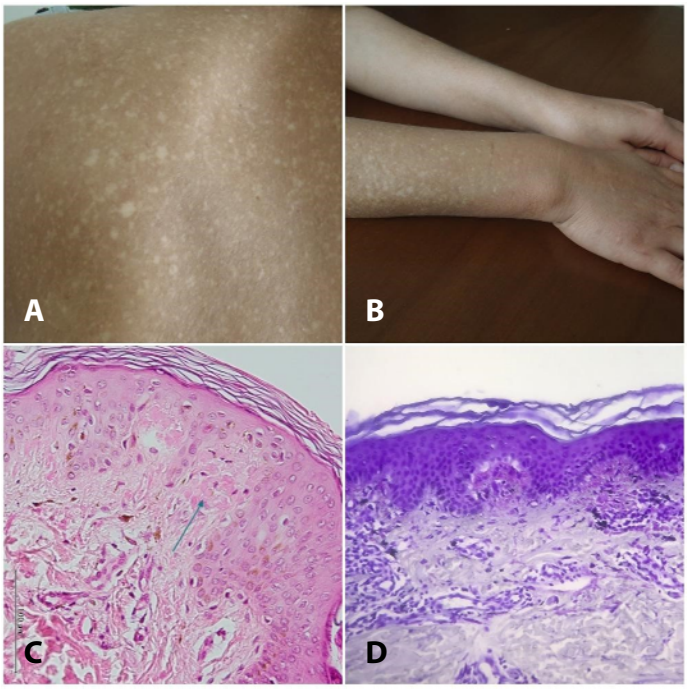

Figure 1. *Case 1.* ***A)*** *Diffuse hyperpigmentation studded by hypopigmented macules over back.* ***B)*** *Sparing of dorsa of hands.* ***C)*** *Histopathology. Mild acanthosis, homogenous eosinophilic globular deposits in the papillary dermis (arrow) and melanophages in the upper dermis. H&E, 400×.* ***D)*** *Purple globules of amyloid in the papillary dermis. Crystal violet, 400×.*

dyspigmentation on her trunk and extremities. The skin lesions were not pruritic and they first started at 6 years of age. She had no relevant past medical history and was taking no regular medications. Two of her paternal aunts and cousins had similar lesions. Her parents were consanguineous.

Dermatological clinical examination revealed diffuse mottled hyper and hypopigmented macules of the trunk and extremities (**Figure 1A)**. The dorsal aspect of the hands and feet, ventral surface of forearms, and face were spared (**Figure 1B)**. No atrophy, telangiectasia, or erythema was noted. The patient's hair, nails, mucous membranes, palms, and soles were normal. There was no systemic finding. Laboratory tests such as CBC, blood sugar, lipid profile, and liver function tests were normal.

Histopathological evaluation of the skin biopsy specimen from hyper/hypopigmented areas indicated mild acanthosis and homogenous eosinophilic globular deposits in the papillary dermis, which were also remarkable in scanning microscopy. In addition, there was pigment incontinence and a mild perivascular infiltrate in the superficial dermis (**Figure 1C)**. Positive staining with crystal violet confirmed the nature of globular dermal deposits for the diagnosis of amyloidosis (**Figure 1D)**. Thus, clinicopathologic diagnosis of ACD was made and phototherapy was started. The lesions were still present following 100 sessions of narrow-band UVB twice weekly. Topical treatment was not helpful with combination of corticosteroid and tretinoin. Acitretin was not considered because of her age and poor compliance with long-term contraception.

Case 2

The second case was a 39-year-old Iranian woman who presented to our outpatient dermatology clinic with non-pruritic hyper/hypopigmented macules on her trunk and extremities. The skin lesions first appeared when she was 5 years old and were located on her upper and lower extremities; subsequently spread to her trunk was noted. The patient had reported that four of her 10 siblings (two sisters and two brothers) had similar lesions. The patient had no relevant past medical history except cleft lip and palate, which was treated surgically. She was taking no regular medications.

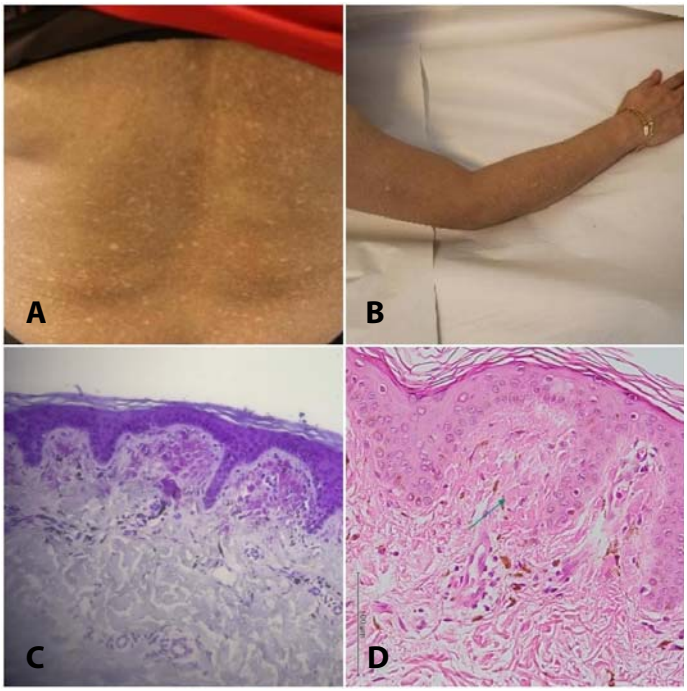

Figure 2. *Case 2.* ***A)*** *Diffuse hyperpigmentation and hypopigmented macules over trunk.* ***B)*** *Similar lesions on upper extremity sparing hand.* ***C)*** *Histopathology. Purple amyloid deposits in the papillary dermis. Crystal violet, 400×.* ***D)*** *Homogenous eosinophilic globules (arrow) and melanophages in the papillary dermis. H&E, 400×.*

Dermatological clinical examination showed diffuse hyper/hypopigmented macules of the trunk and extremities (**Figure 2A)**. The dorsal aspect of the hands, face, and medial aspect of the forearm were spared as in our first case (**Figure 2B)**. The patient's hair, nails, mucous membranes, palms and soles were normal.

Histopathological evaluation of the skin biopsy revealed intact epidermis with papillary dermis expansion with aggregates of homogenous hyaline bodies and pigment incontinence in the papillary dermis (**Figure 2C)**. Crystal violet stain was positive for amyloid (**Figure 2D)**. Considering the diagnosis of ACD, treatment with a combination of corticosteroid and tretinoin creams was commenced, but was not helpful. Topical application of 50% dimethyl sulfoxide (DMSO) resulted in irritation of the skin and did not ameliorate the lesions. She did not use

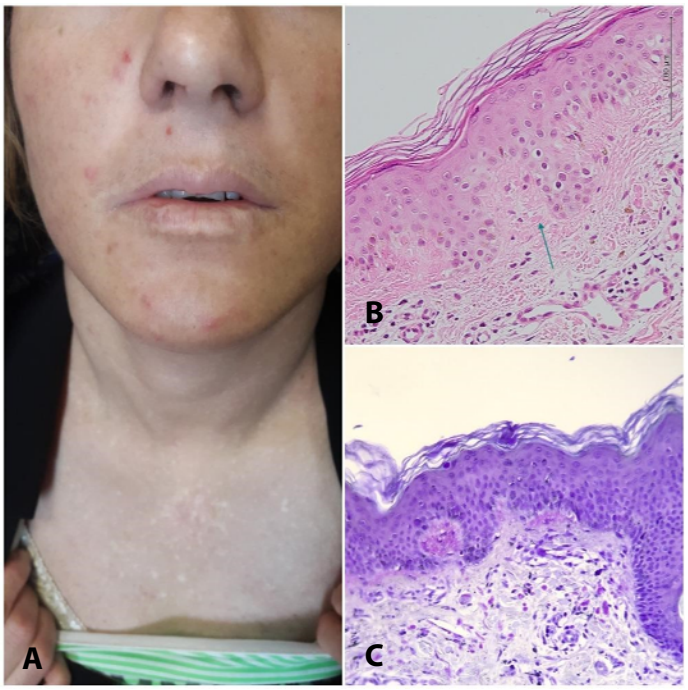

Figure 3. *Case 3. **A)** Mild hyperpigmentation and superimposed guttate hypopigmented macules over the chest with relative sparing of face and neck. **B)** Histopathology. Homogenous pink deposits in the papillary dermis (Arrow). H&E, 400×. **C)** Purple globules of amyloid in the papillary dermis. Crystal violet, 400×.*

contraception; so, acitretin was not a proper therapeutic option.

Case 3

A 32-year-old Iranian woman was referred to our outpatient dermatology clinic with dyspigmentation involving neck, trunk, and extremities. The problem was first noticed in childhood; however, she did not remember the exact age. Two brothers, two sisters, and two paternal uncles also had the same dyspigmentation. The parents were consanguineous. She had no history of any internal disease.

Dermatological examination showed diffuse hyperpigmentation studded with hypopigmented macules, which involved all the body except for face, dorsum of hands and feet, and palms and soles (**Figure 3A)**. Histopathological examination of the skin biopsy showed hyaline homogenous deposits in the papillary dermis, which were crystal violet-positive (**Figure 3C**, **D)**. She missed follow up; therefore, no treatment was started.

Case Discussion

Amyloidosis cutis dyschromica is a rarely reported subtype of primary cutaneous amyloidosis in Iran [2]. Amyloidosis cutis dyschromica has been most commonly reported in Asian and South-East Asian ethnic groups and it has been less frequently reported in the countries in our regional area of Turkey, Pakistan, and Saudi Arabia [6-8]. The first case in the present report is an Afghani woman, a related ethnicity. The other two patients were Iranian. ACD usually presents as diffuse hyperpigmentation gradually studded with hypopigmented macules. The lesions usually appear initially on the trunk and then progress to the extremities [1]. However, some patients report the first lesions on the extremities [3]. Both of these presentations were reported in our patients. Although ACD is usually asymptomatic in opposition to the other subtypes of primary cutaneous amyloidosis, pruritus is reported in 19% of cases [1].

Although most of the reported cases are familial, sporadic cases apparently unrelated to geneology have been reported. Consanguinity of the parents is not a ubiquitous feature [3, 8]. The mean age of diagnosis is 30 years and the mean age of onset of ACD in the familial cases is 6 years (lower than the sporadic cases), [1]. This time lag in diagnosis is significant and suggests a need for more awareness of the condition.

Histological findings of the ACD lesions include homogenous eosinophilic deposits in the papillary dermis and superficial reticular dermis with a few melanophages. Special stains for amyloidosis such as Congo red, crystal violet, and thioflavine T usually highlight the amyloid deposits. Immuno-histochemistry investigation shows positivity of cytokeratin markers (AE1/AE3, CK5/6, and CK34βE12) in the amyloid globules. Amyloid is seen as non-branching hollow thin fibrils under electron microscopy [7, 8].

No clue of systemic amyloidosis was detected in the reported cases of ACD, which indicates that systemic work up is not necessary [1]. Some associated diseases with ACD include morphea and

atypical Parkinsonism [7, 9]. One of the cases, which has been presented in the present article, had surgically repaired cleft lip and palate. One of the significant findings in the reported cases of ACD is relative sparing of face, hands, and feet. This was true of all three cases documented in this case report. Involvement of the face is reported in only 20% of cases [1]. Actually, considering the sparing of sun-exposed areas in the majority of the reported cases, the possibility of a role for impaired DNA repair after exposure to UVB rays is in question as the pathogenesis of ACD [10]. The prevalence of ACD in some ethnic groups and familial cases suggests genetic factors as the cause of ACD. Some authors have suggested autosomal dominance with incomplete penetrance as the mode of inheritance [1]. However, it has been shown that a loss-of-function mutation in *glycoprotein non-metastatic gene B* (*GPNMB*) was the cause of autosomal recessive ACD in 5 Taiwanese families [11].

Amyloidosis cutis dyschromica has been treated with various topical and systemic medications. Topical treatment has not been successful with corticosteroids, urea 10%, and tazarotene in reports. [1, 6]. Oral antioxidants (vitamins E and C**)** did not result in significant improvement [4]. Seven of the 8 patients who were treated with acitretin have been reported to be improved [1]. Treatments with topical corticosteroid, retinoids, DMSO, and narrow-band UVB phototherapy were disappointing in our patients.

Conclusion

In summary, ACD should be considered in any patient especially in the pediatric group who presents with dyspigmentation, and obtaining a thorough history including family history is necessary. Although no specific preventive or therapeutic measures have been successful for ACD yet, early histopathological examination of the biopsy specimen and complementary assessments with amyloid special stains and/or immunohistochemical studies will prevent unnecessary extensive investigations. The rarity of the disease makes it difficult to assess the therapeutic efficacy of treatments.

Potential conflicts of interest

The authors declare no conflicts of interests.

References

1. Mahon C, Oliver F, Purvis D, Agnew K. Amyloidosis cutis dyschromica in two siblings and review of the epidemiology, clinical features and management in 48 cases. *Australas J Dermatol*. 2016;57(4):307-311. [PMID: 25866143].
2. Dehghani F, Ebrahimzadeh M, Moghimi M, Noorbala MT. Familial amyloidosis cutis dyschromica: a case report. *Acta Med Iran*. 2014;52:163-5. [PMID: 24659076].
3. Hermawan M, Rihatmadja R, Sirait SP. Familial amyloidosis cutis dyschromica in three siblings: report from indonesia. *Dermatology reports*. 2014;6:5375. [PMID: 25386328].
4. Qiao J, Fang H, Yao H. Amyloidosis cutis dyschromica. *Orphanet J Rare Dis*. 2012;7:95. [PMID: 23234252].
5. Yang W, Lin Y, Yang J, Lin W. Amyloidosis cutis dyschromica in two female siblings: cases report. *BMC Dermatol*. 2011;11:4. [PMID: 21320354].
6. Al-Dawsari NA, Shahab RK. Amyloidosis cutis dyschromia: a rare form of primary cutaneous amyloidosis. *Dermatol Online J*. 2014;20:22328. [PMID: 24746296].
7. Fernandes NF, Mercer SE, Kleinerman R, Lebwohl MG, Phelps RG. Amyloidosis cutis dyschromica associated with atypical Parkinsonism, spasticity and motor weakness in a Pakistani female. *J Cutan Pathol*. 2011;38:827-31. [PMID: 21645034].
8. Karadag A, Simsek G. Familial amyloidosis cutis dyschromica *Turk J Med Sci*. 2010;40:151-4. [DOI:10.3906/sag-0903-3].
9. Morales Callaghan AM, Vila JB, Fraile HA, Romero AM, Garcia GM. Amyloidosis cutis dyschromica in a patient with generalized morphoea. *Br J Dermatol*. 2004;150:616-7. [PMID: 15030364].
10. Moriwaki S, Nishigori C, Horiguchi Y, Imamura S, Toda K, Takebe H. Amyloidosis cutis dyschromica. DNA repair reduction in the cellular response to UV light. *Arch Dermatol*. 1992;128:966-70. [PMID: 1626966].
11. Yang CF, Lin SP, Chiang CP, Wu YH, H'Ng W S, Chang CP, Chen YT, Wu JY. Loss of GPNMB Causes Autosomal-Recessive Amyloidosis Cutis Dyschromica in Humans. *Am J Hum Genet*. 2018;102:219-32. [PMID: 29336782].