Amyloidosis Cutis Dyschromica, A Rare Subtype of Primary Cutaneous Amyloidosis: Case Report and Literature Review

Jagdish Sakhiya, Dhruv Sakhiya[1], Mehul Patel, Feral Daruwala

Department of Dermatology, Sakhiya Skin Clinic PVT LTD, Surat, [1]MBBS Student. B.J. Medical College, New Civil Hospital Asarwa, Ahmedabad, Gujarat, India

Sir,

In 1970, Morishima *et al*. introduced amyloidosis cutis dyschromica (ACD), a rare variant of primary cutaneous amyloidosis (PCA). ACD is characterized by the presence of hyperpigmented and hypopigmented or depigmented macules of varying sizes in generalized fashion associated with no or little pruritus, prepubertal onset, and focal amyloid deposition in the papillary dermis.[1,2] We present a case of ACD developed in a 9 yearold Indian girl, who was treated with combination of acitretin, the excimer light and fractional CO2 laser.

A 9-year-old Indian girl born to parents of first degree consanguineous marriage presented with generalized, asymptomatic hyperpigmentation since 3 months of age and, three months later mottled hypopigmented macules developed involving the face, abdomen, back, and both upper and lower extremities [Figure 1a-d]. The hypopigmented macular lesions initially appeared on her face and, then gradually extended to involve the abdomen, back, and both upper and lower extremities within a month. There was no associated pruritus, erythema, telangiectasia, atrophy or blisters. There was no preceeding episodes of photosensitivity, inflammatory cutaneous conditions or systemic illness. Her mental developmental milestones were normal and family history was non-contributory. A general physical examination, as well as systemic examination, was unremarkable and routine laboratory parameters were within normal limits. Cutaneous examination revealed diffuse hyper pigmentation with mottled spotty, well-defined and hypo pigmented macules ranging from pinpoint to 3mm diameters in size and some of the hypo pigmented macules coalesced to form macule of 1 × 1 cm. Hair, teeth, nails and oral mucosa were normal. Ophthalmology and ENT assessments were non-contributory. For histopathological examination, punch biopsy samples were taken from both hyper- and hypopigmented macular lesions, from the sun-protected site, i.e., lower back, stained with hematoxylin-eosin stain and observed under light microscopy. The pathological section from both lesions revealed a few widened papillae which had small globular pink amorphous deposits of amyloid in association with occasional melanophages. The amyloid deposits were present at the interface and associated with moderately hyperplastic rete ridges. The epidermis showed moderate compact and lamellated orthohyperkeratosis. Occasional dyskeratotic cells were seen within the upper epidermis [Figure 2]. Later on, the presence of these amyloid deposits was confirmed by congo red staining which had been shown apple-green birefringence with polarised light [Figure 3]. Based on these typical clinical features, histopathological findings, and positive Congo red staining; the diagnosis of ACD was confirmed. After diagnosis, the patient was started on combined therapy of oral acitretin (25 mg oral daily) with 308nm excimer light at a dose of 200mJ/cm2, monthly and, fractional CO2 laser (10,600nm) 1 × 1 spot size along with 4 mJ power once per month. And in the form of repigmentation, partial improvement was observed within the mottled hypopigmented macules of the face [Figure 4]. Acitretin drug therapy was prescribed for 6 months and, until now, the sixth session of the laser has been provided. Currently, the patient was on a similar treatment at the time of article writing.

How to cite this article: Sakhiya J, Sakhiya D, Patel M, Daruwala F. Amyloidosis cutis dyschromica, a rare subtype of primary cutaneous amyloidosis: Case report and literature review. Indian Dermatol Online J 2021;12:330-4.

Received: 29-Apr-2020. **Revised:** 07-Jun-2020
Accepted: 08-Jul-2020. **Published:** 02-Mar-2021.

Address for correspondence:
Dr Jagdish Sakhiya,
Sakhiya Skin Clinic PVT LTD.
2nd Floor, Ayush Docter House,
Station-Lal Darwaja Road,
Surat - 395 003, Gujarat, India.
E-mail: sakhiya.acedemic@rediffmail.com

Access this article online

Website: www.idoj.in

DOI: 10.4103/idoj.IDOJ_293_20

Quick Response Code:

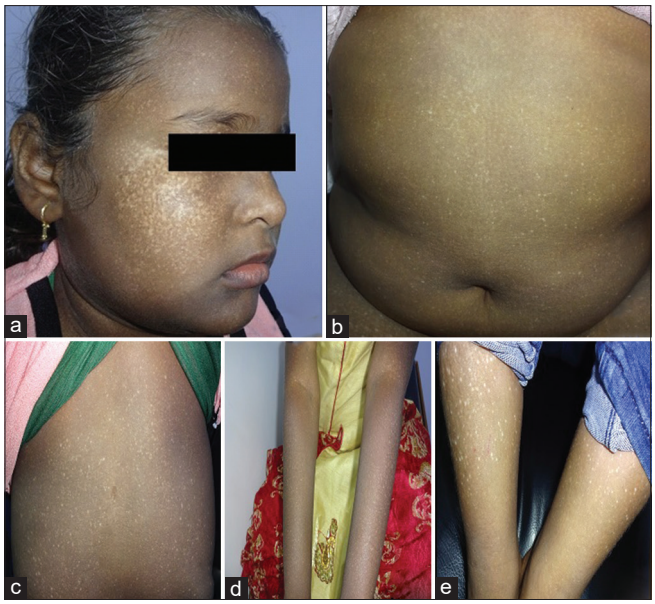

Figure 1: Pretreatment, multiple hyperpigmented and mottled hypopigmented macules over the (a) face (b) abdomen (c) back (d) upper extremities (e) lower extremities

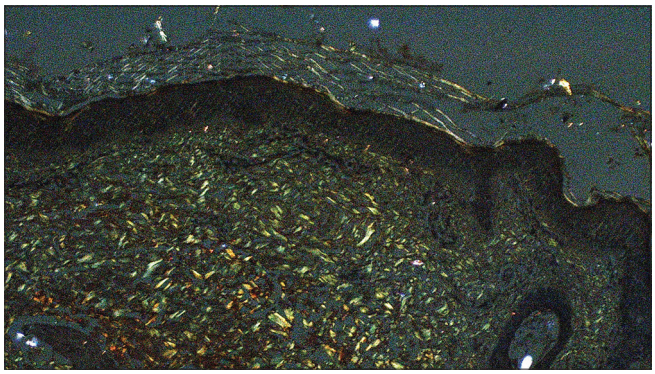

Figure 3: Congo stain showing amyloid deposits in papillary dermis (Congo red, ×5)

Cutaneous amyloidosis has been classified into three major types: PCA, secondary cutaneous amyloidosis, and systemic cutaneous amyloidosis. Of these, PCA is classified into three subtypes: Lichen or papular, macular, and nodular or tumefactive. Lichen amyloidosis is the most common type and clinically characterized by an intensely pruritic eruption. Multiple discrete hyperkeratotic papules may coalesce into plaques and are often located on the extensor surfaces of the legs. Macular amyloidosis presents as brownish macules and has been often distributed in a rippled pattern on the upper aspect of the back. Nodular amyloidosis is a rare form of PCA and presents as a solitary or multiple erythematous to brownish waxy nodules on the legs or the trunk. Rare variants of PCA include familial poikiloderma-like cutaneous amyloidosis, bullous, vitiliginous, anosacral, and ACD.[1,2] ACD is mostly reported from the Southeast Asian countries.[3] To date, from the Indian subcontinent, only seven cases of ACD have been reported. The clinical, histopathological

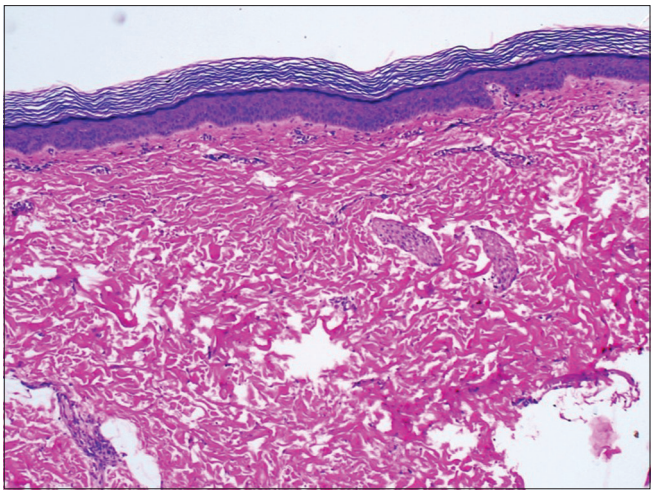

Figure 2: Eosinophilic globular deposits of amyloid in papillary dermis (H and E, ×5)

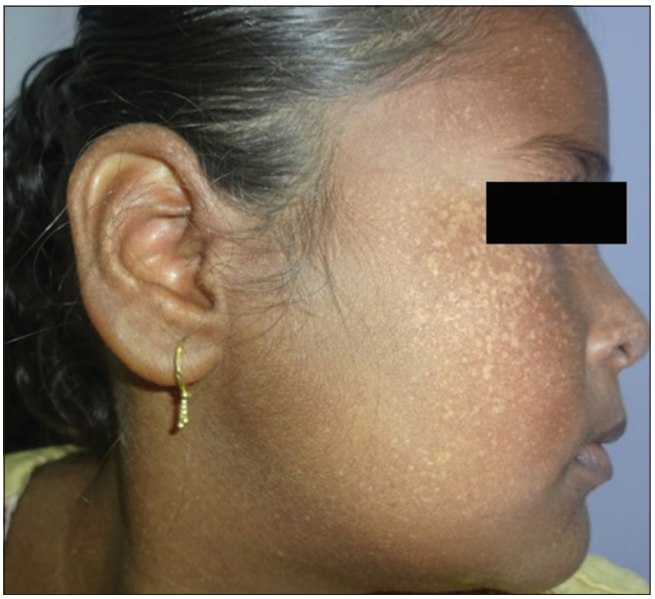

Figure 4: Post treatment, partial improvement in hyperpigmented and mottled hypopigmented macules over the face

and treatment profile of these published cases of ACD has been compiled in Table 1.[4-10]

ACD must be differentiated from other causes of dyschromia including dyschromatosis universalis hereditaria, xeroderma pigmentosum and poikiloderma-like amyloidosis. The former two conditions do not exhibit amyloid deposits in the skin. The latter shows a similar clinical cutaneous picture as ACD but with additional features such as poikilodermic lesions, lichenoid papules, blisters, photosensitivity, short stature and palmoplantar keratoderma.[1] In the presented case, amyloid deposition could be seen in the histopathology report and absence of the above mentioned additional feature confirmed the diagnosis of ACD.

The occurrence of familial cases and disease onset before puberty suggests a genetic aetiology of ACD. The genetic

Table 1: The clinical and treatment profile of published cases of ACD from Indian Subcontinent

Author	Age at diagnosis (years)	Age at the onset (years)	Sex	Pruritus	Histopathology findings	Distribution of skin lesions	Treatment and response
Vijaikumar *et al*, 2001[4]	25	15	M	Mild pruritus	Hyperpigmented lesion: Mildly hyperkeratotic epidermis, amorphous eosinophilic masses in the papillary dermis. Congo red stain: Eosinophilic masses showed apple-green birefringence under polarized light indicating a deposit of amyloid substances in hyperpigmented lesion.	Face, trunk and extremities	Antioxidant therapy† 6 months; no change in skin lesions
Choonhakarn and Wittayachanyapong, 2002[5]	20	15	M	No pruritus	Hyperpigmented lesions: Amyloid deposition in the papillary dermis. Congo red stain: Apple-green birefringence with polarized light indicating presence of the amyloidal deposits in both type of lesion.	Trunk only	No treatment
Kurian *et al*. 2013[6]	26	Childhood	F	No pruritus	Hypopigmented lesion: Atrophic epidermis with loss of rete ridges, eosinophilic extracellular nodular deposits, mild perivascular aggregates of chronic inflammatory cells of which lymphocytes predominate. Congo red stain: Eosinophilic deposits stained brick red indicating presence of the amyloidal deposits in both type of lesion.	Trunk and extremities	NR
Garget *et al*. 2011[7]	19	4	F	No pruritus	Hyperpigmentation: Amorphous eosinophilic material in the papillary dermis with slightly widened dermal papillae, irregular elongation of rete ridges and a sparse subjacent infiltrate of lymphocytes and melanophages. No abnormality in the reticular dermis.	Face and trunk, extremities	Acitretin 0.75 mg/kg/day; response not reported
Verma and Joshi, 2015[8]	41	6	M	No pruritus	Congo red Stain: Pinkish amorphous amyloid deposited in the papillary dermis.	Palms, soles, dorsa of hands, feet and face	No treatment
Tiwari *et al*. 2018[9]	30	10	M	No pruritus	Hyperpigmented macular lesions: Increased melanin in basal layer cells, few melanophages in papillary dermis. Depigmented lesion: Melanocytes were very much decreased in the basal layer Histopathology: Small, globular, pink, amorphous amyloid deposits in papillary dermis in both type of lesion. Congo red Stain: Pinkish amorphous appearance indicating presence of the amyloidal deposits in both type of lesion.	The proximal part of upper and lower limbs and face sparing scalp, palm, soles, hands, feet, and genitalia	Acitretin (25 mg oral daily)
Verma *et al*. 2019[10]	32	12	M	No pruritus	Hyper- and hypopigmented macular lesions: Relatively normal epidermis with orthokeratosis. There were widened papillae with deposition of globular pink deposits in the interface region in association with occasional melanophages suggestive of amyloidosis. Congo red stain: Amyloid deposits in papillary dermis	Trunk and extremities	Acitretin 25mg twice a day; response not reported

Contd...

Table 1: Contd...

Author	Age at diagnosis (years)	Age at the onset (years)	Sex	Pruritus	Histopathology findings	Distribution of skin lesions	Treatment and response
Present case	9	3 months of age	F	No pruritus	Hyper- and hypopigmented macular lesions: Small globular pink amorphous deposits of amyloid in association with occasional melanophages, amyloid deposits associated with moderately hyperplastic rete ridges, moderate compact and lamellated orthohyperkeratosis, occasional dyskeratotic cells. Congo red stain: Apple-green birefringence with polarized light indicating presence of these amyloidal deposits in both type of lesion.	Face, abdomen, back, and both upper and lower extremities	Combined therapy of acitretin (25 mg oral daily for 6 months) with six sessions of excimer light and fractional CO_2 laser; partial improvement in skin lesions of the face

†Antioxidant therapy; vitamin C, beta-carotene, vitamin E, selenium, copper, manganese and zinc

basis of ACD is not known. In particular, biallelic mutations in GPNMB, encoding glycoprotein (transmembrane) nonmetastatic melanoma protein B, have been mainly assumed to be involved in the pathogenesis of ACD.[11] It has recommended that genetic factors may lead to the disruption of DNA repair in keratinocytes. Moriwaki *et al*., Vijaikumar, and Thappa observed slow DNA repair in keratinocytes due to ultraviolet C damage and reduced repair following ultraviolet B damage.[2,4] However, the cutaneous findings in the presented case revealed that hyperpigmented macules and mottled hypopigmented macules distributed over the entire skin surface, and the face, back, and both upper and lower extremities often had a similar presentation as the abdomen which was the non-sun-exposed skin area. These findings argue against a primary role of photosensitivity in the presented case. Onset before puberty may be a crucial contributory factor in the pathogenesis of ACD in this case.

Histopathological examination showed amyloid deposits in the papillary dermis. Amyloid stains positively for crystal violet and Congo red. In rare instances, amyloid is not detected with the former stains, immunochemistry for anti-cytokeratin antibodies should be obtained if suspicion remains. Here, in this case, congo red stain was used for a definite diagnosis of ACD.[12]

Various treatment modalities have been described for the treatment of ACD with varying success rates. Protection from sun exposure and the use of broad-spectrum sunscreen should be advised for all the patients. Variable results have been obtained with topical corticosteroids, keratolytic, dimethyl sulfoxide, UV-B and psoralen–UV-A phototherapy, dermabrasion, capsaicin, and CO2 laser. However, success is limited. Prudent management is of great value in this condition. As per the literature review, systemic acitretin treatment seems to have the most promising results.[13] It is a synthetic retinoid, is the pharmacologically active metabolite of etretinate, may act by repairing the keratinization defect that causes the degeneration of keratin fibrils to amyloid. The excimer light is a quite effective modality for treating hypopigmentation, on this ground; we thought to combine it with acitretin. Fractional CO2 laser passes light down to the deeper layers of the skin, causing controlled damage to the cells and, triggering the skin's natural healing process. This process allows the cells to be trained to grow back stronger, firmer and faster, therefore the skin becomes smoother, tighter and more even in tone. Regarding this mechanism, fractional CO2 laser was used for even distribution of pigmentation in surrounding areas. The healing time for the laser is 2-3 days. In particular, the higher frequency of excimer light and high power of fractional CO2 laser may cause post-inflammatory hyper-pigmentation in dark and dry skin, as a cosmetic point of view, this is a grave matter. As expected, the combination of acitretin with the excimer light and fractional CO2 laser with specific settings worked well for this condition and resulted in improved cosmesis.

Histopathological evaluation with specific stain congo red is the best clue for the diagnosis of ACD. The partial improvement over facial skin was noted with combined treatment of acitretin with excimer light and fractional CO2 laser.

Consent for publication

Written informed consent was obtained from the patient's legal guardian(s) for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not

be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgement

We would like to thank all the authors for the contribution to this work.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Morishima T. A clinical variety of localized cutaneous amyloidosis characterized by dyschromia (amyloidosis cutis dyschromica). Jpn J Dermatol B 1970;3:43-52.
2. 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.
3. Tan T. Epidemiology of primary cutaneous amyloidoses in Southeast Asia. Clin Dermatol 1990;8:20-4.
4. Vijaikumar M, Thappa DM. Amyloidosis cutis dyschromica in two siblings. Clin Exp Dermatol 2001;26(8):674–6.
5. Choonhakarn C, Wittayachanyapong S. Familial amyloidosis cutis dyschromica: Six cases from three families. J Dermatol 2002;29:439–42.
6. Kurian SS, Rai R, Mahukar ST. Amyloidosis cutis dyschromica. Indian Dermatol Online J 2013;4:344–6.
7. Garg T, Chander R, Jabeen M, Barara M, Mittal M, Jain M. Amyloidosis cutis dyschromica: A rare pigmentary disorder. J Cutan Pathol 2011;38:823–826.
8. Verma S, Joshi R. Amyloidosis cutis dyschromica: A rare reticulate pigmentary dermatosis. Indian J Dermatol 2015;60:385-7.
9. Tiwary AK, Mishra DK, Chaudhary SS. Amyloidosis cutis dyschromica: A rare dyschromic subtype of primary cutaneous amyloidosis. Pigment Int 2016; 3:33.
10. Verma K, Sharma RK, Gulati A, Gupta M. Amyloidosis cutis dyschromica: A rare dyschromic pigmentary disorder. Indian J Dermatopathol Diagn Dermatol 2019;6:45-7.
11. Yang CF, Lin SP, Chiang CP, Wu YH, H'ng WS, Chang CP. Loss of GPNMB Causes Autosomal-Recessive Amyloidosis Cutis Dyschromica in Humans. Am J Hum Genet 2011;102:219–232.
12. Huang WH, Wu CY, Yu CP, Chiang CP. Amyloidosis cutis dyschromica: Four cases from two families. Int J Dermatol 2009;48(5):518-21.
13. 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.