Dyschromatosis Universalis Hereditaria: A Case Report From Turkey

Herediter Universal Diskromatozis: Türkiye'den Bir Olgu Sunumu

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ABSTRACT Dyschromatosis universalis hereditaria (DUH) is a rare and clinically heterogenous genodermatosis characterized by an admixture of hyperpigmented and hypopigmented macules in a generalized distribution. Although initially it was reported mostly in Japan, subsequent cases have been reported from other countries. Coexisting with Systemic findings as well as nail and hair abnormalities have also been reported. We present here a 4-year-old girl with generalized and progressive reticulate hyper-and hypopigmentation of the skin. Her tongue also showed mottled hyperpigmentation and her hair was blond. Although she was born of consanguineous parents, other family members were not affected. Histopathological examination revealed an increase in the melanin content of the basal layer and pigmentary incontinence. Based on the clinical and histopathological findings, she was diagnosed as DUH and the interesting clinical features of the disease were discussed.

Key Words: Skin diseases, genetic; pigmentation disorders

ÖZET Dyschromatosis universalis hereditaria (DUH) vücutta yaygın dağılım gösteren, hiperpigmente ve hipopigmente maküllerin birarada görüldüğü nadir ve klinik olarak heterojen bir genodermatozdur. Önceleri en çok Japonya'da bildirilmiş olmasına rağmen, sonradan başka ülkelerden de bildirimler olmuştur. Eşlik eden tırnak, saç anomalileri ve sistemik bulgular da rapor edilmiştir. Bu makalede vücudunda yaygın ve ilerleyici tarzda hiper ve hipopigmentasyonları olan 4 yaşında bir kız hasta sunulmaktadır. Dilde de benekli hipopigmentasyonu olan hastanın saç rengi sarı idi. Akraba evliliğinden doğmuş olmasına rağmen ailenin diğer üyeleri etkilenmemişti. Histopatolojik değerlendirmede bazal tabakada melanin miktarında artış ve pigment inkontinansı saptandı. Klinik ve histopatolojik bulguların ışığında DUH tanısı konuldu ve hastalığın ilgi çekici klinik özellikleri literatür bilgileri eşliğinde gözden geçirildi.

Anahtar Kelimeler: Genetik deri hastalıkları; pigmentasyon bozuklukları

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Dyschromatosis is a term used to describe different dermatoses presenting with hyper-and hypopigmentation of the skin. Dyschromatosis universalis hereditaria (DUH) is a generalized and random distributed form of dyschromatosis. DUH was found to be an autosomal dominantly inherited disease presented with a defect in melanosome synthesis rate. Causative gene was found to be located at chromosome 1q11-1q21.[1,2] It was initially described by Ichikawa and Hiraga in 1933 in

Japan.[3] DUH most commonly occurs in Japan and most of the literature reported in journals has been written in Japanese. Here, we describe the first case of DUH from Turkey and discuss with review of the literature.

CASE REPORT

A 4-year-old girl born of consanguineous parents (the grandmother of her mother and grandfather of her father were siblings) after full-term and normal vaginal delivery, presented with progressive and asymptomatic mottled hyperpigmentation involving almost the whole body which had been present since birth. Gradually spotty hypopigmentation had developed among the hyperpigmented macules (Figure 1). On general examination her size and weight were below normal for age (between 25-50 percentiles). Her developmental milestones were delayed. Personal and family histories were unremarkable. None of her parents nor her two brothers had a history of similar disorder. She was not exposed to chemicals or radiation both in intrauterine life or postpartum.

Cutaneous examination revealed that the lesions were denser on the trunk. The palms and soles were also involved. Oral mucosa and tongue showed mottled hyperpigmentation. Different from the other family members, her hair was blond but teeth and nails were normal (Figure 2).

Systemic examination did not reveal any associated abnormalities. Mixed type astigmatism was found with ocular examination. Routine blood tests as well as audiogram were normal.

A biopsy specimen taken from a pigmented macule on the trunk showed pigmented basal layer of epidermis with pigment incontinence and pig-

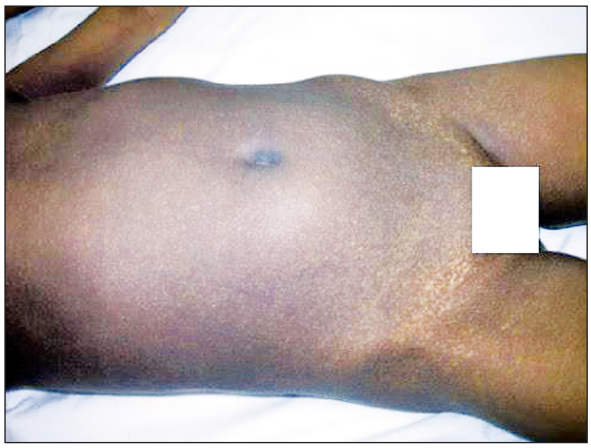

FIGURE 1: Generalized hyper- and hypopigmented macules giving skin a mottled appearance predominantly on the trunk

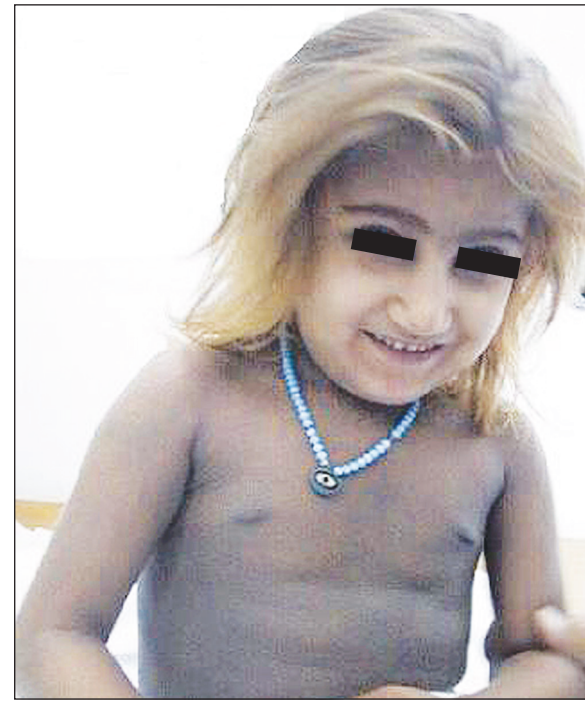

FIGURE 2: Periorbital pigmentation and blond hair.

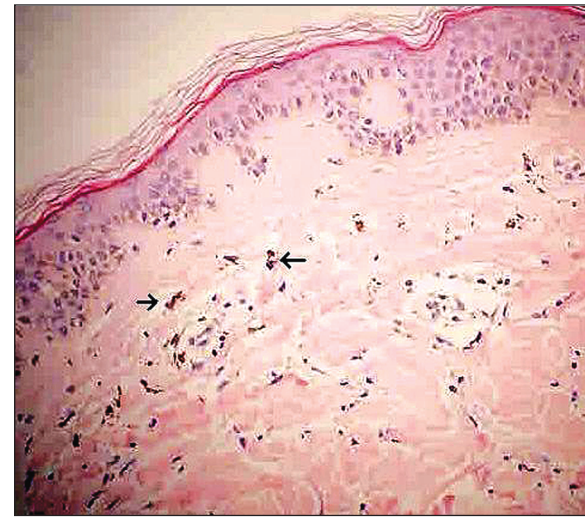

FIGURE 3: Pigment incontinence in the basal layer of epidermis and pigment-laden macrophages (arrows) in the upper dermis (Hematoxylin & Eosin, x100).

ment-laden macrophages in the upper dermis (Figure 3). Based on the typical appearance and histopathological findings, the patient was diagnosed as DUH.

DISCUSSION

Dyschromatosis hereditaria is a rare hereditary skin disorder characterized by asymptomatic hypo-and hyperpigmented macules of irregular size and shape which usually appear early in life.[4] In some, the condition commences in adulthood, explaining the late detection.[5] Sethuraman et al[6,7] classified this disorder into 3 types: DUH, dyschromatosis symmetrica hereditaria (DSH) and unilateral dermatomal pigmentary dermatosis. DUH is the generalized form with predominantly trunk involvement, however similar lesions can also be seen on the extremities and sometimes face.[4,8] There are reports of affected family members in two, three or five generations and these reports strongly support an autosomal dominant inheritance pattern for DUH.[1,3,8-11]

TABLE 1: Differential diagnosis of generalized pigmentary skin changes with hyper- and hypopigmentation.

Disease	Skin macules and distribution	Additional features	Inheritance
Dyskeratosis congenita	Reticulate hyperpigmentation predominantly on neck, upper chest, upper arms	Telangiectasia, atrophy, hypopigmented macules, onychodystrophy, leukoplakia, bone marrow dysfunction, predisposition to malignancy, epiphora	XR
Naegeli-Franceschetti-Jadassohn syndrome	Reticulated hyperpigmentation predominantly on abdomen, periocular and peroral region	Dental abnormalities, hypohidrosis, palmoplantar hyperkeratosis, onychodystrophy	AD
Dermatopathia pigmentosa reticularis	Reticulated hyperpigmentation predominantly on trunk	Alopecia, onychodystrophy, absent dermatoglyphics, hypo- or hyperhidrosis, punctat palmoplantar keratoderma	AD (not certain)
X-linked reticulate pigmentary disorder	Brown reticulated hyperpigmentation (generalized or following Blaschko lines)	Xerosis, recurrent infections and multiple systemic abnormalities in male patients; amyloid deposits in dermis	XR
Dowling-Degos disease	Reticulated hyperpigmentation predominantly on flexural sites	Comedone-like lesions on the back and neck, pitted facial scars, epidermoid cysts	AD
Reticulate acropigmentation of Kitamura	Atrophic, reticulated or lentigo-like brown hyperpigmentation predominantly on acral sites	Palmoplantar pits, breakage of epidermal ridges	AD
Revescz syndrome	Reticulated hyperpigmentation	Exudative retinopathy, bone marrow failure, ataxia, hair abnormalities, psychomotor retardation	?
Mendes da Costa syndrome	Reticulated hyperpigmentation predominantly on face and limbs	Traumatic bullae, dwarfism, atrichia, mental retardation	XR
Cantu syndrome	Reticulated hyperpigmentation predominantly on face, forearms and feet	Alopecia, follicular hyperkeratosis, palmoplantar keratoderma	XR
Linear and whorled hypermelanosis	Reticulated or zosteriform hyperpigmentation folowing the lines of Blaschko	None	Sporadic
Gougerot and Carteaud syndrome	Elevated papillomatosis and reticulated hyperpigmentation predominantly on neck and upper trunk	None	Sporadic
Dyschromatosis symmetrica hereditaria	Acral mottled hyper- and hypopigmentation	Males predominantly affected	AD
Epidermolysis bullosa with mottled pigmentation	Mottled hyper- and hypopigmentation predominantly on lower abdomen, groin, axillae, proximal limbs	Intraepidermal blisters, palmoplantar keratoderma, photosensitivity	AD
Incontinentia pigmenti	Hyperpigmentation in stage 3, hypopigmentation in stage 4	Alopecia, nail and dental abnormalities, CNS and eye involvement	XD
Xeroderma pigmentosum	Hyper- and hypopigmentation predominantly on sun-exposed areas	Xerosis, atrophy, telangiectasia, skin tumors	AR
Hypomelanosis of Ito	Whorled, linear or patchy hypomelanosis predominantly on trunk and limbs	CNS, musculoskeletal, eye and hair involvement, heart defects	Sporadic

AD, autosomal dominant; AR, autosomal recessive; XD, X-linked dominant; XR, X-linked recessive; CNS, central nervous system

Zhang et al,[2] mapped the gene of DUH at chromosome 1q11-1q21 and ultrastructural findings suggested a defect in melanosome production and distribution in the epidermal melanin units with no significant alteration in the number of melanocytes as the pathogenetic mechanism of DUH.[1,11,12] Recently, pathological mutations of the double-stranded RNA-specific adenosine deaminase gene (ADAR1 or DSRAD) have been identified in four dyschromatosis symmetrica hereditaria pedigrees but similar mutations could not be found in DUH.[13] However, more evidence is required to establish the genetic background of DUH.

Exclusion of the associated abnormalities is important in DUH. These include small stature and high tone deafness,[14] abnormalities in erythrocyte, platelet and trpytophan metabolism,[15] epilepsy,[16] insulin-dependent diabetes mellitus,[11] photosensitivity along with neurosensory hearing defects[17] and ocular abnormalities.[18,19] Although the weight and height of our patient were below normal, no endocrine or neurologic abnormality was found to explain her status.

Both DUH and DSH occur most commonly in Japan, but few Caucasian, Indian, Afro-Caribbean, Arabian, Korean and Chinese cases have been reported.[1-23]

In addition to generalized pigmentary disorders (Table 1), postinflammatory hyperpigmentation and exposure to physical, chemical, pharmacological agents or radiation, should be considered in the differential diagnosis.

To the best of our knowledge, this is the first case report of DUH from Turkey. The history of consanguineous parents strongly suggests a genetic pathology for the defect in melanosome synthesis. Since DUH is a rare entity, evidence related to genetic and environmental factors that possibly trigger the disease could only be gathered from cumulating case reports in literature.

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