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THE HAIR IN CHILDHOOD AND OLD AGE

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Summary

More than 20 syndromes, most congenital, have hypertrichosis as a feature. An excessive growth of non-androgen-dependent hair has been reported in association with many acquired diseases and medications, some of which, as cyclosporine, can be administered also in children. Even though primary hypertrichosis is benign in most cases, it may result in cosmetic disfigurement and psychosocial trauma; a pediatric assessment is necessary to rule out associated diseases. Lanugo hair can occur in otherwise healthy individuals but can be associated with polymyositis and neoplasms. Hirsutism can be idiopathic, but often can be associated with an adrenal or ovarian cause. Thns all women with hirsutism require careful evaluation. More, growing evidence has linked hyperandrogenism to increased risk of cardiovascular disease, genital tract neoplasms, and non-insulin-dependent diabetes mellitus. An application from the study of hairs comes from oligoelements. A recent study investigating the zinc status of eighty newborn babies with neural tube defects and their mothers compared with controls found a positive association between this defects and decreased hair zinc levels. As far it concerns the color of hairs our group has demonstrated that heterochromia of the scalp hair can be a sign of pigmentary mosaicism even withont underlying malformations. The present elucidation of pathogenesis of androgenetic alopecia has lead to second generation steroidal 5α reductase inhibitors, such as Gl-198745 (a combined type 1 and type 2, 5α reductase blocker), W09704002, Turosteride, Mk-963, MK-434, Episteride, and MK-386. A variety of non-steroidal inhibitors such as zinc and saw palmetto are also under investigation . The possibility of gene therapy for androgenetic alopecia has been advanced in animal by the development of a cream capable to deliver DNA to hair follicles. Finally, the study of the stem cells of the hair follicle will give us new possibilities of treatment.

Riassunto

L'ipertricosi può presentarsi isolata o essere un sintomo di oltre 20 sindromi, per lo più congenite. Inoltre l'ipertricosi può associarsi a malattie acquisite ed anche a vari farmaci, tra cui la ciclosporina. Vashi e coll. hanno esaminato 11 bambini (7F, 4M) con ipertricosi idiopatica di cui quattro con la forma generalizzata e gli altri sette con la forma localizzata. Mentre nei primi la forma era congenita, negli altri il fenomeno si era manifestato dalla nascita fino al quarto anno di vita. Una bambina con ipertricosi diffusa aveva anche una iperplasia gengivale. È interessante ricordare che l'ipertricosi lanuginosa può osservarsi in individui altrimenti normali ma può anche associarsi a polimiosite o

a neoplasie sottostanti (carcinomi del basso intestino nelle donne, carcinomi polmonari negli uomini). Per quanto riguarda l'irsutismo, oltre alle ovvie indagini endocrinologiche, bisogna prestare attenzione ad un maggiore rischio di malattie cardiovascolari, tumori dell'apparato genitale e diabete mellito non-insulino dipendente. Un'interessante novità viene dallo studio degli oligoelementi negli annessi cutanei. Dato che è noto che un deficit di zinco può provocare negli animali difetti della chiusura del tubo neurale, 80 bambini con questo problema ed 80 controlli sono stati esaminati con la spettrofotometria ad assorbimento atomico. I livelli di zinco del capello, ma non quelli serici, dei bambini malati erano significativamente più bassi die controlli suggerendo che una supplementazione di zinco potrebbe ridurre questo problema. Nel campo del trattamento dellalopecia androgenetica si stanno sviluppando degli inibitori della 5α reduttasi di seconda generazione come il Gl-198745 (un inibitore combinato di tipo 1 e tipo 2), il W09704002, la turosteride, il Mk-963, MK-434, l'episteride, ed il MK-386.

INTRODUCTION

This paper will not focus in depth the problems oh hair diseases related with genodermatoses. These abnormalities are numerous and varied but such diseases are rare and the patients are generally cared in special centers. In this article the other causes of deficit or abundance of hairs are discussed with special emphasis on new clinical observations concerning the association of hair abnormalities with underlying diseases or with drug administration. The role of zinc as a possible indicator (when deficient) of neural tube defects and as non-steroidal inhibitor of 5α reductase, is also discussed.

CLINICAL DISCUSSION

The other causes of alopecia [1] or hypertrichosis [2] are listed in Table 1a, 1b and in Table 2a,

Table Ia
*Diffuse Alopecia **

Drug induced hair loss
Telogen Effluvium
Telogen gravidarum
Chronic Telogen Effluvium
Early androgenetic alopecia
Diffuse alopecia areata
Radiotherapy
Iron deficiency
Starvation/Malabsorption/ Crash diet
Hypothyroidism and hyperthyroidism
Chronic renal failure and hepatic failure
Syphilis
Acute lupus erythematosus
Advanced malignancy

2b. Hypertrichosis, that is an excessive growth of non-androgen-dependent hair, may be localized or generalized, congenital or acquired. More than 20 syndromes, most congenital, have hypertrichosis as a feature. Not taking into account large congenital melanocytic nevi that may be hypertrichotic and at increasing risk for developing a malignant melanoma, hypertrichosis has been reported in association with many acquired diseases (Table 1b) and numerous medications

Table Ib
*Diffuse Hypertrichosis ***

Multiple Sclerosis
Schizophrenia,
Head Injury
Encephalitis
Starvation
Anorexia Nervosa
Porphyrias
Cushing's Syndrome
Dermatomyositis
Hypothyroidism
Hyperthyroidism
POEMS Syndrome

Table 2a
*Drug induced alopecia**

Telogen Effluvium
Heparin
Warfarin
Propranalol/Metoprblol
Captopril/Enalopril
Allopurinol
Boric acid
Phenytoin
Glibenclamide
Amphetamines
Levadopa
Bromocryptine
Methysergide
Interferon
Albendazole / Mebendazole
Cimetidine
Colchicine (low dose)
Sulphasalazine
Penicillamine
Gold
Anti thyroid action
Carbimazole
Propylthiouracil
Amiodorone
Lithium
Hypolipidaemic agents
Clofibrate
Triparanol
Pro-androgen action
Oral contraceptive pill
Danazol
Testosterone
Anabolic Steroids

(Table 2b) some of which, as cyclosporine, can be administered also in children.

Table 2b

Drug induced hypertrichosis **

Minoxidil
Cyclosporine
Phenytoin
Amiodarone
Psoralens
Tamoxifen
Tiopronin
Diazoxide
Corticosteroids
Zidovudine

** *adapted from: Sperling LC (2001).*
NB: Almost all chemotherapy agents can produce generalised hair shedding.
• *from Sinclair RD, Dawber RP (2001)*

Vashi et al. [3] have reviewed generalized and localized symmetrical hypertrichosis in children in a case series of 11 prepubertal male and female (7F, 4M) patients who had idiopathic hypertrichosis. While four patients showed the generalized form the other 7 had the localized one. All patients with generalized form manifested the condition at birth while in the other group the age of onset ranged from birth to 4 years. One girl with generalized hypertrichosis had gingival hyperplasia and the girl with faun tail deformity had bony diastematomyelia with spina bifida occulta. Primary hypertrichosis, although rare in children are benign in most cases, but may result in cosmetic disfigurement and psychosocial trauma for patients and families. A dermatological and pediatric assessment is necessary in all cases to rule out associated diseases.

It should be remembered that lanugo hair (that is the fine, thin, lightly pigmented hair that covers the human fetus that is normally shed before birth) as hypertrichosis lanuginosa can occur in otherwise healthy individuals but can also present associated with polymyositis and as a rare paraneoplastic condition (colorectal cancer in women and lung cancer in men). Hirsutism (the excessive growth of androgen-dependent hair in a woman) can be idiopathic, but often can be associated with an adrenal or ovarian cause. Thus all women with abnormal menstrual cycles or with severe or sudden-onset hirsutism require careful evaluation. More, growing evidence has linked hyperandrogenism to increased risk of cardiovascular disease, genital tract neoplasia, and non-insulin-dependent diabetes mellitus.

An interesting application from the study of hairs comes from the investigation on oligoelements. As far it concerns the problem of neural tube defects it is known that folic acid supplementation has reduced the incidence of this event. Since it is known that zinc deficiency can provoke this defect in animals, a recent study [4] has investigated the zinc status of eighty newborn babies with neural tube defects and their mothers compared with eighty apparently normal newborns and their mothers. Serum and scalp hair zinc levels were analyzed by atomic absorption spectrophotometry. The hair zinc levels, but not the serum levels, of the affected babies and their mothers were significantly lower ($P < 0.001$) than the controls. Thus this study has found association between neural tube defects and decreased hair zinc levels, suggesting to investigate whether zinc supplementation would reduce the overall incidence of this defect.

As far it concerns the color of hairs, the recent paper of our group [5] has demonstrated that heterochromia of the scalp hair can be a sign of pigmentary mosaicism even without underlying recognizable malformations.

The present development in tbe treatment of some forms of alopecia is due to the elucidation of pathogenesis of androgenetic alopecia, especially with regard to the role of 5α reductase. After the first specific antagonist drugs, second generation steroidal 5α reductase inhibitors, such as GI-198745 (a combined type 1 and type 2, 5α reductase blocker), W09704002, Turosteride,

Mk-963, MK-434, Episteride, and MK-386 have been developed and are undergoing further investigation as are a variety of non-steroidal inhibitors such as zinc and saw palmetto [1]. The possibility of gene therapy for androgenetic alopecia has been advanced in animal (mice) by the development of a topical cream containing liposomes capable to deliver entrapped DNA to hair follicles.

CONCLUSIONS

The field of hair disorders in childhood and old age is presently very interesting. From one side, in children, the fine analysis of the hair can establish a diagnosis which would be otherwise delayed or misdiagnosed (e.g. trichorrexis invaginata in Netherton's syndrome) from the other side, in elderly people, hair changes can be an useful marker of an underlying disorders that can be sometimes fatal if untreated. The study of the stem cells of the hair follicle will give us new possibilities of treatment in the future both for genetic and acquired disorders.

References

1) **Sinclair RD, Dawber RP (2001).** Androgenetic alopecia in men and women. *Clinics in Dermatology.* **19:** 167-178.
2) **Sperling LC (2001).** Hair and systemic disease. *Dermatologic Clinics.* **19:** 711-726.
3) **Vashi RA, Mancini AJ, Paller AS (2001).** Primary generalized and localized hypertrichosis in children. *Arch Dermatol* **137:** 877-84.
4) **Srinivas M, Gupta DK, Rathi SS et al (2001).** Association between lower hair zinc levels and neural tube defects. *Indian J Pediatr* **68:** 519-22.
5) **Restano L, Barbareschi M, Cambiaghi S, Gelmetti C (2001).** Pigmentary mosaicism presenting with heterochromia of the scalp hair. *J Am Acad Dermatol* **45:** 136-9

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