

A Possible Continuum from Reversible to Irreversible forms of Alopecia

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Case Report

Primary cicatricial alopecias are a diagnostically challenging group of disorders characterized by a primitive follicular inflammation resulting in destruction of hair follicles and irreversible hair loss. On the contrary, non-cicatricial alopecias are more common non scarring hair loss such as male and female pattern hair loss, Alopecia Areata, telogen effluvium as well as other less common conditions. Nevertheless, clinical practice shows that not only the two clinical forms are so well defined but also that a non scarring alopecia remains so over time. On the other hand some Authors reported the association of Alopecia Areata with disorders such as Lupus Erythematosus, Lichen Planus [1].

The purpose of our report is to demonstrate the possibility of the progression of a non scarring alopecia into a scarring one through the description of some clinical cases we observed.

Case 1

A 43 years-old man who presented six years history of relapsing episodes of small patches of AA localized on the same sites: right eyebrow, beard, right thigh. Apart from a personal history of a late puberty treated with steroid cause of a precocious Androgenetic Alopecia, he was healthy. An uncle was affected by AA. Eight months before our observation the relapsing areas became more persistent and new areas of hair loss appeared on the scalp. Those areas seemed to be more localized in the occipital zone, strictly in correspondence with the belt of the hat that the patient used to wear. A nail pitting could be observed. A visible loss of follicular ostia and a perifollicular erythema with hyperkeratosis was detected. It was not so surprising extracting anagen hair with gelatinous sheath from the active border of the areas in support of the clinical diagnosis of Lichen Plano-Pilaris, confirmed by histological examination (Figure 1).

Case 2

A 55 years-old female developed an Alopecia Universalis associated with Vitiligo and an allergic contact Dermatitis due to nichel sulphate at the age of 25. She had been treated with topical immunotherapy (DNCB) but each application caused a strong local reaction even with systemic symptoms such as high fever and arthralgias. The therapy was stopped after 4 months, the patient refused any other therapy and in the following years the Alopecia Areata evolved in cicatricial Alopecia (Figure 2).

Case 3

A 32 years-old man was affected by Alopecia Universalis from the age of 25. In partial resolution with topical immunotherapy, after 4 months he developed an eruption of multiple discoid Lupus Erythematosus lesions (DLE) on his back also. Despite discontinuation of treatment the lesions persisted (Figure 3).

Case 4

A 66 years-old woman, had been seen 19 years prior to our observation due to Ofiasic AA, involving also the frontal portion of the scalp. She had been treated with minoxidil and dithranol solving the

issue. No familiar history for AA and Atopy. Chronic thyroiditis. For one year, the patient noted the retreat of the frontal hairline in the area previously affected by Ofiasic Alopecia Areata, and the thinning of the eyebrows. Histological examination confirmed the clinical diagnosis of Frontal Fibrosing Alopecia (FFA) (Figure 4).

Case 5

A 61 years-old woman, suffered from Alopecia Areata in childhood. At the age of 20, she had a reactivation of the Alopecia in an ophiasis form. The disease took a chronic course over the years despite the various therapies practised.

At the time of our observation, the Ophiasic Alopecia persisted, associated with the thinning of the eyebrows and the frontal area of the scalp. Histological examination confirmed the clinical diagnosis of FFA (Figure 5).

Case 6

A 48 years-old woman, suffering from Alopecia Androgenetica (AGA) from the age of 26, developed a front setback at the age of 37, together with loss of eyebrows and Fibrosing Alopecia in a Pattern Distribution (FAPD) in the previous baldness area. The patient reports no itching (Figure 6).



Figure 1: 43 y.o. man who presented relapsing episodes of small patches of Alopecia Areata. Eight months before our observation, the alopecic areas became more persistent and new areas of hair loss appeared on the scalp. A visible loss of follicular ostia and a perifollicular erythema with hyperkeratosis and hyperchromia were detected. Anagen hair with gelatinous sheath could be extracted from the active border of the areas supporting the clinical diagnosis of lichen plano-pilaris, confirmed by histological examination.

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Figure 2: 45-y.o. female, affected from Alopecia Universalis and Vitiligo evolved in atrophians after treatment with topical immunotherapy.



Figure 3: Man 32 y.o. affected by Alopecia Universalis from the age of 25. In partial resolution with topical immunotherapy developed an eruption of multiple discoid lupus elements also on the back and discontinued the treatment, but DLE lesions persisted.

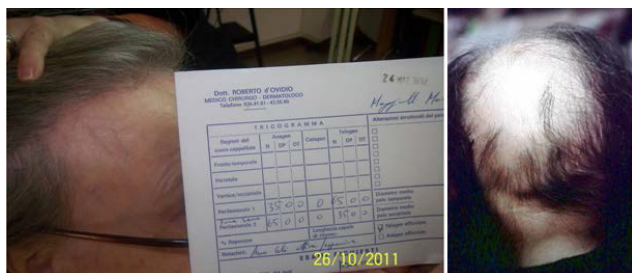


Figure 4: FFA 66 y.o. after chronic AA ophiasic-multilobularis 19 y. before (the picture in the right).

Considerations

The clinical history of our patients gives us the opportunity to discuss about the overlap between different patterns of hair loss. In 1996, Whiting noticed that significant degrees of inflammation and fibrosis occurred in 37% of cases of Androgenetic Alopecia (AGA) with a greater ratio between upper and lower follicle inflammation than in control subjects examined (Chronic Telogen Effluvium – healthy controls) [2]. Even Female Pattern Hair Loss (FPHL), a common potentially reversible hair disorder of the central scalp, may develop in a permanent hair loss in a subset of women [3]. Recent evidence shows that, although Androgenic Alopecia may have a classic clinical pattern, a significant number of occult inflammatory and scarring scalp processes may also mimic this pattern with enough frequency to induce authors to question the possibility of making this diagnosis solely on clinical criteria [4].

Alopecia Areata (AA), a non – cicatricial immunomediated hair loss, may show a scarring pathological pattern in a small proportion of longstanding and not responder patients [5]. Normal human anagen hair follicles (HF) bulge represents a site of relative immune privilege (IP) in human skin and this presumably protects the HF epithelial stem cell reservoir from autoaggressive immune attack. A loss of bulge IP may play a central role in the pathogenesis of cicatricial Alopecias [6]. CD 200 cells localized in this portion of the hair follicle seem to be important in maintaining self tolerance [7]. Importantly, these elements are the precursors of the primary and secondary hair matrix cells and are compromised in the course of Androgenetic Alopecia [8].

Multiple events can lead to loss of IP, such as increased IFN- γ , activation of mast cells and / or NK/NKT cells. The mast cell degranulation with the subsequent activation of fibroblasts (TGF) and microvascular inflammation can lead to phenomena of induction of catagen, fibrosis and follicular atrophy [9-11]. This particular mechanism could explain the cases of Alopecia Universalis which became atrophians after treatment with topical immunotherapy. The minimal persistent inflammation is probably associated with a



Figure 5: FFA successive to old, resistant and persistent form of Ophiasis.

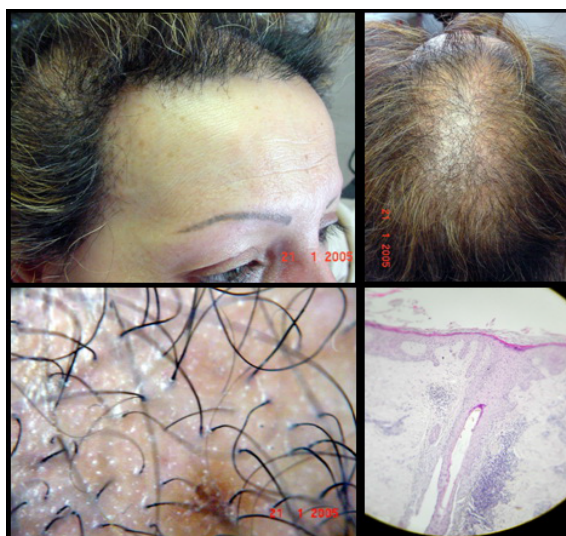


Figure 6: Woman 42 y.o. affected by AGA from the age of 26, developed 11 y. after a front setback, loss of eyebrows and Fibrosing Alopecia in Pattern Distribution and Frontal Fibrosing Alopecia in the previous baldness area.

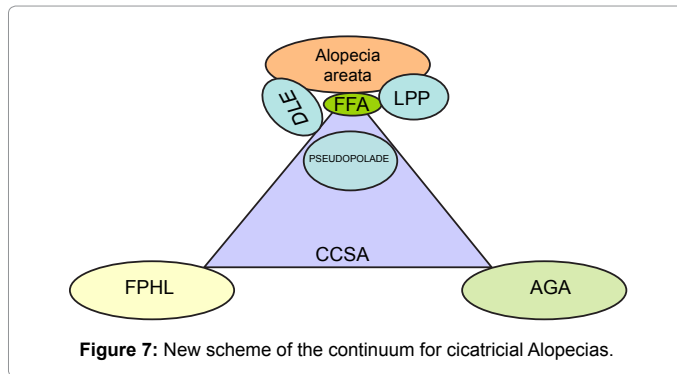


Figure 7: New scheme of the continuum for cicatricial Alopecias.

mast cell activation [11]. Another possibility is the interference of particular subpopulation of lymphocytes, such as Natural Killer T cells (NKT) which are able to recognize lipidic and glycolipidic antigens presented by CD1d which belongs to a family of antigen presenting molecules that are structurally and distantly related to the classic major histocompatibility complex class I (MHC I) proteins [12]. CD1d is constitutively expressed in normal anagen follicle on Outer Root Sheath keratinocytes. So epidermal cells of the immuno-privileged hair follicle other than dendritic cells, can also present an autologous or heterologous lipid antigen to NKT cells [13]. These cells seem to play a primary role in the pathogenesis of AA [14]. In Lichen Planus and also in cutaneous Lupus Erythematosus the implication of cytotoxic T and NK cell is well recognized [15,16]. We have already mentioned also the possible role of the deficit of elements CD200+, responsible of the immune privilege of the area of the bulge, in cicatricial alopecia [7].

In conclusion, in the light of clinical and histological findings, the known scheme of the continuum for cicatricial Alopecias [17] should be revisited (Figure 7), since a persistent damage to the follicle may rarely change a reversible Alopecia to a permanent one, probably through the immunopathomechanism of the immuno privilege collapse and spreading of epitopes [18]. On the other side, it is possible to hypothesize a sort of Koebner Phenomenon, where, in subjects susceptible to scarring Alopecia, a more common and reversible follicular damage (as in AA) or with slow progression to fibrosis (as in Androgenetic Alopecia) could trigger the more rare and irreversible disease [19].

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