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Case Report

Botulinum Toxin A Delivery via MMP Technique: An Emerging Therapeutic Approach for Frontal Fibrosing Alopecia

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Abstract: Frontal Fibrosing Alopecia (FFA) is a disease of unknown etiology and pathogenesis whose prevalence has been increasing since its first description in 1994. With no cure, treatments only control the inflammatory process and disease progression, but do not reverse the changes induced by it. We report the case of a patient with early-stage FFA who underwent three monthly sessions of 30 units of Botulinum Toxin Type A administered by MMP® (Microinfusion of drugs through the skin) technique. The results showed a substantial improvement in the patient's clinical condition with inhibition of the inflammatory process and an evident increase in follicular density in the treated area.

Keywords: Frontal Fibrosing Alopecia; Botulinum toxin A; Microinfusion; MMP; Treatment.

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1. Introduction

FFA is a slowly progressive disease characterized by a receding frontal and temporoparietal hairline, perifollicular erythema, and eyebrow loss [1]. It mainly affects postmenopausal Caucasian women [1]. However, a growing number of cases of FFA in younger adult women and other ethnicities have been reported [2].

Considered a clinical variant of lichen planopilaris (LPP), FFA has similar histological features to those found in LPP, such as the presence of a lichenoid inflammatory infiltrate involving the isthmus and infundibulum [3, 4]. Depending on the stage of the diagnosis, FFA presents different histopathological characteristics. In the early stages, it may present a lymphohistiocytic and lichenoid inflammatory infiltrate around the outer root sheaths in the infundibular and isthmus regions and mild perifollicular lamellar fibrosis. The late stages of FFA are characterized by more severe perifollicular fibrosis, with reduced follicular density until scar tissue replaces the pilosebaceous units [5].

Early diagnosis of FFA is based on the presence of the follicular triad, characterized by inflammatory infiltration of leukocytes in velus, intermediate, and terminal hairs at different stages of the follicular cycle [6]. The follicular triad is predominant in velus and intermediate hairs that are located in greater quantities in the frontal hairline implantation line, suggesting that the follicular triad in this region is related to the receding frontal and temporoparietal hairline in FFA [6].

The medications commonly used to treat FFA are antiandrogenic and corticosteroid drugs [7]. Although these drugs can control the progression of the disease, they cannot

reverse the hair loss caused by FFA. Therefore, it would be worth exploring alternative approaches for treating FFA, such as the administration of botulinum toxin A, which has been shown to be effective as an alternative treatment for androgenetic alopecia and folliculitis decalvans [8, 9]. In the light of this, the purpose of this study was to evaluate the effectiveness of botulinum toxin A in treating a patient in the early stages of FFA. To overcome the limitations of the traditional topical administration method that uses needles and syringes to deliver the medication into the skin, botulinum toxin A was administered using MMP as a delivery system [10]. The results obtained with this approach were very promising, suggesting that botulinum toxin A combined with MMP could be a viable alternative treatment option for FFA.

2. Case Report

A 57-year-old postmenopausal female patient with no known allergies or associated comorbidities was admitted to the clinic with clinical features of frontal fibrosing alopecia, including eyebrow loss, hairline recession in the frontotemporal region, perifollicular erythema, hyperkeratosis with loss of follicular openings, and hair thinning in the frontal and parietal areas (Figure 1).

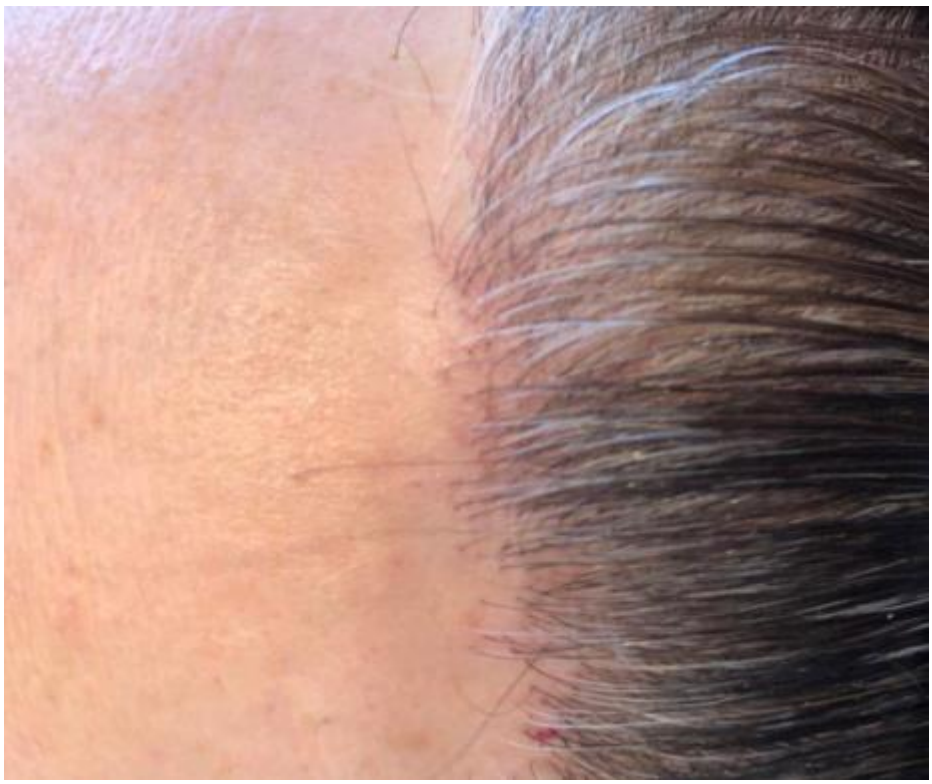

Figure 1: Recession of the hairline in the frontotemporal region with follicular openings, perifollicular erythema, and hair thinning.

The clinical diagnosis of FFA was confirmed by histopathological examination, which showed moderate leukocyte infiltration, follicular epithelial dissociation, and absence of sebaceous glands (Figure 2).

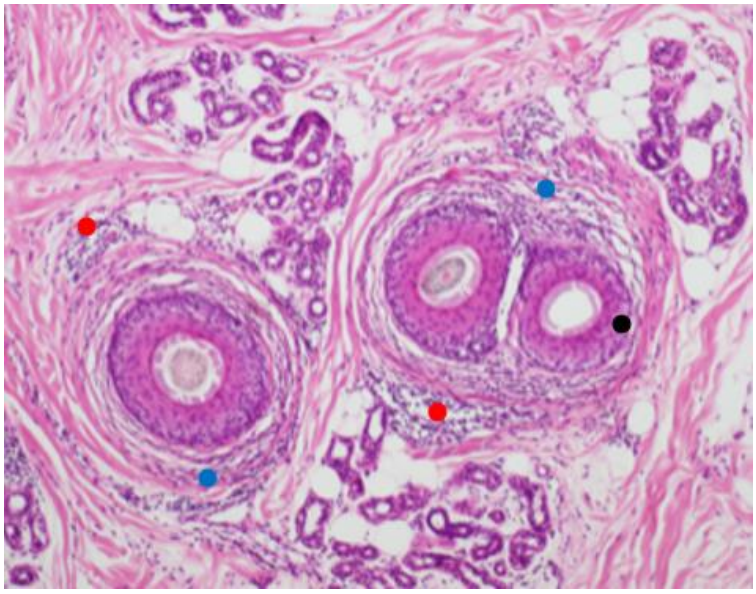

Figure 2: Anatomopathological examination – Horizontal section showing scarring alopecia with interface alteration at the isthmus' level with a concentric fibroplasia around the (blue dots), lymphocytic inflammation (red dots) and a characteristic atrophy of the epithelium (black dot). Note the absence of sebaceous glands. HE staining, original magnification 20x.

The patient was treated with three sessions of botulinum toxin A (30 units/session) administered monthly using the MMP® technique [10, 11]. The MMP technique is a microneedling procedure that was first described in 2013 and uses a tattoo machine to deliver medication into the skin [10, 11]. The MMP machine consists of microneedles with a fine diameter that are arranged parallel to each other (Figure 3A). The MMP machine is powered by a single energy source and has an adjustable operation velocity (Figure 3B). The needles embedded with the medication penetrate the skin, and the medication is delivered into the intercellular space (Figure 3C).

Figure 3: MMP – (Microinfusion of drugs through the skin) technique.

The results obtained from combining the use of MMP to deliver botulinum toxin A in the scalp of the FFA patient showed a decrease in the area of hair loss, an increase in follicular density, a marked decrease in perifollicular erythema, the growth of new hairs, and resistance to the traction test after three months of treatment (Figure 4).

3. Discussion and conclusion

Alopecias can be classified as cicatricial and non-cicatricial [12]. Non-cicatricial alopecias result from a process that does not cause irreparable damage to the hair follicle [12]. On the other hand, cicatricial alopecias such as FFA result from active destruction of hair follicles, which are irreversibly destroyed and replaced by fibrotic tissue [13].

Currently, there are various types of treatments prescribed for FFA, including topical, systemic or a combination of both. The most prescribed topical treatments are corticosteroids, minoxidil and calcineurin inhibitors. Systemic treatments include 5 alpha-reductase inhibitors, hydroxychloroquine, and retinoids. Intralesional triamcinolone is also used, especially for the eyebrows. Recent treatments include pioglitazone, naltrexone, tofacitinib, lasers and hair transplantation. However, treatments differ according to the location, presence of inflammation, itching, stage of the disease and patient response [14].

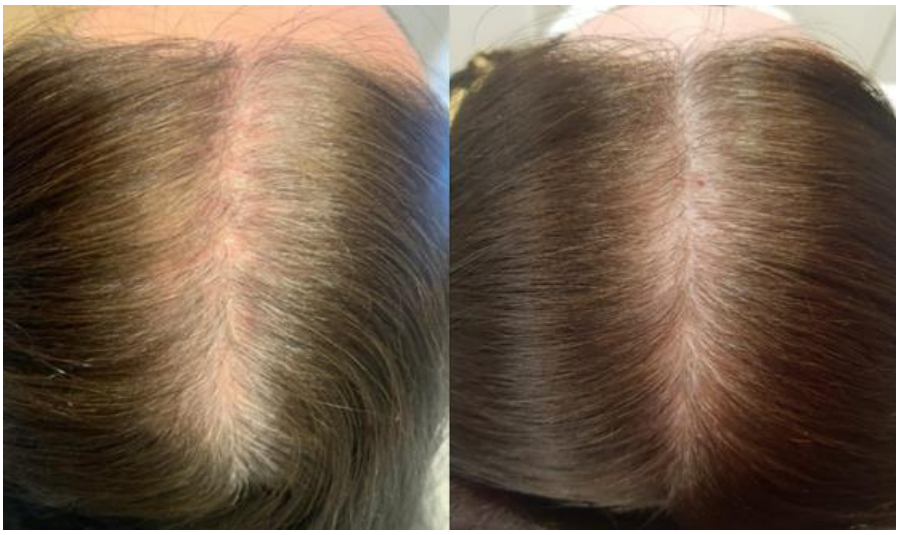

Figure 4: Illustrative photos of the obtained results. **A**. Before the treatment showing perifollicular erythema and hair thinning in the parietal/mid frontal region. **B**. after the treatment showing a substantial increase in hair density and a marked decrease in perifollicular erythema.

Despite the variety of treatments currently prescribed for FFA and other conditions causing alopecia, there is still no validated or approved treatment for these diseases. Consequently, various groups are researching ways to establish protocols and more effective treatment alternatives for these syndromes. However, some studies have shown that botulinum toxin A can be effective in non-cicatricial and cicatricial alopecia such as androgenetic alopecia and folliculitis decalvans respectively [8,9]. On the other hand, MMP has been demonstrated to successfully deliver medication such as triamcinolone acetonide in patients with alopecia [10]. We therefore decided to determine the potential of botulinum toxin A delivered by MMP technique as an alternative treatment against FFA. The results obtained in our study showed that three sessions of botulinum toxin A delivered by MMP in a patient with early-stage FFA were able to reverse the clinical picture by inducing increased hair density and reducing the inflammatory process observed clinically by reducing perifollicular erythema.

This result is very significant, as the first report of the use of botulinum toxin A delivered by MMP technique in the treatment of FFA, opening up the possibility of an alternative therapy against this disease. However, many studies will still be necessary for this approach as a therapeutic process to be established and regulated as a treatment for scalp alopecia syndromes.

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Conflicts of Interest: None.

Supplementary Materials: None.

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