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.

Natural light reveals hair the color of lead and with 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, Dr. Carola Durán-McKinster said 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, found the diseases were fatal in 8 of 10 children with Chédiak-Higashi syndrome, all 7 children with Griscelli syndrome, and 8 of 10 with traditional Elejalde syndrome. Four children who did not fit diagnostic criteria for any systemic syndrome survived.

Children with silvery hair syndromes have skin that is so hypopigmented at birth they may resemble children with albinism, though after exposure to sunlight, their skin becomes deeply, bronzed, said Dr. Durán-McKinster, who is on the dermatology faculty at Universidad Nacional Autónoma de México. Careful examination of an infants' hair is critical to making a diagnosis, often with important prognostic and treatment implications.

A decrease or total loss of hair or skin color 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. Gene mutations that express two critical proteins involved in this process, myosin 5A and Rab27, are key to abnormalities in two silvery hair syndromes, Elejalde and Griscelli, respectively.

Dermatologists may readily recognize the 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 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.

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

A prompt and accurate diagnosis 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 this news organization are wholly owned subsidiaries of Elsevier. ■

Root Cause May Involve One of Four Diagnoses

Dr. Durán-McKinster described the following silvery hair syndromes:

► **Chédiak-Higasi.** In this rare, autosomal recessive disorder, giant inclusion bodies are found in granule-containing cells. Children are immunocompromised. Lymphocytes and histiocytes accumulate in the liver, spleen, lymph nodes, and bone marrow, causing hepatosplenomegaly, bone marrow infiltration, bleeding, and hemophagocytosis. High doses of methylprednisolone and splenectomy may help; allogeneic bone marrow transplantation is done when possible.

► **Griscelli syndrome.** Children with this severe, autosomal recessive immunodeficiency syndrome can develop hemophagocytic syndrome, with infectious episodes, and pancytopenia, hypertriglyceridemia, hypofibrinogenemia, and hypoproteinemia. Treatment of choice is allogeneic bone marrow transplantation.

► **Elejalde syndrome.** This is also an autosomal recessive disease with severe neurologic abnormalities, including hypotonia, mental retardation, and progressive psychomotor impairment until death. Ocular abnormalities and abnormal melanocytes and melanosomescan also occur.

► **Silvery hair without associated abnormalities.** Children with a syndrome resulting from a mutation of the gene that encodes for melanophilin have silvery hair and bronzed skin after sun exposure, but do not exhibit immunologic or neurologic complications.

FDA Mulls Revision of Warning Labels for Indoor Tanning Beds

BY ALICIA AULT
Associate Editor, Practice Trends

The Food and Drug Administration is considering changing the warning labels on indoor tanning beds to be shorter and more forceful, according to a report that the agency submitted to Congress and posted on its Web site in early December.

Congress required the FDA to take a closer look at the warning labels as part of the FDA Amendments Act of 2007. Legislators were concerned that the current labeling does not effectively communicate the risks of skin and eye damage and skin cancer. The FDA missed the statutorily imposed September deadline, but did fulfill Congress' request to study the issue.

Currently, every "sunlamp product" is required to carry the warning paragraph established by the FDA in 1985. It contains various statements about the potential for damage, the need to wear protective eyewear (which is bolded), and a caution that a physician should be consulted if the tanner is using medications or has a history of skin problems. It also states, "Repeated exposure may cause premature aging of the skin and skin cancer."

The agency was directed to use consumer testing to determine whether these statements have had any impact. It conducted focus group meetings in October 2007 in Baltimore and Rockville, Md., with 48 participants. Each meeting was attended by "experienced indoor tanners" and those who had never used the devices. Participants were split into three groups: high-school teenagers aged 14-17 years; adults with a college degree; and adults without a college degree.

The groups were asked to review the current warning and a new, shortened version, and they were asked questions about each. The participants also were asked to look at a photo of a tanning bed and to state where they would be most likely to notice a warning.

According to the FDA's report, most of the participants said the new, alternate warning was easier to understand and they would be more likely to pay attention to it. The newer warning had a clearer format with bullet points stating, among other things, that ultraviolet radiation causes skin cancer, injury to the eyes and skin, and skin aging. It also said to avoid overexposure, wear protective eye wear, read instructions carefully, and to consult a physician before tanning.

The participants suggested placing the warning next to the control panel or on the head side of the canopy of the tanning bed and said that it should be away from other labels so "as not to detract from the label's importance."

The FDA would need to propose a rule to require new labels. According to the report, it "is considering amending the warning label requirements for sunlamp products to include specific formatting requirements to more clearly and effectively convey the risks that these devices pose for the development of irreversible damage to the eyes and skin, including skin cancer." It has also begun consumer education efforts, primarily through its Web site. ■

Reassurance, Basic Advice Best for Some Dermatoses

BY BETSY BATES
Los Angeles Bureau

LAS VEGAS — As a pediatric dermatologist, Dr. Fred Ghali is often faced with worrisome hemangiomas, grim genetic dermatoses, or serious drug eruptions, so he relishes being able to say to a family: "No worries."

Such is the case with three common but sometimes unrecognized diagnoses presenting to his practice in Grapevine, Tex. He spoke about the following conditions at a dermatology seminar sponsored by Skin Disease Education Foundation:

► **Pseudo acne.** Most parents recognize children are maturing earlier these days, but they still panic when they see what they think is acne developing in their 5- or 6-year-old. The white papules on a young child's nose are likely "pseudo acne," small milia created when a child constantly rubs his or her nose, often in response to nasal allergies. If these miniature epidermal cysts rupture, they may take on an inflammatory appearance resembling acne. Less nose-rubbing will help, and topical comedolytics and antibiotics may be prescribed if necessary.

► **Striking striae.** These deep, dark, horizontal marks lining the back of 13- or 14-year-old boys, usually "[white] children who are extremely skinny," appear as welt-like striations. Dr. Ghali first theorized that the bands of discoloration might be caused by carrying heavy backpacks or doing wacky skateboard maneuvers. However, adolescents with this condition "have lots of vertical growth over a short period of time," he said. The striae tend to fade over time and resolve far better than striae of pregnancy. No treatment is needed.

► **Retention keratosis.** Darkly pigmented, nonpruritic regions in the flexural areas of a child's neck or underarm might point to a diagnosis of acanthosis nigricans, but in a child of normal weight, with no other signs of metabolic illness, this condition is easily dispensed with. "Just walk in with a little bit of alcohol and wipe it off. You can look like a hero," said Dr. Ghali. The condition is common in young children.

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