Case Report

Graft versus Host Disease Presenting as Fibrosing Alopecia in a Pattern Distribution: A Model for Pathophysiological Understanding of Cicatricial Pattern Hair Loss

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ABSTRACT

A case of cutaneous graft versus host disease (GvHD) presenting as fibrosing alopecia in a pattern distribution (FAPD) is discussed, possibly providing a mechanistic model for a better understanding of the pathogenic events underlying cicatricial pattern hair loss. The implication of a follicular inflammation and fibrosis associated with patterned hair loss has emerged from several independent studies. Eventually, Zinkernagel and Trüeb reported a peculiar type of cicatricial pattern hair loss with histopathological features consistent with lichen planopilaris (LPP) associated with androgenetic alopecia (AGA). With regard to its pathogenesis, LPP is regarded to constitute a T-cell-mediated autoimmune reaction. An as yet unknown antigenic stimulus from the malfunctioning hair follicle may initiate a lichenoid tissue reaction that triggers apoptosis of the follicular epithelial cells in the susceptible individual. GvHD is a complication following allogeneic tissue transplantation and is induced and maintained by immunocompetent cells from the donor tissue that particularly attack epithelia of fast-proliferating tissues in the recipient. Due to its analogies with lichen planus, GvHD constitutes a valid immunologic model for lichen planus, LPP and ultimately FAPD. Specifically, the presentation of GvHD of the scalp combines features of AGA and of LPP, as originally proposed in earlier observations on permanent alopecia after bone marrow transplantation.

Key words: Cicatricial pattern hair loss, fibrosing alopecia in a pattern distribution, graft versus host disease

INTRODUCTION

Patterned hair loss or androgenetic alopecia (AGA) is understood to represent a hereditary and androgen-sensitive, progressive thinning of the scalp hair. Its pathogenesis is related to a polygenic hereditary background and peculiarities of androgen-metabolism, resulting in androgen-dependent, progressive thinning of hair associated with a decrease of anagen duration in the hair cycle, miniaturization of the hair follicle, and gradual transformation of the terminal to vellus hair in the affected areas. Therefore, diversity of hair shaft diameter or anisotrichosis is a diagnostic dermoscopic feature of AGA. It is best appreciated in a central hair part at low magnification and is very useful to detect the condition, particularly in women.

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Treatment of AGA aims at blocking the effect of androgens with antiandrogens, such as cyproterone acetate and spironolactone, or 5 alpha-reductase inhibitors, such as finasteride and dutasteride, and at increasing the duration of anagen with the hair growth-promoting agent minoxidil. The limited success rate of treatment with these agents means that additional pathogenic factors may be considered.

The implication of a follicular inflammation and fibrosis associated with patterned hair loss has emerged from several independent studies: an early study referred to an inflammatory infiltrate of activated T cells and macrophages in the upper third of the hair follicles, associated with an enlargement of the follicular dermal sheath composed of collagen bundles (perifollicular fibrosis) in the regions of actively progressing alopecia. Subsequently, Whiting demonstrated in morphometric studies in patients with male pattern AGA treated with minoxidil that 55% of patients with microinflammation had regrowth in response to treatment, in comparison to 77% in those without inflammation and fibrosis. Ultimately, Mahé et al. proposed the term microinflammation, in as much as the process involves a slow, subtle, and indolent course, in contrast to the inflammatory and destructive process in the classical inflammatory scarring alopecias.

Eventually, Zinkernagel and Trüeb reported a peculiar type of cicatricial pattern hair loss with histopathological features consistent with lichen planopilaris (LPP) associated with AGA and named it fibrosing alopecia in a pattern distribution (FAPD).

With regard to its pathogenesis, LPP is regarded to be a T-cell-mediated autoimmune reaction that triggers apoptosis of the follicular epithelial cells. This autoimmune process is thought to be in response to some antigenic challenge, but a specific antigen has yet not been identified. Harries et al. provide the first evidence that LPP may result from an immune privilege collapse of the hair follicle’s epithelial stem cell niche. Where a causal or triggering agent is identified, this is termed a lichenoid reaction rather than lichen planus. This may include drug reactions, viral hepatitis, and cutaneous graft versus host disease (GvHD).

Herein, we report a case of cutaneous GvHD presenting as FAPD, providing a model for a better understanding of the pathogenic mechanisms possibly underlying cicatricial pattern hair loss.

**CASE REPORT**

A 58-year-old woman presented with the complaint of symptomatic (pruritus) and accelerated hair loss. She had a personal history of acute myeloid leukemia with bone marrow transplantation preceding by 3 years and GvHD of the lung, gut, oral cavity, skin, and nails, that was treated with extracorporeal photopheresis. Her systemic medication consisted of tacrolimus, mycophenolate mofetil, fluconazole, valaciclovir, atovaquone, atorvastatin, sitagliptin, pantoprazole, ramipril, pregabalin, magnesium, calcium, and vitamin D3.

Clinical examination revealed a thinning of hair of the central scalp area [Figure 1] associated with diversity of hair shaft diameters and perifollicular scaling and follicular dropout limited to the respective area on dermatoscopic examination [Figure 2]. Associated nail alterations were longitudinal ridges and melanonychia.

A diagnosis of FAPD was made, and the patient was prescribed a compound of 5% minoxidil and 0.2% triamcinolone acetonide b. i. d. for the crown area.

**DISCUSSION**

Cicatricial pattern hair loss is the term proposed by Olsen in 2005 to acknowledge the existence of follicular inflammatory phenomena and fibrosis with follicular dropout in biopsies of women with AGA.

In 1994, Kossard originally reported on scarring alopecia in a pattern distribution in postmenopausal women with progressive frontal hairline recession that was associated with perifollicular erythema within the marginal hairline, producing a frontal fibrosing alopecia extending to the temporal and parietal hair margins. Scalp biopsy specimens revealed histological features that were indistinguishable from those seen in LPP. FFA has meanwhile also been described in premenopausal women and men though with a significantly lesser frequency. Moreover, it has been recognized to represent a more generalized rather than localized process of inflammatory scarring alopecia, with extension beyond the frontotemporal hairline to include the parieto-occipital hair line, involve peculiar facial papules as evidence of facial vellus hair involvement, and loss of peripheral body hair. More recently, also lichen planus-type nail involvement has been reported, again pointing to a close relationship of FFA to lichen planus. It has been speculated to what extent a background of AGA may contribute to this particular clinical presentation.
of the disease, specifically in patients suffering of lupus erythematosus presenting with FFA. Nevertheless, the localization of FFA in androgen-independent areas, the lack of evidence of associated AGA (diversity of hair shaft diameters) in some patients with FFA, and the limited success rate of antiandrogen therapy, including 5 alpha-reductase inhibitors, all point to the fact that AGA represents only a facultative comorbidity of FFA, setting the condition apart from FAPD.

An important question that arises is how the lichenoid tissue reaction pattern is generated around the individual androgenetic hair follicle in FAPD. Follicles with some form of damage or malfunction might express cytokine profiles that attract inflammatory cells to assist in damage repair or in the initiation of apoptosis-mediated organ deletion. Alternatively, an as yet unknown antigenic stimulus from the damaged or malfunctioning hair follicle might initiate a lichenoid tissue reaction in the immunogenetically susceptible individual. Remarkably, in healthy murine skin, clusters of perifollicular macrophages have been described as perhaps indicating the existence of a physiological program of immunologically controlled hair follicle degeneration by which malfunctioning follicles are removed by programmed organ deletion. It has therefore been proposed that various forms of clinically perceptible, permanent alopecia might represent a pathological exaggeration of this type of programmed organ deletion, resulting in a lichenoid tissue reaction pattern and true scarring alopecia. Further studies are required to elucidate a presumable role of androgenetic factors in addition to that of the lymphohistiocytic infiltrate, perifollicular lamellar fibrosis, and apoptosis-mediated follicular regression in FAPD.

GvHD is a common complication following allogeneic tissue transplantation and is induced and maintained by immunocompetent cells from the donor tissue (graft) that particularly attack epithelia of fast proliferating tissues in the recipient (host), such as those from the gastrointestinal tract, liver, and the skin. The skin is the most common organ involved. While the cutaneous, mucosal, and nail manifestations of chronic GvHD are well recognized, involvement of the hair follicle has so far found lesser attention. Miyazaki et al. reported the first case of GvHD with follicular involvement.

Due to its analogies with lichen planus, GvHD constitutes a model that may lead to a better understanding of the pathophysiological features of lichen planus, LPP, and ultimately FAPD. Specifically, the presentation of chronic GvHD on the scalp may be that of FAPD with features of both AGA and of LPP, as originally proposed by Basilio et al. in their earlier observations on permanent alopecia after bone marrow transplantation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

This case report represents an integral part of Hudson Dutra Rezende’s traineeship in Dermato-Trichology at
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