Chediak-Higashi Syndrome with Hyperpigmentation

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Chediak-Higashi syndrome (CHS) is a disease of infancy and childhood in which the initial finding is an anomalous pigmentation. The skin is pale in general, but on the exposed parts of the patient born of dark-skinned parents it may have "slate gray" coloration or hyperpigmentation.

We report herein a case of CHS with hyperpigmentation in a Korean boy. At birth and when the child was adopted he had fair skin but a few months later some exposed parts of his skin became progressively pigmented.

Since this phenomenon is not so uncommon in Japanese or black children, the later development of hyperpigmentation of the exposed skin could be a characteristic skin manifestation of CHS, especially in the Mongoloids and black races.

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Chediak-Higashi syndrome (CHS) is a very rare autosomal recessive disorder characterized by partial oculocutaneous albinism, giant cytoplasmic granules in leukocyte, and increased susceptibility to infections.

Although the usual cutaneous manifestation of CHS is hypopigmentation, a few cases of hyperpigmentation of the skin have been described in the literature. Since this phenomenon is rare in Caucasians, hyperpigmentation of CHS has been infrequently reported.

We report a case of CHS with hyperpigmentation focusing on the patients cutaneous manifestation and emphasize that the hyperpigmentation could be one of the cutaneous manifestations of CHS.

REPORT OF A CASE

A 23-month-old Korean boy was admitted to the Pediatrics Department of St Mary's Hospital with a two-week history of cough and fever. His family history was unknown as he was an adopted son of the present parents. He had suffered from an recurrent upper respiratory infection since the age of seven months. On admission, the patient's temperature was 38.7°C, pulse rate 138/min and respirations 50/min. He had multiple nontender swelling of cervical lymphnodes. The vesicular respiratory sound was auscultated at the right lower lung field. The liver was palpable 4cm below the costochondral margin in the midclavicular line and the spleen was also palpable in a 5 finger width. A chest X-ray revealed patch infiltrations in the bilateral lower lung fields, especially in the right. An abdominal sonography showed the hepatosplenomegaly.

The patient's hemoglobin and hematocrit levels and platelet count were decreased to 7.2gm/100ml, 22.8% and 43,000/mm³ respectively. The white blood cell count was 4,700/mm³, with 12%
adopted, his skin color was lighter than that of a healthy Korean infant. When he was fourteen months old, marked hyperpigmentation of the sun-exposed skin area was observed. His hair color was dark brown with a silvery tint.

Skin sections from the hypo and hyperpigmented skin showed normal histology except for the mild epidermal atrophy of the hypopigmented skin. A Fontana-Masson stained section from the hyperpigmented lesion of the forearm revealed a number of variable sized melanin granules throughout the epidermis and some melanophages in the upper dermis; some of them being larger than normal (Fig. 4A). A Fontana-Masson stained section from the hypopigmented skin from the back showed a scarce melanosomes distributed segmentally in the basal layer (Fig. 4B). Dopa-stained section from the hypo and hyperpigmented lesion showed normal number of dopa-positive melanocytes in the basal layer. However, compared with a decreased dopa reaction was observed in sections from the hypopigmented lesion than those from the hyperpigmented lesion. Electron microscopy of the hyperpigmented skin showed multiple giant melanin granules within the cytoplasm of keratinocytes (Fig. 5) and melanocytes (Fig. 6). Most of these granules were fully melanized and distributed individually in the cytoplasm.

The patient was treated with ascorbic acid and antibiotics such as ceftriaxone dihydrate and aztreonam. He was discharged from the hospital after two weeks with some clinical improvement.

segmented neutrophils, 86% lymphocytes, and 2% monocytes. On a light microscopy of the peripheral blood smear, large peroxidase-positive lysosomal granules were observed in the lymphocytes and neutrophils. A bone marrow biopsy was done and these granules were also found within the bone marrow precursor cells (Fig. 1).

Clinical and laboratory findings were consistent with a diagnosis of an accelerated phase of CHS. No neurological abnormalities were found. Eye examination revealed a hypopigmented fundus because of the atrophy of the retinal pigment epithelium. Photophobia and nystagmus were absent.

He showed diffuse light to dark brown colored hyperpigmented patches on the face, neck, arms and legs, sparing the antecubital and popliteal fossae (Figs. 2 and 3). At birth and when he was

Fig. 1. Bone marrow biopsy showed peroxidase-positive lysosomal granules within the bone marrow precursor cells (PAS stain; × 100).

Fig. 2. This photographs shows hyperpigmentation on the arms and whitish discoloration on the trunk.

Fig. 3. Diffuse hyperpigmentation on the legs, sparing the popliteal fossae.
DISCUSSION

Approximately 200 cases of CHS have been reported in the literature. Many of them made no mention of the skin findings in detail because they were mostly reported by pediatricians, and some by ophthalmologists and pathologists.

According to the literature, the most common dermatologic findings of CHS are tyrosinase-positive partial oculocutaneous albinism with very light skin and light-colored hair. Pigmentation of exposed skin was noted by Higashi for the first time but was not mentioned in most other cases in the literature, except for Pierinis case. Recently, Fukai et al. stressed for the first time that the incidence of hyperpigmentation in CHS is higher in Mongoloids than in Caucasoids. Fukai et al. explained this phenomenon by the difference in the degrading capacity of the melanosome, i.e., a degrading defect in Mongoloids and nearly normal capacity in Caucasoids. In our opinion, race is
an important factor in the hyperpigmentation. Sun-exposure also affects the hyperpigmentation in CHS. Stegmaier et al. mentioned that their patients had pale skin until they were exposed to sun-light. Therefore, as in normal skin UV-irradiation induces hyperpigmentation by increased melanogenesis, in CHS patients a sun-light induces hyperpigmentation as well. However this phenomenon is probably due to a defect in degrading the melanosomes or melanosome complexes despite the increased melanogenesis induced by UV exposure. Most reports of the hyperpigmentation in CHS occur in Mongoloids and Negroids, who revealed increased melanin pigment in the sun-exposed area. In normal skin, the melanosomes in Negroids are individually dispersed inside the keratinocytes, whereas the melanosomes in Caucasoids and Mongoloids are present in groups. In addition to the cutaneous albinism on the trunk, hyperpigmentation of the sun-exposed skin such as the face, arms and legs, sparing antecubital and popliteal fossae, was evident in our case. A light microscopic study of the hyperpigmented lesion of our case revealed abundant melanin pigment in clumps of large granules dispersed throughout the epidermis and melanophages in the upper dermis. Electron microscopy of our case showed that giant fully melanized granules were dispersed individually as in Negroids.

Recognition of cutaneous pigmented changes of CHS can be crucial for the early diagnosis and treatment of this potentially fatal disease because pigmented changes were the earliest feature noticed before immunodeficiency manifested itself in most of the reported cases. However, since hyperpigmentation of sun-exposed skin areas had been observed in a few cases, some authors indicated the existence of a wide variation on the pigmented changes in CHS. It is now recognized that there may be a spectrum of pigmented abnormalities in which albinism is one extreme. Because the hypopigmentation is difficult to notice and hyperpigmentation is not so uncommon in Mongolods, the hyperpigmentation may be a characteristic initial feature of CHS. Thus, we consider that hyperpigmentation as well as hypopigmentation is one of the important cutaneous manifestations of CHS, especially in Mongoloids.

REFERENCES