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Case Report

Treating Frontal Fibrosing Alopecia with Regenerative Approaches: A Case Report

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ABSTRACT

One of the many types of scarring alopecia is Frontal Fibrosing Alopecia (FFA), which is especially common in post-menopausal women. It presents a variety of clinical manifestations and is characterized by a distinct clinical pattern of progressive recession involving the frontotemporal and parietal hairline. Its aetiology is still poorly understood, but autoimmune, hormonal, genetic, inflammatory, behavioural and environmental factors are thought to be important in its aetiology. Alternatives to these approaches are also regenerative, including the use of Platelet-Rich Plasma (PRP) and Polydeoxyribonucleotides (PDRN), which exhibit immunoregulatory and tissue remodelling functions. This study aimed to describe a regenerative intervention in a case of frontal fibrosing alopecia in a female patient whose clinical examination revealed significant hairline recession and bitemporal skin atrophy. The proposed treatment consisted of six sessions of intradermal therapy with PRP associated with PDRN. Additionally, the patient was treated with minoxidil 2.5 mg/day, dutasteride 0.5 mg/day and hydroxychloroquine 400 mg/day. When the patient returned after six months, the area of atrophy was much improved, perifollicular scaling at the hairline and vellus hair had not recurred, and there was no sign of inflammation in the eyebrow area. The results strongly suggest that early diagnosis and therapy capable of limiting the inflammatory process, such as regenerative approaches, are important to preventing FFA's progression.

Keywords: Frontal Fibrosing Alopecia, Platelet-Rich Plasma, PDRN, Regenerative medicine

INTRODUCTION

Frontal Fibrosing Alopecia (FFA) is a type of primary lymphocytic scarring alopecia that is slowly progressive and predominantly observed in postmenopausal women, with an incidence that has been increasing in recent years [1,2]. It is characterised by a distinct clinical pattern of progressive recession involving the frontotemporal and parietal hairline [3]. In addition to hair loss with scarring, FFA can frequently cause skin atrophy along the frontal scalp line, affect eyebrows, lead to the loss of eyelashes and body hair, and generate perifollicular erythema and follicular hyperkeratosis [2,4,5].

The aetiology of the disease is not fully elucidated yet, although it has been confirmed that autoimmune, hormonal, genetic, inflammatory, behavioral and environmental factors have important roles in its pathophysiology [4,6]. Interferon-gamma (IFN-γ) induced an immune response mediated by T helper (Th)-1 cells in the infundibular and isthmus regions and essentially in the bulge area [7,8]. These fibrotic remnants are accompanied by a decrease in keratinocytes and an increase in Transforming Growth Factor-beta (TGF-β), indicating that hair loss begins [9,10]. Many different therapies have been reported to be beneficial for the same. Still, there are relatively few published guidelines for the treatment of the disease, which use topical corticosteroids and calcineurin inhibitors, intralesional corticosteroids and oral anti-inflammatory and immunosuppressive [1].

Regenerative approaches, both autologous and commercial, have gained significant prominence in the medical literature for

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treating various alopecias. However, most studies focus on non-scarring alopecias, such as androgenetic alopecia and alopecia areata [11,12]. Autologous PRP, which is an autologous concentrate of platelets, induces the release of biomolecules such as interleukins and growth factors, with both immuno-modulation and tissue regeneration [13]. Polynucleotides, particularly PDRN, have considerably attained a large use in dermatology. Extracted from salmon sperm, PDRN consists of DNA fragments that, upon binding to the A2 adenosine receptor, promote modulation of the inflammatory response and apoptotic processes, enhancing tissue repair [14]. There is a scarcity of studies involving PRP in treating FFA and no reports of its association with PDRN. Therefore, this study aimed to describe a successful regenerative approach using PRP associated with PDRN in a case of FFA with significant hairline recession and bitemporal skin atrophy.

MATERIAL AND METHODS

This is a descriptive study with a qualitative approach, describing a case report, of frontal fibrosing alopecia. The patient was treated by professionals at the Passoni Clinic, a dermatology clinic specializing in hair sciences located in Sao Paulo, Brazil.

The patient signed an Informed Consent Form (ICF) outlining the study's objectives and guaranteeing confidentiality, privacy, and anonymity, in accordance with ethical guidelines for research with human subjects according to Resolution 466/12 of the Brazilian Ministry of Health.

CASE PRESENTATION

A 49-year-old Caucasian female patient undergoing treatment with anxiolytics for anxiety presented to the Passoni Clinic in March of 2023 with receding hairline and atrophy in the frontotemporal region as shown in Figure 1A. Previously, she had received intradermal therapy with corticosteroid (triamcinolone acetonide) at a different centre at the site of disease progression. Clinical examination revealed a significant hairline recession and bitemporal cutaneous atrophy. Trichoscopy of the hairline indicated hyperemia, perifollicular scaling, and an absence of vellus hairs as shown in Figure 1B, while the trichoscopy of the eyebrows showed mild hyperemia and perifollicular scaling.

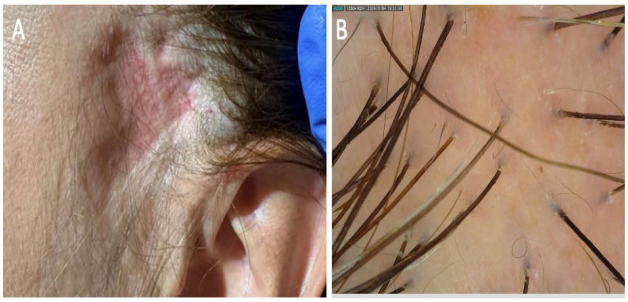

Figure 1: (A) Skin atrophy in the temporal region; (B) Trichoscopy of the scalp with signs of hyperemia and scaling.

A clinical treatment involving intradermal applications of PRP combined with PDRN (Skymedic, United Kingdom) was initiated. Six sessions were performed in total, with an interval of one month between each. Additionally, oral pharmacotherapy was prescribed, including 2.5 mg/day of minoxidil, 0.5 mg/day of dutasteride, and 400 mg/day of hydroxychloroquine.

To prepare the PRP, 4 tubes of blood containing sodium citrate were collected and centrifuged at 1,200 RPM for 8 min. After centrifugation, the supernatant plasma was collected to inject into the patient.

The patient reported good tolerability of the treatment, reporting only local pain at the time of application. After six months, the patient showed significant improvement in the atrophic area, the absence of perifollicular scaling in the hairline, the presence of vellus hairs, and no signs of inflammation in the eyebrow region as shown in Figure 2.

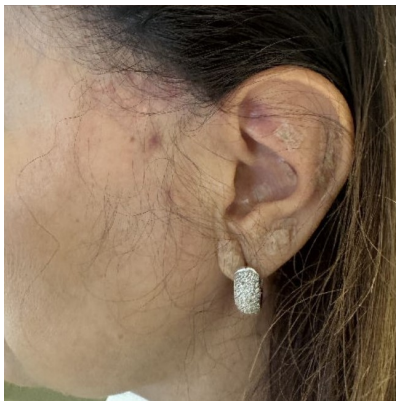

Figure 2: Temporal region 6 months after treatment.

RESULTS AND DISCUSSION

Since 1994, when it was first described, frontal fibrosing alopecia cases have increased considerably worldwide. At that time, reports of the disease's incidence primarily involved postmenopausal Caucasian women [15]. The pathogenesis of FFA is not yet fully elucidated, but it is already known that a persistent inflammatory response and a collapse of immune privilege develop and lead to the destruction of epithelial hair follicle stem cells and epithelial-mesenchymal transition in the area bulge [16]. This process can be induced by IFN-γ. In FFA, an autoimmune reaction of cytotoxic T cells against the hair follicle in the infundibular region and, to a more variable degree, in the isthmic region, seems to play an important role [3].

The treatment of FFA is considered a challenge for clinicians. Due to its irreversible nature, the main goal of treatment is to reduce inflammation and achieve disease stabilization due to its scarring nature [15]. In other words, all forms of treatment aim to reduce the symptoms and signs of the disease and slow its progression, but they rarely stimulate hair growth [2]. Over the years, several medications have been used to treat FFA, mycophenolate mofetil [17]. The use of phototherapy and including topical steroids, steroid injections, hydroxychloroquine,

doxycycline, tetracycline and surgical procedures have also been described [4]. Systemic medications, such as antimalarials (hydroxychloroquine) or 5α-reductase inhibitors, appear to be among the preferred treatment options currently, although there is a need for continued monitoring and high risks of adverse events [2].

5α-reductase inhibitors are among the most effective treatment options for FFA [15]. A case report has been made of a patient who experienced not only frontal hair growth with the 5α-reductase inhibitor finasteride, but also a marked reversal of skin atrophy [17]. A study reported that oral finasteride (2.5 mg/day) combined with minoxidil 2% halted the progression of alopecia in some patients after 12-18 months of treatment [18].

Another study compared finasteride and hydroxychloroquine, and the authors found that both drugs were equally effective, safe, and well tolerated in patients with FFA [19].

The use of PRP in alopecia has been widely studied in recent years. PRP has been used as a new therapy for some types of non-scarring alopecia, such as androgenetic alopecia and alopecia areata. The mechanism of action of PRP is based on the release of growth factors that promote follicular regeneration. Among them, Vascular Endothelial Growth Factor (VEGF) induces angiogenesis of the follicular plexus; Insulin-like Growth Factor (IGF-1) helps maintain the anagen phase and Platelet-Derived Growth Factor (PDGF) induces the proliferation of dermal papilla cells [20]. However, there is a lack of studies on the use of PRP in scarring alopecia.

PDRN, despite little study for hair diseases, has been shown to be effective for the treatment of FFA in this patient. This molecule binds to the A2 receptor and induces an anti-inflamatory response by inhibiting the activation of the NF-KB pathway [21]. In addition, PDRN also decreases the production of Matrix Metalloproteinases (MMP) and induces collagen production [22].

CONCLUSION

Although the incidence of frontal fibrosing alopecia has increased in the last two decades, there are still gaps regarding its etiology and pathology. Several treatment possibilities have been reported in the literature, including anti-inflammatory and immunosuppressive agents, as well as 5-alpha-reductase inhibitors and antimalarial agents, which have offered a good therapeutic response in FFA, especially when used in combination, as was the case with the patient in this study. More recently, it has been reported that PRP may be effective in some types of cicatricial alopecia, such as lichen planopilaris and frontal fibrosing alopecia. However, it is considered that further clinical trials are needed in order to provide more robust evidence. Furthermore, the use of PDRN has shown to be a promising new agent for the treatment of FFA. It is suggested that early diagnosis and therapy that can limit the inflammatory process are crucial to prevent the progression of frontal fibrosing alopecia.

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