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Hair Shaft Abnormality in Children: a Narrative Review

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Abstract

Background

Hair is an ectodermal structure, and its formation is regulated by master genes important in embryology. Hair shaft consists of three major regions: the medulla, cortex and cuticle. Hair shaft abnormality will divide structural hair abnormalities into two broad categories - those associated with increased hair fragility and those not associated with increased hair fragility. We conducted a review study to assess hair shaft abnormality in children.

Materials and Methods

We conducted a review of all papers published on hair shaft abnormalities. A literature search was performed using PubMed, Scopus and Google Scholar on papers publish from 1990 to 2016. The search terms were: hair shaft abnormality, Hair loss, Hair fragility. All abstracts and full text English-language articles were studied.

Results

While common developmental and structural features are shared in hair follicles and hair shafts. Anomalies of the hair shaft are separated into those with and those without increased hair fragility.

Conclusion

Although hair has no vital function, it may serve as an indicator for human health. Clinical and morphological hair abnormalities can be clues to specific complex disorders. Hair shaft abnormalities can be inherited or acquired, can reflect a local problem or a systemic disease.

Key Words: Abnormality, Hair loss, Hair fragility, Hair shaft.

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1- INTRODUCTION

Hair is an ectodermal structure, and its formation is regulated by master genes important in embryology. The mammalian hair follicle develops from the epidermis (1). The major biochemical components of human hair are the intermediate filaments or keratins and the keratin-associated proteins (2). Keratins belong to the superfamily of proteins that form 8- to 10 nm filaments (IFs) in the cytoplasm of many epithelial cells. The terminology for human hair basic keratins is abbreviated internationally as "hHb" (3).

Keratin-associated proteins are divided into two groups, high-cysteine and high glycine-tyrosine-rich polypeptides, according to the amino acid composition. Cysteine-rich keratins contain high-sulfur (15–30%) proteins and ultra-high-sulfur proteins composed of 30% cysteine residues (4). A trichohyalin gene is only characterized in rabbits so far, and further work is necessary to unravel the human homologue (5).

Hair shafts are made by the hair follicle, a complex miniorgan of the skin, which constitutes the pilosebaceous unit together with its associated structures, the sebaceous gland, the apocrine gland and the arrector pili muscles. Hair follicle formation largely takes place during fetal and perinatal skin development. However, after skin wounding *de novo* hair follicle formation may also occur in adult mouse and rabbit skin (6), and can even be induced in adult human skin (7, 8).

Hair follicle development involves tightly coordinated prototypic ectodermal–mesodermal interactions (9, 10). Ectodermal hair follicle stem cells give rise to all epithelial components of the hair follicle, including the sebaceous gland and apocrine gland, while the mesoderm derived cells will develop into the follicular dermal papilla and the connective tissue sheath. Instead, neural crest-derived melanocyte progenitors give rise to the hair follicle pigmentary unit (11, 12). We conducted a review study to assess hair shaft abnormality in children.

2- MATERIALS AND METHODS

We conducted a narrative review of all papers published on hair shaft abnormalities. A literature search was performed using PubMed, Scopus and Google Scholar on papers publish from 1990 to 2016. The search terms were: "Hair shaft abnormality", "Hair loss", and "Hair fragility". All abstracts and full text English-language articles were studied.

In addition the reference lists of identified articles were scanned and related articles link on PubMed was used to find relevant articles. All studies that contained different types of hair shaft abnormalities (acquired or hereditary), with or without hair loss included.

Articles about scarring alopecia and non-scarring alopecia were excluded. Any study that met the selection criteria, regardless of the publication date, was included in an initial phase of review. Eligible articles were independently assessed for quality by two authors.

3- RESULTS AND DISCUSSION

3-1. Types of hair

While common developmental and structural features are shared in hair follicles (HFs), and hair shafts, there are a variety of hair types in a single organism. In the mouse, there are four distinct hair types making up the coat and specialized hairs such as vibrissae, and tail hair (13), which play important thermoregulatory and sensory roles. In humans, there are also different types of hair, although by structure and localization, these cannot be directly correlated to any specific hair type in mice. Human hair grows everywhere on the external body except for glabrous skin, which is present on the palms of the hands,

soles of the feet and lips. There are specialized types of hair such as the hair that is found on the eyebrows and eyelashes. The density of hair (HFs per area of skin) is determined during development and varies between individuals. The first hair type is formed in fetal life and is called lanugo hair. This type of hair is characterized as fine, non-medullated, and lightly pigmented. Vellus hair replaces lanugo hair on a human fetus in late gestation, and is characteristically short, non-medullated, and not associated to a sebaceous gland.

On the scalp, vellus hair is replaced by pigmented terminal hair before or shortly after birth. On the body, vellus hair is present throughout childhood and is replaced by terminal hair in certain areas of the body (arms, legs), during and after puberty. The pituitary gland secretes hormones that trigger the production of androgens in the ovaries and testicles, promoting replacement of vellus hairs with coarse pubic hair in the pubic region and terminal hair in the axillary region. In addition, adult males develop terminal hair on their face and chest (14). Although hair has no vital function, it may serve as an indicator for human health. Clinical and morphological hair abnormalities can be clues to specific complex disorders. The human hair form and the diameter are determined by the anatomy of the hair follicle (15, 16).

Changes in the hair shaft can occur physiologically such as in pregnancy but in general mirror a disease process. Nissimov and Elchalal (17), described for the first time that hair diameter increases during a normal physiological process. Anomalies of the hair shaft are separated into those with and those without increased hair fragility. Hair shaft abnormalities can be inherited or acquired, can reflect a local problem or a systemic disease (**Table.1**).

Table-1: Features of hair shaft diseases (5)

Classification	Acquired or congenital
	Exogenous or genetic
	Diffuse or localized
Clinical aspect	Dry hair and lusterless
Uncombable hair	Fair hair
	Breaks easily
Diagnosis History	Physical examination
	Light and scanning
	electron microscopy
	Biochemical analysis

It is important to know whether the hairs do never grow, or whether a defect in the hair cycle exists such as in the anagen phase, limiting the duration of hair growth. The fact that alopecia in a given case is caused by hair which is falling out to light traction, while still growing may be a clue for loose anagen hair syndrome. Most of the genotrichoses show a Mendelian trait of inheritance. However, some are non-Mendelian phenotypes representing lethal mutations surviving only by mosaicism. These traits may follow para dominant inheritance as emphasized by Happle and König (18). There are polygenic and monogenic hair disorders. Online Mendelian inheritance in man' gives 66 entries for hypotrichosis and 153 entries for alopecia which illustrates the heterogeneity of the problem. In the daily work, a clinical classification of alopecia which also includes hair shaft

abnormalities as proposed by Happle seems reasonable: (i) total or subtotal absence of scalp hair in early childhood, (ii) more or less diffuse hypotrichosis that may or may not deteriorate during life or even diminish, (iii) absence of hair in distinctly demarcated patches or streaks. Complex systemic diseases may lead to typical hair shaft alterations such as trichorrhexis nodosa, trichorrhexis invaginata, and trichoschisis. Hair shaft disorders include "uncombable hair" with a triangular and canaliculi diameter (19).

If a clinician determines that a hair shaft disorder is likely, further classification and diagnosis can often be done in the office with a hair mount. An algorithmic approach to making the diagnosis of a hair shaft disorder is presented. This algorithm should be used as a guide and not an absolute, as variations and overlaps in hair shaft disorders are seen. Disorders of the hair shaft are typically segregated by those that are congenital or acquired; further classification is based on the presence or absence of hair shaft fragility that can lead to breakage (**Table.1**).

A review of the most common hair shaft disorders is presented below. Although, our emphasis is on the clinical presentation and diagnosis of the hair shaft disorder, we have included a summary of the molecular defects where known. Not only is an understanding of these molecular defects critical in understanding and correlating clinical findings, it is helpful in counseling patients and potentially offering treatment options (20).

3-2. Hair Shaft Alterations and the Dysmorphologist

Hair changes may be a significant finding or even the initial presentation of a syndrome giving the clue to the diagnosis, e.g. Trichothiodystrophy (TTD). Clinically hair in these syndromes may be sparse, slow growing, fragile and brittle, Uncombable hair syndrome, dry and lusterless. The hair color may give further information on the existence of genetic disorders with hair shaft anomalies. Clinical diagnosis in dysmorphology is often like a puzzle, and numerous stones help to complete the whole picture. Hair morphology as a tool for the diagnosis of genetic diseases has been recognized by dysmorphologists (21).

In Keratitis-ichthyosis-deafness (KID) syndrome (keratosis, ichthyosis and deafness), more than 90% of patients have alopecia often associated with hair shaft alterations (22). To investigate hair shaft disorders, about 50 hairs should be visualized under light microscopy. There are exceptions such as Netherton syndrome where repeated samples of hairs may be necessary to confirm the diagnosis. The hair sampling should be performed where clinical hair abnormalities are most prominent. There are hair shaft disorders which have more impressive changes in the occipital area because of maximal trauma such as in TTD and monilethrix.

It is important to compare normal and affected hairs. In patients with hair shaft diseases, hair should be cut just above the scalp to make sure that weathering of hair which is found on the distal parts does not interfere. In case no hair shaft alteration is found, alopecia could result from a defect in the hair cycling process, and therefore in such cases hair should be plucked by a pair of forceps with rubber or plastic tubing over the tips as in loose anagen hair syndrome or in dystrophic anagen hair. Examination under light and scanning electron microscopes is an important step in the diagnosis of hair shaft disorders. A diagnostic clue for breaking hair is a brush on the distal end of the shaft. An important question is also whether cuticles are normal, sparse or even lacking.

3-3. Hair Shaft Alterations in Ectodermal Dysplasias

Ectodermal dysplasias are a large group of heritable conditions characterized by congenital defects of one or more ectodermal structures (23). Selvaag et al. (24), investigated hair samples of patients with various ectodermal dysplasias such as Hypohidrotic Ectodermal Dysplasia (HED), pachyonychia congenita, Tricho-dento-osseous (TDO) syndrome, and Trichorhinophalangeal syndrome type I (TRPS1) by scanning electron microscopy. The hairs of those patients showed twisting, longitudinal grooves, trichorrhexis nodosa and variations in hair caliber (25).

Ectrodactyly, ectodermal dysplasia and cleft palate (EEC) syndrome has initially been described in 1804. Since then the clinical spectrum has been further delineated. EEC syndrome is an autosomal dominant trait involving ectodermal and mesodermal tissue. Marked scalp dermatitis may occur early in the disease (26, 27). Scarring folliculitis in a 16-year-old boy was observed by Trüeb et al. (28).

They documented reduced hair elasticity indicating either an abnormal composition or a disordered arrangement of microfibrils within the apparently normal keratin matrix. Hair is affected in all cases. Hair is light colored, coarse and dry. Axillary and pubic hair may be sparse. An increase in hair pigmentation with age has been observed. A germline missense mutation in the p63 gene underlying EEC syndrome has been reported (29).

3-4. Acquired hair shaft disorders with increased fragility and breakage

Bubble hair occurs when bubbles form within the hair cortex due to high temperatures from styling with blow dryers or curling irons (30). This leads to hair breakage and alterations in hair texture and manageability as seen in this representative case (31). Hair dryers may cause this deformity when they overheat, especially when excess lint and hair are blocking the air intake of the hair dryer (32). In a prior study, a temperature of 175–215 °C for 5 min was sufficient to create these bubbles; however, if the heat is applied to damp hair, the threshold could be even lower (30, 33) .

3-5. Congenital hair shaft disorders without increased fragility

Uncombable hair syndrome (UHS), pili annulati, pseudo pili annulati, and woolly hair UHS presents with characteristic unruly hair that is difficult to style and has the appearance of standing away from the scalp (38). These changes are typically noted in childhood, but acquired UHS has been reported (39). UHS usually occurs without any other associations, although ocular, dental, or ectodermal defects (40) have been reported in the setting of UHS (41, 42). On light microscopic examination of mounted hair, the shaft may have a canal-like longitudinal groove along one or two facets; however, this finding is subtle and difficult to detect (37).

When hair cross-sections are examined (not an office procedure), the characteristic triangular or kidney-shaped appearance of the hair shaft is diagnostic. The irregular and changing shapes of the hair cross-section prevent adjacent hairs from lying flat or forming locks, and this accounts for the stand away appearance. To deal with this problem, the hair should be trimmed to reduce its volume, and the use of a silicone-based leave-in conditioner may aid in managing the hair.

The etiology of this hair shaft disorder is unknown. Pili annulati is a rare hair shaft disorder characterized by bright and dark bands when viewed with reflected light. This banded appearance is attractive and can affect the entire scalp, as well as the axillae, beard, and pubic areas (43, 44). There is no fragility, and the hair can grow long. The bright bands correspond to abnormal air-filled cavities within the hair cortex (45-47). On a hair mount, these

bright bands appear dark because transmitted light is not permitted to pass through. This differs from Pseudo pili annulati in which there are no air-filled cavities, and instead the banded appearance is an optical effect stemming from the partial twisting of the hair shaft in an oscillating manner (48).

Pili annulati is inherited in an autosomal dominant fashion. Initial theories that pili annulati was due to a keratin defect have not been borne out. Immunohistochemical studies of epithelial cytokeratins and linkage studies of keratin gene clusters among families with pili annulati have been found to be normal (48). Recently, the gene for pili annulati has been localized to the telomeric region of chromosome 12q (49). Candidate genes include regulatory proteins involved in the normal formation or degradation of the basement membrane zone of the lamina densa and sublamina densa layers of the hair follicle (43).

3-6. Congenital hair shaft disorders with increased fragility and breakage

Congenital Trichorrhexis nodosa (TN), trichothiodystrophy (TTD), pili torti, trichorrhexis invaginata, and monilethrix Congenital TN, may occur as the sole clinical abnormality in a sporadic case, or in families, with the abnormal fragility of the hair becoming evident shortly after birth. There are no abnormal laboratory findings in these patients. More commonly, TN is noted as an incidental finding in patients with other hair shaft disorders associated with fragility, such as pili torti, monilethrix, or TTD (**Figurers 1, 2**).

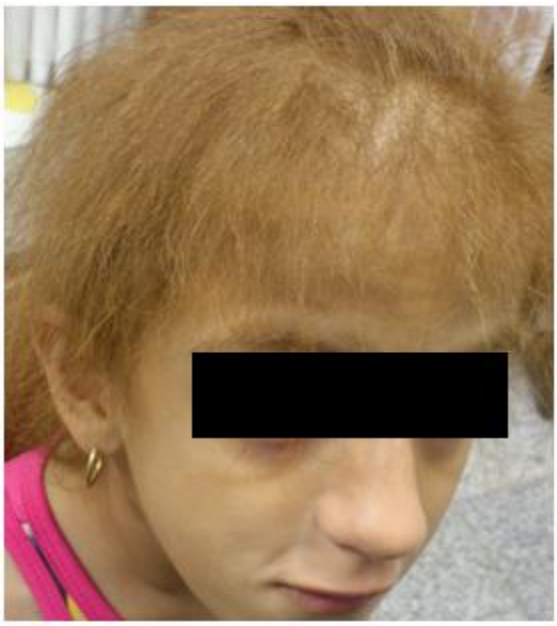

Fig.1: Pilitorti with increased fragility and breakage of hairs in Pierre Robin patient.

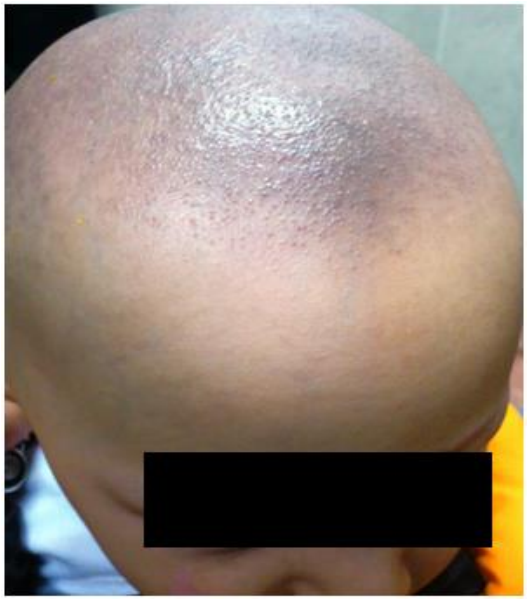

Fig.2: Monilethrix. Monilethrix is a hair shaft disorder with increased fragility and breakage of hairs.

4- DISCUSSION

Argininosuccinic aciduria is an inborn error of urea synthesis which can cause mental retardation. This rare syndrome is caused by a deficiency of the enzyme argininosuccinate lyase, and large amounts of argininosuccinic acid are found in the urine, blood, and cerebrospinal fluid. This abnormality is now tested for and diagnosed in infancy. If unrecognized, neonates present with failure to thrive that can lead to lethargy and coma (66). The hair defect was historically an important diagnostic clue to this systemic disease.

TTD is a term that describes cysteine-deficient brittle hair (67). Hair is an important clinical marker for this rare inherited disorder with a wide variety of phenotypes: these phenotypes range from brittle hair only to a neuroectodermal symptom complex with severe intellectual and developmental impairment. Diagnosis of TTD can be made by examination of the hair. The diagnosis is suspected with a hair mount and light microscopy, which shows hair shafts with an undulating, wavy outline rather than the usual straight outline (68). There may be trichoschisis fractures (69), TN-like fractures, and ribboning, which describes the flattened hair shaft folded over itself like a ribbon (70). Polarizing microscopy further supports the diagnosis, with hair shafts showing alternating bright and dark (tiger tail) bands (67), in the position of darkness. Amino acid analysis of the hair confirms the diagnosis with a cysteine content reduced to less than half of normal values. The wide variety of clinical phenotypes ranges from short, fragile hair alone to a variety of symptoms including, but not limited to, photosensitivity, ichthyosis, brittle hair, intellectual impairment, decreased fertility, and short stature. Neurological abnormalities, developmental delay, and immunodeficiency, may also be present.

TTD is an autosomal recessive disorder, and mutations in three different genes have been implicated in its pathogenesis. These genes, xeroderma pigmentosum group D (XPD), xeroderma pigmentosum type B (XPB), and L-tartrate dehydratase (ttdA), are components of the transcription factor II H (Human), a multiprotein complex that is involved in the nucleotide excision repair pathway (69). Mutations in these

genes are associated not only with TTD but also with the rare genetic diseases Xeroderma pigmentosum (XP), and Cockayne syndrome. Pili torti is characterized by hair that does not grow long and is easily broken; the hair often has a "spangled" appearance due to the unequal reflection of light from the twisted surface. Patchy hair breakage and coarse stubble are typically seen in the occiput and temporal areas due to friction. Pili torti can also involve the eyebrows and eyelashes. A diagnosis is made by light microscopic observation of flattened hair twisted at 180 along its axis and occurring in groups of 3–10. Sometimes this twisting can be difficult to visualize with a hair mount due to the flattening of the hair; thus, if the diagnosis is suspected, the hair may be viewed by light microscopy without mounting media.

Although pili torti hair may be seen in isolation, it is commonly associated with other congenital defects and therefore, if identified, further evaluation for possible neurological and ectodermal disorders is an important part of the clinical evaluation (71). The twisting of the hair is likely due to irregularities in the inner root sheath, which may induce an uneven molding of the hair shaft (72). New research suggests that these alterations may occur in the face of mitochondrial dysfunction, and may be influenced by the presence of reactive oxygen species (73).

5- CONCLUSION

Although, hair has no vital function, it may serve as an indicator for human health. Clinical and morphological hair abnormalities can be clues to specific complex disorders. Changes in the hair shaft can occur physiologically such as in pregnancy but in general mirror a disease process. Anomalies of the hair shaft are separated into those with and those without increased hair fragility. Hair shaft abnormalities can be inherited or acquired, can reflect a local problem or a systemic disease.

6- CONFLICT OF INTEREST: None.

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