Dyschromatosis Universalis Hereditaria

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Dyschromatosis universalis hereditaria is a rare pigmentary disorder initially described in the Japanese literature. The pattern of inheritance is believed to be autosomal dominant, but many sporadic cases have been reported.

We encountered a family in which dyschromatosis universalis hereditaria occurred in seventeen members of three generations. In the two members whom we observed, typical skin lesions were distributed all over the body except palms and soles. By pedigree analysis, we found an autosomal dominant pattern of inheritance.

The differential diagnosis of the other reticulate pigmentary disorders is discussed with a review of dyschromatosis reported in the Korean literature.
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Key Words: Dyschromatosis universalis hereditaria, Autosomal dominant

Dyschromatosis is characterized by spotted hyperpigmentation mingled with patches of hypopigmentation. Two types of dyschromatosis have been reported: localized dyschromatosis, also known as Dyschromatosis Symmetrica Hereditaria (DSH)[1-6] and widespread dyschromatosis, also known as Dyschromatosis Universalis Hereditaria (DUH).[7-9] Although both types of dyschromatosis have a similar primary lesion clinically but vary in the extent of cutaneous involvement, it is not fully dismissed that they are different clinical expressions of the same pathologic process.

The early reports of DUH were confined to Japanese patients,[7-9] but identical or closely similar syndrome has been reported among South Africans,[10] the English[11] and Americans.[12] In Korean literature, we could find only two reported cases of DUH. In 1969, Kim[13] reported the first case of DUH in a 21-year-old male who had no family history. Myung et al,[14] in 1979, described an additional case in a 18-year-old female with family history of a similar condition. The affected family members were her mother, maternal uncle and two aunts and maternal grandfather. Several authors[7-8] have suggested that DUH may be inherited by an autosomal dominant gene. But in view of the wide variety of gene penetrance and expression, it is difficult to establish the exact mode of inheritance from the limited numbers of cases. Fortunately, we recently observed a case of DUH present in a family with seventeen affected members, that was transmitted by an autosomal dominant trait in three generations.

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REPORT OF CASES

Case 1.: A 20-year-old man visited the Dermatology Department of Hanyang University Hospital in April, 1988, with mottled pigmented and depigmented macules in a reticular pattern on the trunks

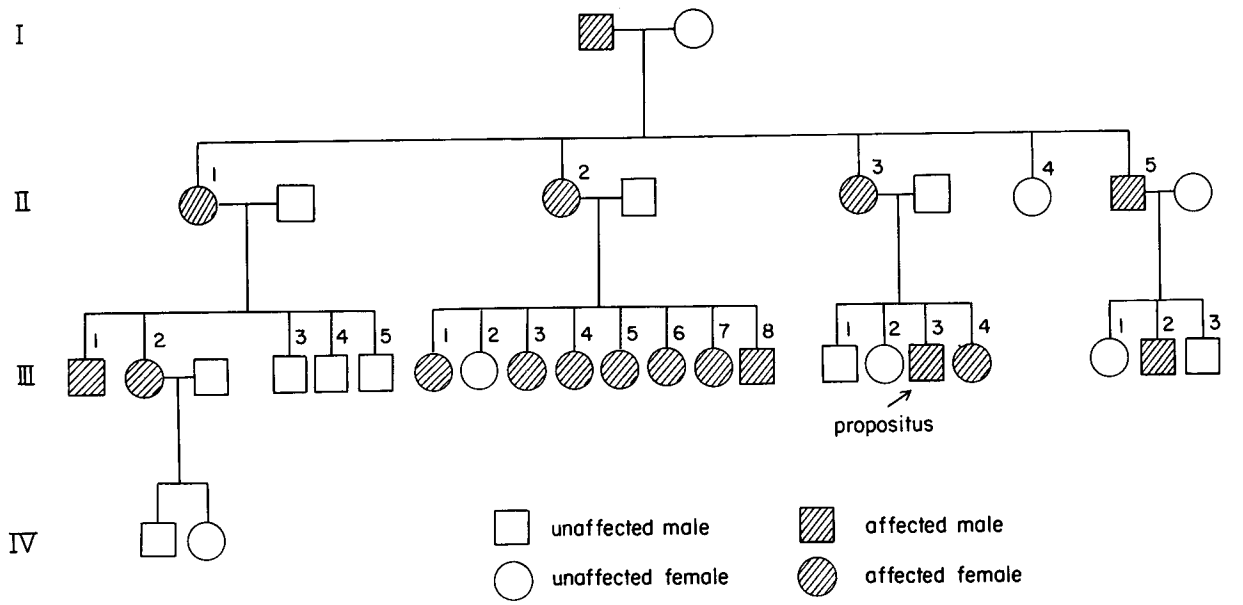

Fig. 1. Pedigree of four generations of family with DUH showing autosomal dominant inheritance.

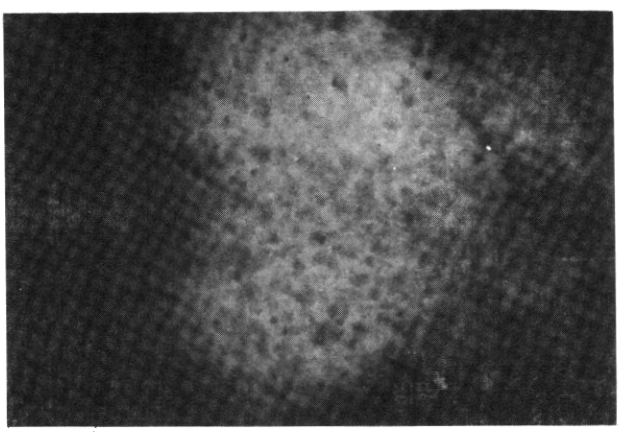

Fig. 2. Mottled pigmented and depigmented macules in a reticular pattern on the trunk of patient 1.

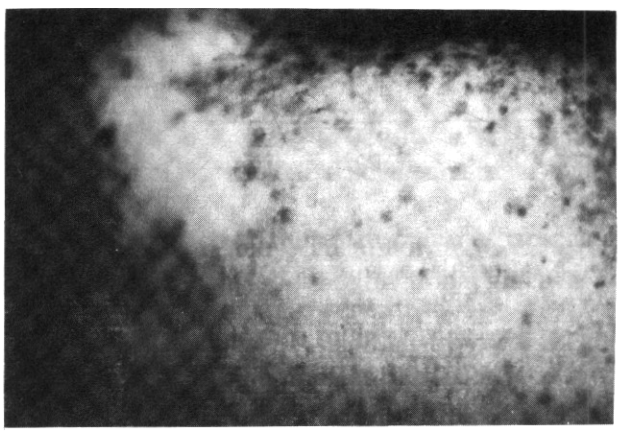

Fig. 3. Well-defined irregular shaped hypopigmented macules on the lower back of patient 1.

and extremities. Pigmentary changes began to show on his buttocks at the age of 3 months and spreaded to the trunk during the next 5 months, then to the extremities slowly but progressively. There was no history of previous inflammation or any other dermatosis, and no seasonal variation in the intensity of pigmentation. In his family, sixteen members including his mother were affected with the same condition (Fig. 1). On the physical examination, 2 to 5 mm-sized multiangular, reticulated brown pigmented and depigmented macules were closely intermingled with each other all over the body (Fig. 2). His face was involved only slightly with small pigmented macules resembling freckles and his palms and soles were spared. On the lower back, a few well-defined, irregular shaped, hypopigmented macules were noted (Fig 3). There were no erythema, scales, wrinkles, or other epidermal changes. There were no subjective symptoms. Hairs, nails, and teeth were normal and no systemic anomaly was detected in the internal organs. Biopsy specimens were taken from the pigmented and depigmented lesions on the back and stained with hematoxylin-eosin and Fon-

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Fig. 4. Decreased melanin granules were observed in the basal layer of the depigmented lesion as compared to the normal-appearing skin (Fontana's silver stain, ×100).

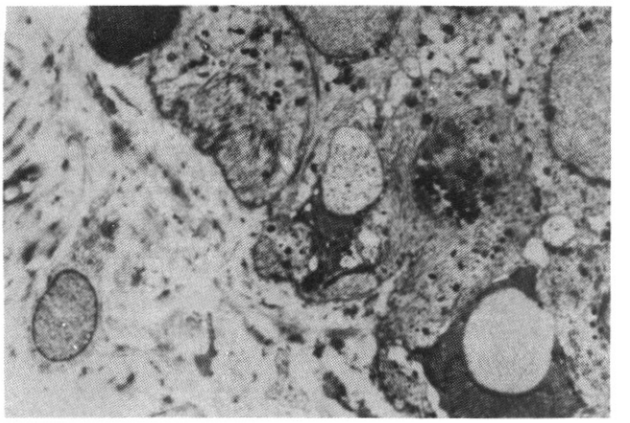

Fig. 6. Electron micrograph of the normal-appearing skin showing degenerative changes of melanocytes, such as dark cytoplasm and vacuolization of the cytoplasm (×3,000).

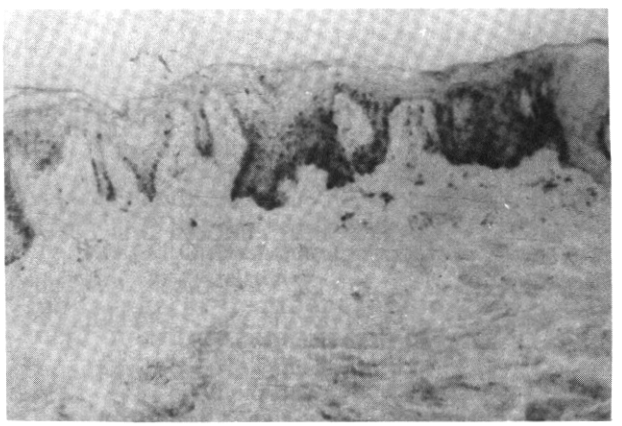

Fig. 5. Increased melanin granules seen in the basal layer and in melanophages in the papillary dermis of the pigmented lesion (Fontana's silver stain, ×100).

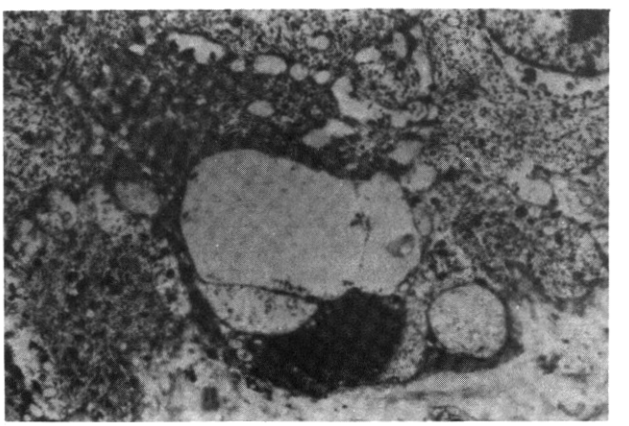

Fig. 7. Electron micrograph of the depigmented lesion showing decreased melanosomes and degenerative changes of the melanocyte (×3,500).

tana's stain for melanin. The specimens showed increased melanin granules in the basal cell layer of the pigmented lesion and decreased melanin granules in the basal cell layer of the depigmented lesion. Melanophages were present in the papillary dermis underneath the pigmented area (Fig. 4, 5). Dopa-oxidase reaction showed no significant change in the total number of dopa-positive dendritic melanocytes in the pigmented vs. depigmented lesion. However, the depigmented lesion had less pigment as compared to the pigmented lesion. For the electron-microscopic study, a second biopsy was performed two months after the first visit. Biopsy specimens were taken from the normal-appearing skin of left forearm and the hyperpigmented/hypopigmented lesions of left side of abdomen. Ultrastructurally, normal numbers of melanocytes were seen at the basal cell layer and there were only differences in the number of the melanosomes according to the areas of pigmentation intensity. The melanocytes and some of the basal keratinocytes of normal-appearing skin and hypopigmented lesion showed degenerative changes such as dark cytoplasm and vacuolization of the cytoplasm (Fig. 6,7).

Case 2: A 51-year-old woman, mother of case 1, also had similar skin lesion, which appeared in early infancy, first on the groin and axilla, and then spread to involve her trunk and extremities. Her palms and soles were spared. Other than the pigmentary changes there were no epidermal changes. The lesions were not pruritic. Her general health

was good and this pigmentary disorder was not associated with any systemic anomalies. There was no history of consanguinous marriages. Permission to take biopsy specimens was refused. The other family members who had affected with this disorder were described by her and her younger sister.

DISCUSSION

Dyschromatosis was first reported as a localized form by Matsumoto[1] in 1923 as "leukopathia punctata et reticularis symmetrica" and later by Dohi and Komaya[2] in 1924 under the title "acropigmentio symmetrica-Dohi". In 1929, 12 cases of a previously unrecognized pigmentary disturbance in Japanese patients were studied by Toyama[3] who first used the term "dyschromatosis symmetrica hereditaria". In 1933, Ichikawa and Hiraga[7] described two families in which both mother and children exhibited a generalized speckled cutaneous pattern composed of both hyperpigmented and hypopigmented small macules. The palms and soles were not involved and there was no associated internal anomaly. They reported this widespread type of dyschromatosis as "dyschromatosis universalis hereditaria".

Both types of dyschromatosis are very rare and only a few cases have been reported. Ito[5] found in his clinic between 1925 and 1944 only 16 cases of DSH, and stated that dyschromatosis is thought

Table 1. Summary of reported cases of dyschromatosis in Korea.

Author	No.	Sex	Onset	Distribution	Family History
Kim[13] (1969)	1	M	3y	Dorsa of hands & feet extremities face & neck	−
	2	F	12y	Dorsa of hands & feet extremities face & neck	−
	3	M	2y	Generalized	−
Chun,[17] et al (1970)	4	M	birth	Dorsa of hands & feet	Mother & maternal grandfather were also affected
Myung,[14] et al (1979)	5	F	10y	Dorsa of hands & feet	One brother was also affected
	6	M	9m	Generalized	Mother, one uncle, two aunts & maternal grandfather were also affected
Kim,[18] et al (1980)	7	M	12y	Dorsa of hands & feet extremities	
	8	F	3m	Dorsa of hands & feet	Daughter of case 7
	9	F	infancy	Dorsa of hands & feet extremities	Mother of case 7
	10	F	15y	Dorsa of hands & feet extremities	
	11	M	2y	Dorsa of hands & feet	Son of case 10
Kim,[19] et al (1987)	12	M	10y	Dorsa of hands & feet extremities	Mother & one brother were also affected
Chung,[20] et al (1987)	13	F	12y	Dorsa of hands & feet	−
Ro,[21] et al (1989)	14	M	15y	Lower extremities abdomen	One brother & father were also affected

*Negative sign indicates no family history; M, male; F, female; y, year; m, month.

to be unique to Japan. But Costa[15] described two similar cases of DSH in South Americans and stated that a similar disorder is frequent in Brazil. In 1964, Siemens[16] also reported a similar case in Europians under the term "acromelanosis albopuncta". Although the early reports of DUH were also confined to Japanese patients,[7-9] Findlay and Whiting[10] recognized it in two Bantu females, and Rycroft et al[11] reported an Iraqi girl who also had small stature and high tone deafness. The Negro girl reported by Petrozzi[12] probably also had the disorder. In Korea, several cases of DSH[13, 14, 17-21] have been reported but there are only two previous reports of DUH.[13, 14] A summary of reported cases of dyschromatosis in Korea is shown in Table 1.

The typical lesions are the same in both type of dyschromatosis, but the extent and severity of the involvement is a major difference differentiating DUH from DSH. The lesions of DSH are symmetrically distributed over extremities, particularly the distal hands and feet where spotted hyperpigmentation is mingled with hypopigmentation and also over the arms and legs. Although precipitating factors are unknown, that DSH is localized to sun-exposed areas suggests a role of ultraviolet radiation. In the physiogenetic study of the skin disease, Ito[4] summarized DSH and xeroderma pigmentosum as well as freckles in a polymeric dominant group caused by common genotype of photosensitivity. He attributed the difference of phenotype to the individuality to the factors of photosensitivity. In DUH, the skin lesions are distributed all over the body, particularly the trunk, abdomen, and limbs. While the face may be affected, it is less commonly involved and, if so, less severely than elsewhere. The palms and soles are usually spared. But Suenaga[8] reported involvement of palms with a few light brown macules in two patients and involvement of the sole in one. Furthermore, in many reported cases of DUH, as well as DSH, there were no seasonal variation in the intensity of pigmentation nor history of photosensitivity. Thus light is not the etiologic agent for all dyschromatosis. In a view of that, Suenaga[8] suggested DUH can not be enlisted in the same genetical group with DSH in spite of remarkable similarity in clinical appearance. Petrozzi et al,[12] in 1971, reported a case of DUH in a malnourished Negro girl and suggested that the abnormal pigmentary finding may represent the manifestations of malnutrition occurring during the early months of life. But in general, it is believed that dyschromatosis does not affect the general health of the patient. Nails, eyes, teeth, and hair are usually normal and there are no neurologic abnormalities. Only isolated patients have been reported to have systemic abnormalities. Suenaga,[8] for example, reported a child with DUH, caries of the dorsal spine, coxa valgae, and signs of nerve root compression.

Histologic features of dyschromatosis are not diagnostic in themselves. In DSH, the epidermis is normal except for an increase in melanin granules seen in the basal layer in the pigmented lesions and a decrease in the hypopigmented lesions. In DUH, histologic findings are similar with those of DSH, but there may be pigment incontinence. Hydropic degeneration of the basal layer and accumulation of the melanin in the upper dermis within melanophages are observed. Tanaka et al[9] reviewed nine cases of previously reported DUH in Japan and divided them into three groups according to the histologic findings. Six patients showed only increase or decrease of melanin pigments in the basal layer, and two patients including their case showed the presence of melanophage in the upper dermis. Finally, two patients showed both of these histologic findings. Because pigment incontinence is observed in other congenital pigmentary anomalies, such as Naegeli's disease and Rothmund-Thomson's disease, the authors suggested DUH in which melanophage is present in the upper dermis, may have some etiological relationship to other congenital pigmentary anomalies.

Both forms of dyschromatosis have been observed to be familial and inheritance is probably autosomal dominant. For DSH, Toyama and Omori[4] first reached this conclusion. Chun and Kim[17] assumed the type of inherity to be non-sex linked dominant inheritance. For DUH, Ichikawa and Hiraga[7] who found DUH in seven members of two families, also suggested an autosomal dominant pattern of inheritance. And there are many family studies in the literature to support a dominant inheritance pattern.[8, 9] In our case of

Table 2. Clinical features of some genetically determined pigmentary disorders

Disease	Distribution, pattern	Hypopigmentation	Pigment incontinence	Comments
Dyschromatosis symmetrica hereditaria	Acral, mottled	+	–	No atrophy, no palmar pits
Acromelanosis progressiva	Acral, diffuse	–	–	Mental retardation
Acropigmentation of Kitamura	Acral, reticulate	–	–	Atrophic lesion, palmar pits, breakage of epidermal ridges
Dyschromatosis universalis hereditaria	Generalized, mottled	+	+	No atrophy, normal nails & teeth
Dyskeratosis congenita	Generalized, reticulate	±	+	Atrophy over extensor surfaces, dystrophic nails & teeth, thickened palms & soles, hyperhidrosis, excessive lacrimation, leukoplakia/ leukokeratosis
Franceschetti-Jadassohn syndrome	Generalized, reticulated	–	+	Enamel hypoplasia, palmoplantar keratoderma, hypohidrosis
Incontinentia pigmenti	Generalized, whorl/streak	–	+	Usually females, may have early erythemato-bullous stage with later hyperkeratosis
Incontinentia pigmenti achromians (Ito)	Generalized, whorl/streak	+	–	Hypopigmentation in reverse pattern of incontinentia pigmenti

DUH, seventeen individuals were affected in three generations of one family. To our knowledge, this case has the largest number of family members affected with DUH. By pedigree analysis, we find that DUH is inherited as an autosomal dominant trait. However, many sporadic cases have been reported. In Korean literature, three cases reported by Kim[13] and one case reported by Chung[20] were non-familial cases of DSH. In 1982, Yamada[22] also reported a case of DUH with no family history.

The differential diagnosis of dyschromatosis includes a number of reticulate pigmentary disorders which are thought to be genetically determined.[23-25] The clinical features of the more important of these are listed in Table 2.

We would encourage other physicians to include dyschromatosis, which may be more common than is generally appreciated, in the differential diagnosis of pigmentary lesions occurring in similar patients. The connection between DUH and DSH remains unclear. Additional report of cases and further detailed studies, including dopa-reaction and electron-microscopic findings, are needed to elucidate the mechanism of inheritance of DUH and its association with DSH.

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