# Silvery Hair Points to Deadly Genetic Syndromes

BY BETSY BATES
*Los Angeles Bureau*

LAS VEGAS — Genetic disorders associated with silvery hair are almost uniformly fatal in children, most often as a result of accompanying immunologic or neurologic abnormalities, according to Dr. Carola Durán-McKinster.

Natural light reveals hair the color of lead that has a "peculiar" shine in children with Chédiak-Higashi syndrome, Griscelli syndrome, and Elejalde syndrome, and in the rare child whose unusual pigmentation is not associated with systemic defects, said Dr. Durán-McKinster at a dermatology seminar sponsored by Skin Disease Education Foundation.

A natural history study of children with these syndromes at the National Institute of Pediatrics of Mexico, where Dr. Durán-McKinster is head of pediatric dermatology, determined that the diseases were fatal in 8 of 10 children with Chédiak-Higashi syndrome, all 7 children with Griscelli syndrome, and 8 of 10 children with traditional Elejalde syndrome.

Four children with silvery hair who did not fit diagnostic criteria for any systemic syndrome all survived, she said.

Children with silvery hair syndromes have skin that is so hypopigmented at birth that they may resemble children with albinism.

However, after exposure to sunlight, their skin becomes deeply, persistently bronzed, explained Dr. Durán-McKinster, who serves on the dermatology faculty at Universidad Nacional Autónoma de México.

A careful examination of the hair of infants can be critical to making a diag-

## The Genetics of Silvery Hair

Dr. Durán-McKinster described the following syndromes:

▶ **Chédiak-Higasi syndrome.** In this rare, autosomal recessive disorder, giant inclusion bodies can be found in all granule-containing cells. Children are immunocompromised because of impaired phagocytosis and natural killer cell function. The genetic defect is a mutation of the LYST (lysosomal trafficking regulator) gene on chromosome 1. During an accelerated phase, lymphocytes and histiocytes can accumulate in the liver, spleen, lymph nodes, and bone marrow. High doses of methylprednisolone and splenectomy may be helpful during this phase, but allogeneic bone marrow transplantation is performed whenever possible.

▶ **Griscelli syndrome.** A mutation on the RAB27A gene of chromosome 15 causes this severe, autosomal recessive immunodeficiency syndrome. Many children develop hemophagocytic syndrome early, with frequent infectious episodes. Children may develop pancytopenia, hypertriglyceridemia, hypofibrinogenemia, and hypoproteinemia. Delayed-type cutaneous hypersensitivity and impaired natural killer function contribute to immunodeficiency. Allogeneic bone marrow transplantation is the treatment of choice.

▶ **Elejalde syndrome.** This autosomal recessive disease is caused by a mutation in the gene MYO5A on chromosome 15. Severe neurologic abnormalities are seen, including hypotonia, mental retardation, and relentlessly progressive psychomotor impairment until death. Ocular abnormalities and abnormal melanocytes and melanosomes are associated with the syndrome.

▶ **Silvery hair syndrome without associated abnormalities.** Children with a syndrome resulting from a mutation of the gene that encodes for melanophilin on chromosome 2 have silvery hair and bronzed skin following sun exposure; however they do not exhibit immunologic or neurologic complications.

nosis, often with important prognostic and treatment implications, she stressed.

"Hair can be a very, very good tool to making the diagnosis of genodermatoses," she said. "Pigment in the hair shaft is very special."

A decrease or total loss of color in the hair or skin can arise from a mutation in any of 127 genes involved in the complex pigmentation process, which involves distribution of melanin polymers produced in the melanocytes and transferred to neighboring keratinocytes.

Mutations in genes that express two critical proteins involved in this process, myosin 5A and Rab27, are key to abnormalities in two key silvery hair syndromes, Elejalde syndrome and Griscelli syndrome, respectively, said Dr. Durán-McKinster.

Dermatologists may readily recognize the very light hair characteristic of albinism or poliosis (often, a white forelock) that may be an isolated genetic feature or may be associated with deafness, as in Waardenburg's syndrome.

Unusual silvery-gray hair is much less common, and should be investigated with light microscopy and a biopsy.

Histopathologic findings include a clustering of melanin in basal melanocytes, with nearly absent pigment in adjacent keratinocytes—features especially well visualized with Fontana-Masson stain, said Dr. Durán-McKinster.

Light microscopy of the hair shaft can distinguish a pattern of melanin distribution virtually pathognomonic for Chédiak-Higashi syndrome. The "very, very small clumps" of melanin are evenly distributed, in contrast to giant and small clumps of melanin distributed in an irregular pattern in Elejalde syndrome.

Clinically, the hair of a child with Elejalde syndrome may shine more brightly, since there is more space between melanin clumps to reflect light, she explained.

A prompt and accurate diagnosis of the underlying syndrome can lead to appropriate immunologic or neurologic testing and management, which may include antibiotics and antivirals, intravenous immunoglobulin, blood transfusions, and bone marrow transplantation.

Dr. Durán-McKinster disclosed having no relevant conflicts of interest.

SDEF and SKIN & ALLERGY NEWS are wholly owned subsidiaries of Elsevier. ■