HYPOMELANOSIS OF ITO

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Abstract. Hypomelanosis of Ito appears to be a disorder of hypopigmentation. Findings from histochemical and electronmicroscopic studies indicate that pigment cells from the hypopigmented areas have short dendrites and synthesize less than normal amounts of melanin. The syndrome may have two forms: a cutaneous and neurocutaneous variety. In the more severe neurocutaneous variety, the phenotypic pigmentary abnormalities probably reflect a biochemical defect in all tissues derived from the neuro-ectodermal anlage.

Key words: Melanin; Pigment disease; Hypomelanosis; Congenital

Hypomelanosis of Ito is a rare disorder of the pigmentary system. Discussion persists about whether this disease should be classified as a disorder of hyper- or hypopigmentation (1) or whether it is a variant of incontinentia pigmenti (2). We believe the features of hypomelanosis of Ito are sufficiently characteristic to distinguish it easily from incontinentia pigmenti.

We should like to report another case, with unusual clinical findings, and contribute new data on the histology of the hypopigmented areas, which indicate that pigment cells of the hypopigmented areas are not producing normal quantities of melanin.

We divide hypomelanosis of Ito into two different syndromes: a more common cutaneous type in which the disease is limited to pigmentary changes and mild abnormalities of perspiration; and a neurocutaneous variety in which the patients manifest severe nervous system defects and bony abnormalities in addition to the hypopigmentation and sweating abnormalities.

CASE REPORT

The patient, a 23-year-old female, was the first of three siblings. The mother, who was 19 years old at delivery, had moderately severe toxemia and hypertension during the pregnancy but the delivery was normal. For the child...

Fig. 1. The breasts are asymmetric. Whorls of depigmented skin are visible on the flanks.
the neonatal period was uneventful. At 3 months of age
the infant's pediatrician thought the baby might have suf­
fered a brain injury at birth. At 6-8 months, whorled
hypopigmented areas began to appear over her trunk
without a preceding rash. At 16 months a diaphragmatic
hernia was repaired surgically. The child had two seizures
associated with tonsillitis and fever around the same time.
At age 4 years the child was thought to have a peptic ulcer,
but no radiographic studies were performed. At age 5
years the patient had chicken pox, possibly complicated
by mild encephalitis.

Her intellectual and motor development were retarded.
The child sat at 5 months and crawled at 7 months. She
could not walk until 18 months. Her gait was clumsy and
she fell frequently, sustaining a skull fracture in early
childhood. She spoke only six to eight words at 4 years of
age. Psychologic examination at age 9 indicated an I.Q. of
21. She was placed in a state training school for the men­
tally retarded and remains there to the present time. At
age 10 she was started on sodium phenobarbital (Lumi­
nal®; Winthrop Lab., N.Y., USA) and diphenylhydantoin
sodium (Dilantin®; Parke, Davis & Co., Detroit, Mich.).

Fig. 3. Representative sections of normal (a) and
hypopigmented skin (b) examined by electron
microscopy, showing the relative decrease in melanosome
in the hypopigmented area (×23,000). The epidermal
basement membrane is visible at the bottom of each
photomicrograph. The nucleated cells in both illustrations
are melanocytes surrounded by keratinocytes.
The number of seizures.

On physical examination the patient has hypertelorism and an epicanthal fold. She has an alternating strabismus. The fundi are normal but she requires spectacles to correct a moderate myopia. Her gums are hyperplastic and her cheeks and chin hirsute, all side effects of the diphenylhydantoin sodium.

The syndrome of hypomelanosis of Ito has also been termed Incontinentia Pigmenti Achromians. We agree with others (2) that incontinentia pigmenti achromians is a meaningless term and should be discarded in favor of hypomelanosis of Ito.

Hypomelanosis of Ito probably has two forms, cutaneous and neurocutaneous. Approximately two-thirds of the patients have the cutaneous variety manifested mainly by mild abnormalities of perspiration and depigmentation. In this group the pigmented loss begins late in childhood, persists until early adulthood, and then may disappear. Other than the mild cosmetic disfigurement, these children seem to be normal. In the patients with the neurocutaneous syndrome, depigmentation develops earlier in infancy and is accompanied by severe, central nervous system dysfunction, seizures, and bone abnormalities. In a previous paper (6), we suggested that cutaneous pigmentary abnormalities, especially if present at birth, might be a manifestation of a more generalized defect of all neuro-ectodermal derivatives. A genetic or enzymatic defect of the neuroectodermal anlage present during the critical developmental stages of the embryo could affect all organs derived from the neural crest. Thus mental retardation, seizures, and coordination defects, which are so easily attributable to trauma at birth, anoxia or infections, are in fact more probably due to a biochemical injury in the first or second trimester of pregnancy.

Others have examined the appearance of pigment cells in several different forms of congenital hypomelanosis (3). A patient with probable hypomelanosis of Ito was grouped with other patients who had a nevus depigmentosus. The findings were similar to ours. Split-dopa preparations showed the pigment cells to be clumped, with short, sparse dendrites. Preparations examined by electron microscopy had a significant decrease in the numbers of melanosomes within pigment cells and keratinocytes. Thus our study indicates that the pigmentary abnormality of patients with the neurocutaneous variety of hypomelanosis of Ito cannot be distinguished from that of the more benign form of cutaneous hypomelanosis of Ito, although the genetic defects in these two disease forms must differ greatly. The findings of our study indicate that hypomelanosis of Ito is a disease of hypopigmentation.

**REFERENCES**

2. Jelinek, J. E., Bart, R. S. & Schiff, G. M.: Hypomelanosis of Ito

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