Dyschromatosis Universalis Hereditaria with Hypospadias: A Rare Association

Abstract

Dyschromatosis universalis hereditaria (DUH) is a rare genodermatosis, which presents as hyper- and hypopigmented macules all over the body.Although a benign condition, rarely DUH is associated with abnormalities of dermal connective tissue, nerve, and systemic conditions. We report a case of DUH associated hypospadias and complicated with hydronephrosis that has not been described earlier.

Keywords: *Dyschromatosis universalis hereditaria, genodermatosis, hypospadias*

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Introduction

Dyschromatosis universalis hereditaria (DUH) is a rare genodermatosis. Usually hyper- and hypopigmented macules are present all over the body with increased predilection of lesions on the trunk. Few cases are reported from India.[1] DUH is associated with abnormalities of dermal connective tissue and nerve.[2,3] One case of DUH had end-stage renal disease.[4] We report a case of DUH, without any family history of similar disease, associated hypospadias complicated by hydronephrosis. To our knowledge, there are no reports of such association of DUH with hypospadias till date.

Case Report

A 7-year-old boy presented to OPD with hyper- and hypopigmented lesions over arms, legs, trunk, and buttocks since 3 years. The lesions appeared first on trunk and gradually involved other parts like bilateral hands and legs. There was no history of photosensitivity or photophobia. The child was born out of nonconsanguineous marriage and similar disease was not present among the family members. His parents denied exposure to chemical or history of prolonged drug intake. Physical examination revealed numerous asymptomatic, hyperpigmented macules (size 0.5–1 cm) interspersed with hypopigmented macules with increased predilection on the trunk [Figure 1]. Palms and soles were not involved. Examination of hair, nails, teeth, and mucosae appeared normal. There was no apparent atrophy, erythema, or telangiectasia. The patient had penile hypospadias present since 3 years of age [Figure 2]. It was not associated with any disturbance in urinary stream or difficulty in voiding urine. Systemic examination did not reveal any abnormality. Routine investigations were within normal limits. Clinical diagnosis of DUH, amyloidosis dyschromia cutis, Dyschromatos is symmetric a here ditaria, dyskeratosis congenital, generalized Dowlinge-Degos disease were considered. Histopathology from the pigmented macule showed mildly hyperplastic epidermis with moderate increase in pigmentation throughout the epidermis with frequent melanin incontinence and scattered melanophages, which was compatible with diagnosis of DUH [Figures 3 and 4]. Ultrasonography of kidney and urinary bladder showed left side secondary hydronephrosis. Parents were counseled regarding the benign nature of the skin condition and patient was referred for surgical correction of the penile hypospadias.

Discussion

DUH is inherited as autosomal dominant condition; however, few autosomal recessive and sporadic cases are also reported.[5] DUH was first reported by Ichikawa and

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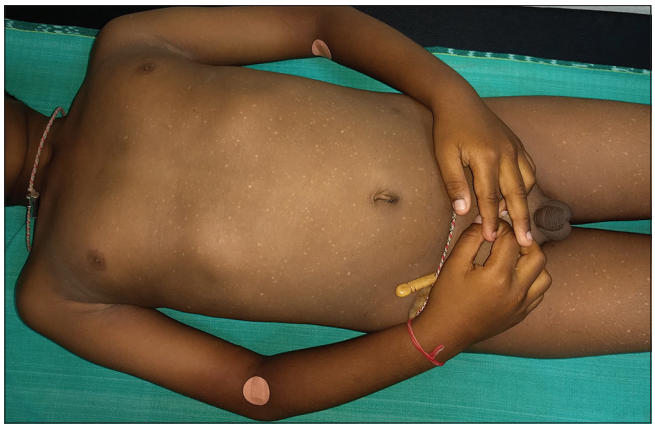

Figure 1: Hypo and hyperpigmented macules with widespread distribution

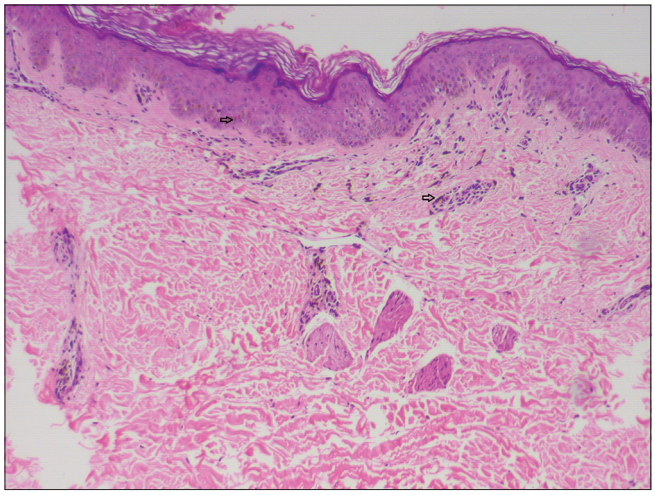

Figure 3: Increase pigmentationof basal layer with Melanin incontinencein superficial dermis (H and E ×100)

Higara,[6] which presents with hyper- and hypopigmented macules all over the body. Skin lesions usually present in the first years of life and they predominantly present over trunk and extremities. Involvement of face, palm, and soles are rare.

DUH must be differentiated from xeroderma pigmentosum since both can present with mottled pigmentation. However, the xeroderma pigmentosum lesions have increased predilection for photoexposed areas and may turn malignant. Atrophy and telangiectasia are uncommon and lesions have a benign course. Other differential diagnosis of DUH include Dyschromatos is symmetric a here ditaria, dyskeratosis congenital, generalized Dowlinge-Degos disease, incontinentiapigmenti (Bloch–Sulzberger), Naegelie–Franceschetti–Jadassohn syndrome, chronic arsenic toxicity, and chronic radiodermatitis.

Although etiology of this disorder is not yet known, the locus has recently been mapped to be chromosome 6q2.[7] Recently, ABCB6, an ATP binding cassette (ABC) transporters has been identified as the first pathogenic gene associated with DUH.[8] ABC transporters transport various

Figure 2: Penile hypospadias

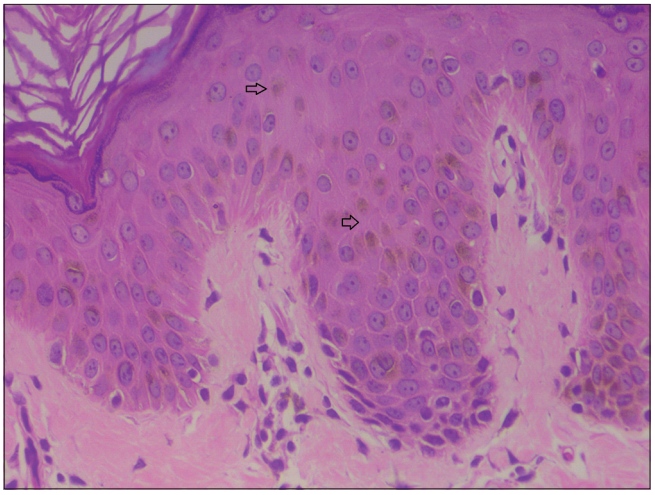

Figure 4: High-power view showing increased basal layer pigmentation (H and E ×400)

molecules across cell membranes and disruption can cause dysfunction of tyrosinase and abnormal melanin synthesis. It also plays a role in melanosome transport to surrounding keratinocytes.[8] ABCB6 protein has wide range function at different sites of body; hence, mutation of ABCB6 domains can produce disease of diverse phenotypes. However, not all DUH patients have the ABCB6 mutation. It is possible that DUH is a disease of genetic heterogeneity.[9]

Association of DUH with abnormalities of dermal connective tissue, nerve tissue, or other systemic complications is reported.[2,3] DUH has been reported to be associated with a wide range of cutaneous and systemic diseases such as tuberous sclerosis, learning difficulties, mental retardation,

short stature, and high tone deafness,[10] X-linked oculo-cutaneous albinism,[11] epilepsy,[12] erythrocyte, platelet and tryptophan metabolism abnormalities,[13] renal failure,[4] and primary ovarian failure.

Ultra-structurally skin in DUH has defective melanosome synthesis rate or melanocyte activity and not the melanocyte number. Histopathology has focal increase or decrease in melanin content of the basal layer (depending on the type of the lesion biopsied) and occasional pigmentary incontinence.

Our case has clinical and histopathological features of DUH. But, we could not find similar disease in the family, suggesting a sporadic inheritance in our case. Second, association of hypospadias with secondary hydronephrosis has never been reported in the literature. Although we could not establish the pathogenesis behind this association, still we believe it may be the first case. Although hypospadias is a disease of heterogenicity, Sonic hedgehog, WNT and BMP signaling play a major role and there was no established genetic association with DUH. Therefore, whether the occurrence of hypospadias is a true association or a coincidence remains inconclusive. Authors believe though DUH is a benign disease, other systemic associations need to be carefully ruled out in every case by thorough clinical examination and history-guided investigations so that any association can be treated earlier.

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Conflicts of interest

There are no conflicts of interest.

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