ALOPECIA AREATA AND HYPERTRICHOSIS: A CASE REPORT

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Key words: Alopecia areata, hypertrichosis, human hair follicle

Parole chiave: Alopecia areata, ipertricosi, follicolo pilifero

Abstract

Hypertrichosis is an abnormal hair growth for age, sex, race or for a particular body area of an individual. For this special clinical condition a differential diagnosis is proposed with hirsutism: male-pattern hair growth in a female or child. It typically involves the upper lip, chin, cheeks, breast areola, linea alba and the top of the pubic triangle and it is, usually, due to androgen excess. The most common cause in females is the polycystic ovary syndrome but other causes, in both sexes, include hyperandrogenic insulin resistance acanthosis nigricans syndrome, androgen-secreting tumors, and androgen drug intake. When in women it is accompanied to other masculinization signs it is usually defined virilization. This clinical condition is associated with a more complete voice change, changes in libido, and clitoromegaly. Two different mechanisms are proposed to explain hypertrichosis's development: conversion of vellus to terminal hairs and changes in the hair-growth cycle. Hair cycle is characterized by the switch from a period of very rapid growth, pigmentation, and hair-shaft production (anagen, the active-growth phase, with classification ranging from stages I to VI) to a short, apoptosis-driven phase of organ involution (catagen). After catagen, the hair follicle enters a period of relative quiescence (telogen) before it reenters anagen. This regenerative cycle is made possible by an abundance of keratinocyte and melanocyte stem cells located for the most part in the so-called bulge area. Alopecia areata is a...
multifactorial autoimmune disease, which involves several genes, characterized by well-circumscribed patches of hair loss especially from the scalp and typically it presents as one or more well demarcated isolated, round smooth areas of complete hair loss patches of no scarring alopecia on skin of overtly normal appearance without clinical signs of skin inflammation, in which the scalp feels slightly depressed because of loss of the supportive effect of the hair shafts. The pattern of scalp involvement may be patchy, mosaic, confluent or diffuse. Different forms of AA may evolve into one another during a single episode or with recurrent episodes. The pathobiology of this chronic, relapsing hair-loss disorder is not fully understood but studies shown that hair follicle melanocyte- and/or anagen-associated autoantigens play a key role in AA pathogenesis which is based, also, on immune privilege collapse; thus the available therapies are disappointing. In contrast to scarring hair loss induced by other chronic, inflammatory skin diseases, lesional hair follicles in AA, generally, do not scar and can regrow. Mild disease has a high rate of spontaneous remission, and even cases of severe AA universalis can spontaneously experience complete hair regrowth. The impact of this skin disease on the lives of patient tends to be underestimated or even dismissed as simply a “cosmetic problem.” Alopecia areata exemplifies such a condition, owing to its substantial disease burden and its often devastating effects on the patient’s quality of life and self-esteem.

Abstract

L’ ipertricosi è una condizione caratterizzata da crescita di peli anomala per età, sesso, razza e localizzazione a livello dell’ intera area corporea. È necessario porre questa particolare condizione clinica in diagnosi differenziale con l’ irsutismo in cui si assiste a crescita di peli a disposizione caratteristica per il sesso maschile nelle donne e nei bambini. L’ irsutismo coinvolge aree del corpo caratteristiche come la cute sovrastante il labbro superiore, l’ areola mammaria, la linea alba e la parte più alta del triangolo pubico e nella maggior parte dei casi esso è dovuto ad un eccesso di androgeni circolanti. Tale reperto clinico-laboratoristico nel sesso femminile è più frequentemente determinata dalla sindrome dell’ ovale policistico (PCOS) o sindrome di Stein-Leventhal; in entrambi i sessi può venirsì a determinare in seguito a tumori androgeno secretanti, aumentata assunzione farmacologica di androgeni e la presenza di una forma sindromica caratterizzata da ipeandrogenismo, insulinorresistenza e acanthosis nigricans. Talvolta nel sesso femminile l’ ipertricosi si associa ad altri segni di mascolinizzazione come il cambio della tonalità vocale, variazioni nella libido e clitoridomegalia; tale quadro clinico viene definito virilizzazione. Per spiegare lo sviluppo di ipertricosi sono state formulate due ipotesi: la conversione dei peli vellus in peli terminali e cambiamenti nel ciclo di crescita del capello. Esso è caratterizzato dal cambiamento cicloico da un periodo di crescita rapida, pigmentazione e produzione del fusto (fase anagen di crescita attiva classificata in 6 diversi stadi) e da un periodo breve, di involuzione del capello causato da meccanismi guidati dall’ apoptosi (catagen). Dopo la fase catagen il follicolo pilifero entra in un periodo di relativa quiescenza (telogen) prima di rientrare in anagen. Questo ciclo rigenerativo è possibile grazie alla presenza di numerose cellule staminali presenti per la maggior parte nell’ area del follicolo pilifero chiamata bulge area. L’ alopecia areata è una patologia autoimmune di tipo multifattoriale che coinvolge numerosi geni ed è caratterizzata da chiazze ben circoscritte caratterizzate da perdita di capelli a livello del cuoio capelluto che generalmente si presentano come una o più chiazze ben demarcate, generalmente circolari e lisce; la cute sottostante è normale e non presenta segni di inflamazione. Essa appartiene alle alopecie non cicatriziali e si può manifestare livello del cuoio capelluto come forma in chiazze o reticolare di tipo confluenre o diffuso. Forme diverse di AA possono evolvere l’ una nell’ altra e possono essere caratterizzate da un episodio singolo o dalla loro ricorrenza. L’ ezioiopatogenesi di questa malattia cronica non è stata completamente compresa ma numerosi studi hanno mostrato come la cellula melanocitaria in anagen e/o gli autoantigeni espresso durante la fase anagen possono avere un ruolo chiave nella patogenesi basata, pertanto, sul collasso del privilegio immunologico. Le attuali terapie disponibili sono diverse e al momento non sono disponibili terapie standardizzate. È importante sottolineare che, a differenza di altre patologie croniche di tipo cicatriziale, i follicoli dell’ alopecia areata possiedono ancora cellule staminali e quindi è possibile una ricrescita del capello. La malattia in forma lieve ha una remissione spontanea e anche casi di AA più gravi possono guaire spontaneamente. L’ impatto di tale patologia nella vita dei paziente tende ad essere sottostimata o ad essere minimizzata a puro problema estetico-cosmetologico, tuttavia non bisogna sottovalutare i gravi aspetti psicologici che tale malattia può avere nella vita del paziente.
Introduction

It is important to understand normal hair growth and the normal immunobiology of the hair follicle in order to appreciate the changes that occur in alopecia areata and hypertrichosis thus their clinical presentation and diagnosis. During the normal cycle of hair growth human hair follicles are continuously transformed in a cycle of organ construction and deconstruction. During anagen, which for scalp hair lasts 1 to 8 years, a pigmented hair shaft is generated. This phase of active growth consists of six stages (I through VI). Anagen is followed by catagen, a rapid, apoptosis-driven organ-involution phase that lasts several weeks, during which melanogenesis is switched off and the hair shaft is transformed into a “club hair.” The hair follicle then enters telogen, a phase of relative quiescence that varies in duration (e.g., lasting several months on the scalp), and then returns to anagen.

After hair’s cycle description it is necessary to define the terms used to describe hair. Lanugo hairs are long, unmedullated hairs grown in utero and shed during the end of pregnancy and the first several months after birth. With the exception of the hair on the scalp and eyebrows, most postnatal body hair is of the vellus type. Vellus or intermediate hairs are short, nonpigmented hairs produced by follicles that penetrate only into the papillary dermis; they are variably medullated. Vellus hair shafts are no wider than the inner root sheath of the follicle that produces them. Terminal hairs are produced by follicles that penetrate to the reticular dermis; they are medullated and wider than the inner root sheath of the follicle that produces them. Longer hair is created by increased time spent in the anagen phase, whereas greater hair density can be caused by a decrease in hair shedding as a result of a decrease in the percentage of follicles in telogen phase. Areas of the body with longer, denser hair, such as the scalp, have an increased percentage of follicles in anagen stage. Like the vellus-to-terminal switch, control and alteration of the hair cycle is just beginning to be understood. Follicles in each body area have their own intrinsic growth pattern, which may be altered by systemic influences, such as androgens, thyroid hormone, and growth hormone.

Case report

We observed a 33 years old afghan man, affected by patchy alopecia areata of the beard, eyebrows, hair and trunk from about three years (Fig. 1-4). He reported onset of alopecia after a psychoemotional stressful events with patchy’s outset in the beard.

Figure 1 - AA in the beard region
Figure 2 - Alopecia Areata (reticular form)

Figure 3 - AA (shoulders)
Concerning his past medical history, we excluded history of Alopecia Areata (AA), presence of autoimmune diseases like autoimmune thyroiditis, celiac disease, vitiligo, systemic lupus erythematosus (SLE), type I diabetes or atopy. The patient referred insomnia, night blindness and stranguria. Clinical family history was unremarkable.

Clinical examination revealed patchy hair loss in the anterior and posterior part of trunk and by reticular form in the scalp with a progressive ingrownscent clinical course, without nail involvement. This clinical picture was associated with itching. At the same time a diffuse hypertrichosis with black, curly hair diffuse was present in the whole body. Through an accurate anamnestic exam we excluded pharmacological causes and congenital forms of pathology due to dominant, recessive or X-linked autosomal transmission.

Patient was subjected to laboratory examinations as hepatic, thyroid and renal function, glycemic levels, iron levels, Ab anti HCV and HBV, dehydroepiandrosterone sulfate (DHEAS), vitamin D3 and parathyroid hormone (PTH). They revealed low levels of vitamin D3 (13.5 ng/ml) and high levels of red cells (6.1 M/uL), Hb (19.4 g/dl), Ht (58 %), and eosinophils (5.6% and 0.56K/ul). In order to differentiate hypertrichosis's pathogenesis and, overall, exclude a “de novo” mutation or a mild form of Cornelia de Lange syndrome, patient was subjected to oculistic, cardiological and urological clinical examinations that excluded any alterations. There were no abnormalities in the digital orthopanoramic, that revealed only carious lesions. A genetic counseling excluded Cornelia de Lange syndrome. Pull test’s positivity and videodermoscopy with Trichoscan Dermoscope Fotofinder® revealed the presence of exclamation hairs and cadaver hairs. Anamnestic data, clinical features and laboratory tests lead us to the diagnosis of AA and hypertrichosis. We subjected the patient to HLA genetic test to have a better clinical management of AA, which revealed DQB1*06. DQB1*06 is a protective variant mainly in cases with greater hair loss, although the diagnostic significance of the HLA test for AA was not absolute (1). The patient started systemic therapy using triamcinolone acetonide (40 mg/ml twice a month for three months) and topical therapy with clobetasol propionate. We also treated the patient with oral cholecalciferol (10000 IU in drops formulation five drops every day for three months), associated with cetirizine 10 mg for every day for three months.

Results
Our case is a first case of patchy AA and hypertrichosis generalized in literature. In this patient it is possible to conclude that he is affected by idiopathic hypertrichosis and alopecia areata through clinical and instrumental evaluation that
excludes causes of congenital or acquired generalized hypertrichosis. In this case report it is interesting to note that generalized hypertrichosis is the sole feature in universal hypertrichosis due to idiopathic causes and that Alopecia Areata is not associated with other autoimmune systemic pathologies. In our case two unusual clinical situations occur simultaneously and it is completely new compared to the previous literature.

Discussion and Conclusions
Hypertrichosis is defined as an increase in body hair beyond the normal variation for a patient’s reference group. It is characterized by an increased hair growth with a transformation of vellus hairs into terminal thicker and darker hairs (2). A differential diagnosis is proposed with hirsutism: male-pattern hair growth in a female or child (3). Olsen (4) classified hypertrichotic diseases into congenital and acquired conditions with generalized versus localized hair growth. Alopecia areata (AA) commonly affects individuals aged 4–5 years and 15–40 years and rarely occurs in patients older than 60 years and the incidence rate is 1–2%. The phenotypic manifestations have a discontinuous clinical course with remission, exacerbation or progression of the disease. Hair loss may affect small patches of the scalp or can involve the entire scalp as in ‘alopecia totalis’ or, more rarely, may extend over the body as in ‘alopecia universalis’. Variants of this disorder include ophiasis, reticular patchy alopecia and alopecia areata incognita. Videodermatoscopic signs are characteristic like: exclamation-mark hairs, cadaver hairs (Fig. 5), grey or yellow spots (5).

Figure 5 - Exclamation-mark hairs and cadaver hairs

Clinical signs are nail pitting, growth of white hair in formerly alopecic lesions and association with lots of autoimmune pathologies (lupus erythematosus in 0.6% of patients, vitiligo in 4%, and autoimmune thyroid disease in 8 to 28%)(6, 7). These evidences show the importance of a genetic component further supported by the epidemiological indication that AA shows a familial aggregation, with 10-47% of patients having a positive family history, and the recurrence risk is greater among close relatives (8). In acute alopecia areata, histologic examination reveals a characteristic “beeswarm pattern” of dense, perifollicular lymphocytic infiltrates around anagen hair follicles; in patients with chronic disease, this pattern may be absent (9). As confirmed by histopathology it is probably due to a collapse of immunological privilege (IP): a temporary and rhythmically reoccurring phenomenon which is a unique key feature of hair follicle. Decreased levels of pro-inflammatory molecules or molecular mechanisms and increased anti-inflammatory mechanisms with low expression of MHC I, absence of MHC II molecules, rare intraepithelial T cells, absence of limphatics, expression of Fas
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ligand (FasL, CD95L) to delete autoreactive Fas-expressing T cells, downmodulation or absence of appropriate co-
stimulatory signals, presence of a physical barrier and high local generation of potent immunosuppressant are the most
important mechanisms detected in the area of IP in normal condition. Loss of these immunosuppressive factors may
result from certain stimuli (such as psychoemotional stress leading to neurogenic skin inflammation, trauma or infection)
which promote the migration of IFNγ-producing NK or/and activated T cells into the anagen hair follicle. IFNγ- or
substance P-induce MHC class I expression in the anagen hair bulb (10, 11, 12) facilitating the presentation of follicular
auto antigens to CD8+ T cells that recognize and respond to auto antigens presented by the anagen hair follicle
epithelium with appropriate costimulatory signals and CD4+ T cell help. This will subsequently lead to the development
of an autoimmune response against the anagen hair bulb, ultimately leading to clinically manifest alopecia areata. Thus
is possible to conclude that AA has a multifactorial aetiology and several genes and environmental factors come together
with a different weight in triggering the pathology. It is possible to conclude that this clinical case report is paradoxical
and unusual because of the simultaneous presence of hypertrichosis and alopecia areata. Generalized hypertrichosis of
terminal hair can occur as sole feature in universal hypertrichosis with an increase in thickness and density of hair in
normally hairy areas like thorax, back, and limbs due to idiopathic causes; contemporarily, the presence of patchy
alopecia AA of scalp and trunk starting from the beard region and the presence of a protective form in HLA genetic test
for AA’s diagnose directed us to conclude that this form is probably due to a stressful event which induce a collapse of
IP in a patient with idiopathic hypertrichosis. This is a first case of patchy AA and hypertrichosis generalized in literature
and it is interesting to note that two unusual clinical situations occur simultaneously. Only a previous work reported the
combination of AA universalis and hypertrichosis localized in a finger in a patient suffering of complex regional pain
syndrome (CRPS). In this case hypertrichosis is probably due to the acute inflammatory phase of CRPS (14),
Furthermore inflammation in CRPS includes classic inflammatory mechanisms through action of immune cells
(lymphocytes and mast cells), which, after special tissue trauma, secrete proinflammatory cytokines including
interleukin-1β, interleukin -2, interleukin -6, and tumor necrosis factor (TNF)-α. Also a neurogenic inflammation is
involved; it is mediated by release of proinflammatory cytokines and neuropeptides such as substance P, calcitonin
gene-related peptide, and bradykinin (which also initiates cytokine release) directly from nociceptive fibers in response
to various triggers, probably including psychoemotional stress too (15). A similar hypothesis is implicated in AA and
could explain the combination of AA and CRPS. Our clinical case report is completely new compared to the previous
literature. Generalized hypertrichosis and patchy AA are, in fact, the only clinical features without any other associated
sistemic diseases.
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References

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