

## SPECIALISTFOCUS



# Genetic Hair Diseases



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## Introduction

In recent years, with advances in molecular biology and genetic research, there has been an explosion of knowledge with regards to our understanding of genetic hair diseases. There has been a paradigm shift from simply diagnosing these conditions based on history and physical examination, to the use of more sophisticated investigations, including hair shaft analysis and genetic testing.

Genetic hair diseases can be divided into those causing alopecia or hypotrichosis, hair shaft disorders and pigmentary hair alterations.

## Genetic hair diseases associated with alopecia or hair loss

In the approach to a child presenting with congenital or early onset alopecia, it is important to assess the severity, extent and distribution of the hair loss, and whether there is hair fragility or brittleness. Association with other cutaneous or extracutaneous abnormalities may point to an underlying ectodermal dysplasia or syndrome. Signs to look out for include dysmorphic facies, abnormalities in nails, teeth, and sweating, limb deformities, visual or hearing impairment, mental retardation, presence of cleft lip or palate, and thickened palms and soles. Certain syndromes associated with hair loss may also present with skin tumours, poikiloderma and photosensitivity, or recurrent infections. Some of these manifestations may develop later in life, and thus regular follow-up is important.

## Genetic hair diseases associated with hair shaft disorders

Genetic hair shaft diseases can be divided into those presenting with hair shaft fragility or those that are not brittle. With regards to obtaining hair samples for microscopic evaluation, non-brittle hairs are plucked to include the hair bulb, while brittle hairs should be cut at the base to prevent breakage from pulling at the points of interest. These hairs can be sent for analysis under the light microscopy, spectroscope or electron microscope.

Netherton Syndrome is an autosomal recessive condition due to mutations in the SPINK 5 gene on 5q32, which encodes for LEKTI, a serine protease inhibitor. This condition is associated with brittle hair, atopic dermatitis, and characteristic serpiginous scaly plaques over the body. At infancy, there may be hypernatraemia, failure to thrive and increased allergy to certain foods. Under microscopic examination, the hair shaft in Netherton Syndrome shows a characteristic “bamboo hair” appearance, or trichorrhexis invaginata.

## Genetic hair diseases associated with pigmentary hair alterations

Genetic causes of pigmentary hair alterations would include more commonly encountered conditions such as oculocutaneous albinism (OCA) and piebaldism, to more rare diseases such as Hermansky Pudlak Syndrome, Chediak-Higashi Syndrome, and Griscelli Syndrome.

OCA is caused by a heterogenous group of diseases presenting with absent or reduced production of melanin pigment. Hair is hypopigmented, the skin often tans poorly and burns easily, and the patient may develop numerous nevi, lentiginos and freckles. Risk of developing skin cancers is higher. Patients may also have eye abnormalities such as strabismus and decreased visual acuity. Different gene mutations have been mapped to various chromosomes and their gene products involved in melanin synthesis.

Chediak-Higashi Syndrome is an autosomal recessive condition with a high mortality in childhood. Patients present with silvery grey hair, increased pyogenic infections, as well as hematologic and neurologic abnormalities. There is a mutation in the LYST gene on chromosome 1, which codes for a lysosomal trafficking regulator. There is an abnormality in lysosomal trafficking, resulting in accumulation of giant granules in cells.

Griscelli Syndrome is an autosomal recessive condition presenting with silvery grey hair, immunodeficiency, hematologic and/or neurologic manifestations. It is due to mutations affecting MYO5A and/or RAB27A gene products, which are involved in vesicle trafficking. This results in melanosome accumulation in melanocytes as a result of defective melanosome transfer from melanocytes to keratinocytes.

## Conclusion

Genetic hair disorders encompass a large, diverse group of diseases. They may be associated with cutaneous and extracutaneous manifestations. A multidisciplinary approach is often needed to diagnose and manage these patients. A better understanding of these conditions, due largely to advances in molecular genetics, would pave the way for more accurate diagnoses and effective management of these diseases.

*(This article is based on a lecture given at the NHG ASC 2007)*