# Do you know this syndrome?*

## Você conhece esta síndrome?

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**RELATO DO CASO**

Male patient, native of São Paulo, normal birth at full term, with healthy parents and first cousins. First dermatologic assessment at 3 months of age revealed silver hair color, white eyebrows and eyelashes and skin hypopigmentation, all features not shared with his parents. (Figure 1). An optical microscopy examination of the patient´s hair showed groups of pigment scattered along the length of the hair shafts, contrasting with the normal pattern of fine, diffuse pigmentation (Figure 2). Opthalmic fundus examination revealed foveal hypoplasia and albinism, while analysis of otoacoustic emissions showed delayed auditory development of bilateral retrocochlear origin. A peripheral blood smear showed the presence of giant intracytoplasmic granules in leukocytes (Figure 3). The patient was hospitalized for H1N1 virus infection and febrile neutropenia and then treated as an outpatient for impetigo and ear infections. The child, now aged 18 months, has normal psychomotor development and is being tracked by the dermatology, genetics and immunology departments while awaiting a bone marrow transplant.

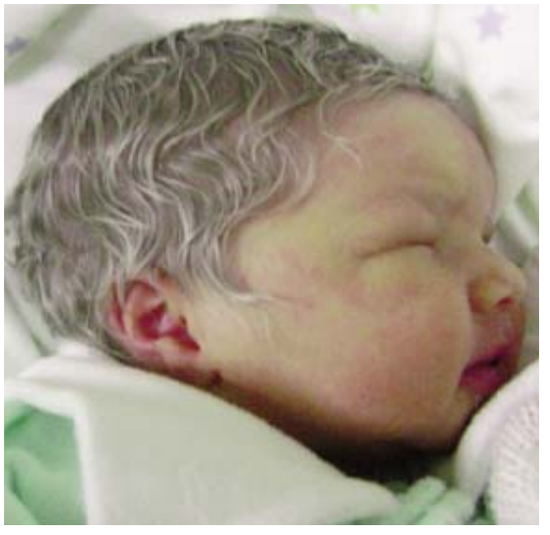

**FIGURE 1:** Silverish coloring of the hair and skin hypopigmentation

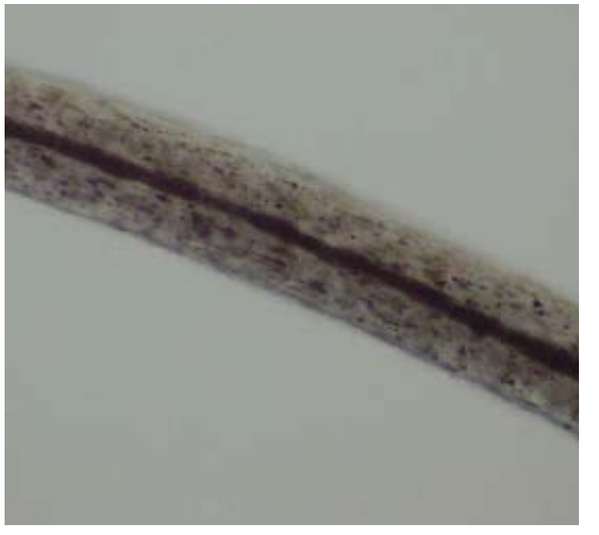

**FIGURE 2:** Pigment granules grouped together and scattered on the hair shaft

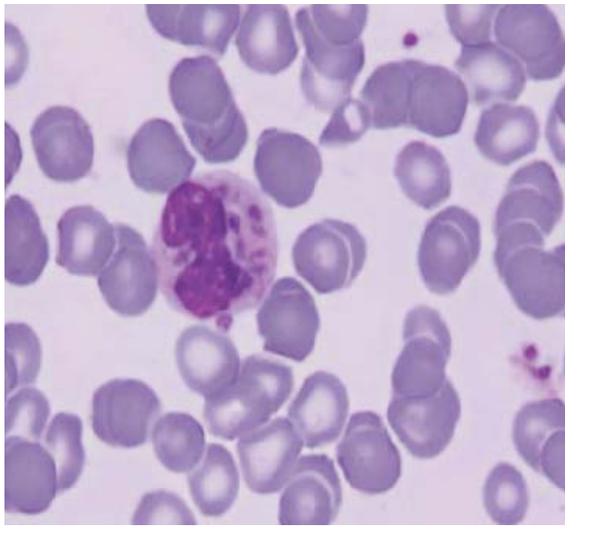

**FIGURE 3:** Peripheral blood smear showing giant intracytoplasmic granules in the leukocytes

Received on 04.11.2010
Approved by the Advisory Board and accepted for publication on 24.03.2011.
* Work undertaken at the Department of Dermatology, Escola Paulista de Medicina, Federal University of São Paulo (EPM - UNIFESP), São Paulo (SP), Brazil.
Conflict of interest: None / *Conflito de interesse: Nenhum*
Financial funding: None / *Suporte financeiro: Nenhum*

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## Você conhece esta síndrome?

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**DISCUSSION**

Chediak-Higashi syndrome (CHS) is a rare autosomal recessive disorder characterized by oculocutaneous albinism, immunodeficiency, progressive neurological disorders, bleeding predisposition and lymphoproliferative syndrome. While the primary defect of the CHS is unknown, the clinical symptoms are attributed to a vesicular trafficking defect secondary to enlarged granules in the lysosomes and melanosomes and platelet dense granules. Skin hypopigmentation is variable, and in some individuals is only noticeable when compared to other family members. The hair is silver-colored or has a metallic sheen. Giant melanosomes can be observed through microscopic examination of the skin. The discovery of groups of large pigment granules in the hair shaft has been used for prenatal diagnosis of CHS. [2] Reduced pigment may be observed in the eyes, and nystagmus, photophobia and decreased visual acuity can result. The iris can be grayish, bluish or brownish. [3] Patients develop recurrent infections, mainly in the skin and airways, and are responsive to antibiotic therapy, although more slowly than immunocompetent individuals. The immune defect is attributed to impaired cytolytic function of T and Natural Killer (NK) cells, and delayed neutrophil and monocyte chemotaxis. [4,5] Mild to moderate bleeding can occur. Bleeding can be severe at the accelerated phase when thrombocytopenia occurs in addition to platelet dysfunction. [6] Neurologic changes may occur in the central or peripheral nervous system, with progressive neurodegeneration. [7] Around 85% of patients progress to the accelerated phase which is characterized by multiple organ linfohistiocitary infiltration, non-malignant but similar to lymphoma and manifested by fever, anemia, neutropenia, thrombocytopenia, hepatosplenomegaly, lymphadenopathy, jaundice and coagulopathy. The diagnosis of CHS is confirmed (i) by finding giant peroxidase-positive cytoplasmic granules in polymorphonuclear cells, as well as in other cells such as leukocytes, platelets, melanocytes, hepatocytes, renal tubular cells, neural and thyroid tissue, or (ii) by genetic analysis, with mutation in the LYST/CHS1 gene on chromosome 1. 8 Death usually occurs in the patient´s first ten years of life from infection or bleeding, or later when the disease progresses to accelerated phase. [9] Curative treatment consists of bone marrow transplantation to correct the immune and hematologic defect, but oculocutaneous and neurological changes nevertheless persist. The main differential diagnosis is the Griscelli syndrome, a rare autosomal recessive disorder caused by mutations in the MYO5A or RAB27A genes. This syndrome manifests with partial albinism, silvery hair, variable neurological involvement and immunodeficiency, and progresses towards the accelerated phase as in CHS, but differs from CHS in view of the absence of giant intracytoplasmic granules in the leukocytes observed either in the peripheral blood smear or by genetic analysis.[10,11] ❑

**Abstract:** Chediak-Higashi syndrome is characterized by varying degrees of oculocutaneous albinism, recurrent infections, bleeding disorders and variable neurological involvement. The treatment consists of bone marrow transplantation, which corrects the immunologic and hematologic defects. Untreated patients die as the result of bacterial infections or develop "accelerated phase" lymphoproliferation. We present a case of Chediak-Higashi syndrome and discuss the clinical and laboratorial features that determine its diagnosis.
Keywords: Chediak-Higashi Syndrome; Diagnosis; Hypopigmentation; Lysosomes

**Resumo:** A síndrome de Chediak-Higashi é caracterizada por graus variados de albinismo oculocutâneo, infecções recorrentes, alterações de coagulação e envolvimento neurológico variado. O tratamento é o transplante de medula óssea, que corrige os defeitos imunológicos e hematológicos. Pacientes não tratados evoluem frequentemente a óbito por infecções bacterianas ou por desenvolverem a "fase acelerada" linfoproliferativa. Apresentamos um caso de síndrome de Chediak-Higashi e discutimos as características clínicas e laboratoriais que determinam seu diagnóstico.
Palavras-chave: Diagnóstico; Hipopigmentação; Lisossomos; Síndrome de Chediak-Higashi

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How to cite this article/*Como citar este artigo*: Fantinato GT, Cestari SCP, Afonso JPJM, Sousa LS, Enokihara MMSS. Você conhece esta síndrome? Síndrome de Chediak-Higashi. An Bras Dermatol. 2011;86(5):1029-38.