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REPIGMENTATION AFTER BOTULINUM TOXIN APPLICATION IN UNIVERSAL VITILIGO LESIONS: A CASE REPORT

Repigmentación Tras la Aplicación de Toxina Botulínica en Lesiones de Vitiligo Universal: Un Reporte de Caso

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ABSTRACT

Objective: To report a case of unexpected facial repigmentation in a patient with stable universal vitiligo who underwent BTA treatment for hyperkinetic rhytids. **Methods**: A 37-year-old patient diagnosed with universal vitiligo since childhood and without active treatment for the condition for over two decades received two sessions of abobotulinumtoxinA (Dysport®) for orofacial harmonization. Clinical evolution was documented through standardized photography and subjective evaluation by the patient. **Results**: After the applications, notable repigmentation was observed in the facial areas treated with BTA, which coincided with the vitiligo macules. The patient reported high satisfaction with the aesthetic results and with the incidental repigmentation. Conclusion: This case suggests that BTA may have therapeutic potential in inducing repigmentation in patients with stable vitiligo, possibly through modulation of the neuroimmunocutaneous pathway. This finding contrasts with existing literature and justifies the need for controlled studies to investigate the efficacy and mechanisms of action of BTA as a new treatment modality for vitiligo.

Keywords: Vitiligo, Botulinum Toxin, Facial Rejuvenation.

RESUMEN

Objetivo: Reportar un caso de repigmentación facial inesperada en un paciente con vitíligo universal estable que se sometió a tratamiento con TBA para arrugas hipercinéticas. **Métodos:** Un paciente de 37 años, diagnosticado con vitíligo universal desde la infancia y sin tratamiento activo para la enfermedad durante más de dos décadas, recibió dos sesiones de abobotulinumtoxinA (Dysport®) para armonización orofacial. La evolución clínica se documentó mediante fotografía estandarizada y evaluación subjetiva del paciente. **Resultados:** Después de las aplicaciones, se observó una repigmentación notable en las áreas faciales tratadas con TBA, que coincidió con las máculas de vitíligo. El paciente refirió alta satisfacción con los resultados estéticos y con la repigmentación incidental. **Conclusión**: Este caso sugiere que la TBA podría tener potencial terapéutico para inducir la repigmentación en pacientes con vitíligo estable, posiblemente mediante la modulación de la vía neuroinmunocutánea. Este hallazgo contrasta con la literatura existente y justifica la necesidad de estudios controlados para investigar la eficacia y los mecanismos de acción de la TBA como una nueva modalidad de tratamiento para el vitíligo.

Palabras clave: Vitíligo, Toxina Botulínica, Rejuvenecimiento Facial.

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RESUMO

Objetivo: Relatar um caso de repigmentação facial inesperada em paciente com vitiligo universal estável, submetida a tratamento com TBA para rítides hipercinéticas. Métodos: paciente de 37 anos, com diagnóstico de vitiligo universal desde a infância e sem tratamento ativo para a condição há mais de duas décadas, recebeu aplicações de abobotulinumtoxinA (Dysport®) em duas sessões para harmonização orofacial. A evolução clínica foi documentada por meio de fotografia padronizada e avaliação subjetiva da paciente. Resultados: Após as aplicações, observou-se uma repigmentação notável nas áreas faciais tratadas com a TBA, que coincidiam com as máculas de vitiligo. A paciente relatou alta satisfação com os resultados estéticos e com a repigmentação incidental. **Conclusão:** Este caso sugere que a TBA pode ter um potencial terapêutico na indução da repigmentação em pacientes com vitiligo estável, possivelmente através da modulação da via neuro-imuno-cutânea. O achado contrasta com a literatura existente e justifica a realização de estudos controlados para investigar a eficácia e os mecanismos de ação da TBA como uma nova modalidade de tratamento para o vitiligo. Palavras-chave: Vitiligo, Toxina Botulínica, Rejuvenescimento facial.

INTRODUCTION

Vitiligo is a chronic autoimmune disease characterized by the selective destruction of epidermal melanocytes, which clinically manifests as achromic macules on the skin[1,2]. With a global prevalence estimated between 0.5% and 2%, the condition is not restricted to the skin, as it's also recognized for its profound psychosocial impact[3,4]. The pathogenesis of the disease is multifactorial, with the convergence theory being the most widely accepted. This model postulates that an autoimmune cascade, mediated by cytotoxic CD8+ T lymphocytes through the Interferon-gamma (IFN-γ) signaling pathway, is the central mechanism of melanocyte destruction[1,2]. Additionally, neuro-immuno-cutaneous dysfunction is a contributing factor, evidenced by an imbalance in the local cholinergic system. Studies show an increase in acetylcholine (ACh) concentration and a reduction in acetylcholinesterase (AChE) activity in vitiligo lesions, suggesting that ACh, a neurotransmitter that can inhibit melanogenesis, accumulates in the affected skin[5].

The therapeutic arsenal for vitiligo aims to control autoimmunity and stimulate repigmentation. In this context, Botulinum Toxin Type A (BoNT-A) emerges as an agent of investigational interest. Known for blocking the release of ACh, its action could, in theory, counterbalance the cholinergic excess observed in vitiligo[5-8]. The neural hypothesis, which involves the release of neuropeptides by nerve endings, is also considered a relevant component, especially in segmental vitiligo[9].

In addition, BoNT-A's ability to modulate the release of other neuropeptides and act on inflammatory pathways expands its therapeutic potential beyond muscle relaxation[10]. However, the literature on its efficacy for vitiligo is scarce and contradictory. A pilot study conducted by BinSaif et al. (2010), as well as that by El-Zawahry et al. (2010), found no evidence of repigmentation after the application of BoNT-A in localized vitiligo lesions, concluding the treatment was ineffective[7,11].

Thus, Botulinum Toxin Type A (BoNT-A) is an agent of investigational interest. Although well-established in aesthetic dermatology for its potent muscle-relaxing effect, resulting from the cleavage of SNARE proteins and the blockage of acetylcholine release at the neuromuscular junction, its action is much broader[9].

Recent studies have elucidated expanded mechanisms of action, demonstrating that BoNT-A is a neuromodulator capable of inhibiting the release of various neuropeptides, including SP and CGRP, which are implicated in pain transmission and neurogenic inflammation.[6,10] This anti-inflammatory and neuromodulatory property provides a basis for its off-label use in conditions like rosacea and opens a theoretical window of opportunity for intervention in diseases where neural dysfunction is a pathogenic component, as postulated in the neural theory of vitiligo[1,9].

The literature on using BoNT-A for vitiligo treatment is, however, extremely scarce and inconclusive. A previous prospective clinical trial showed no efficacy for BoNT-A in repigmenting localized vitiligo lesions. It concluded that isolated neurochemical modulation would be insufficient to overcome the robust cellular immune response that dominates the disease's pathogenesis[6,11].

Given the pathogenic complexity of vitiligo and the biological plausibility of neuro-immuno-cutaneous modulation, the objective of this work is to report a case of successful repigmentation in a patient with stable facial vitiligo treated with BoNT-A, contributing a new perspective for the treatment of this condition.

CASE REPORT

This is a descriptive clinical case report conducted in a private dental office in Salvador, Bahia. The patient was informed about the nature of the treatment and provided a written Informed Consent Form (ICF), authorizing both the procedure and the publication of the case. As this was a case report involving a standard procedure, it was exempted from review by a Research Ethics Committee.

A 37-year-old female patient, a photo model with the initials C.S.G., presented to a private clinic specializing in Orofacial Harmonization in Salvador, Bahia, on August 27, 2024. Her chief complaint was the presence of hyperkinetic facial rhytides. During the medical history and clinical examination, it was found that the patient had vitiligo, self-reported as the universal subtype, which she correlated with emotional factors. This was her only systemic comorbidity. She was diagnosed with vitiligo at six years old and had undergone previous treatments, including pharmacotherapy and phototherapy, until age eleven, when they were discontinued. The patient had since remained without any specific treatment for the condition. She denied pregnancy, lactation, or a history of allergy to the components of BoNT-A.

Although vitiligo is an autoimmune condition, it is classified as a low-risk factor for the development of late adverse reactions to aesthetic procedures, such as those with hyaluronic acid fillers.[8] This classification supported the decision to proceed with the proposed treatment.

Intervention and Application Protocol

For the intervention, Botulinum Toxin Type A (AbobotulinumtoxinA, Dysport® 500 U) was used. The lyophilized product was reconstituted with 2.0 mL of sterile 0.9% sodium chloride. The dosage for application followed the equivalence of 2.5 Speywood Units (U) to 1 international Unit (u). The application procedure was performed using 1 mL syringes with 30G x 6mm needles, after rigorous antisepsis of the treatment area with a 2% aqueous chlorhexidine digluconate solution.

Two sessions were performed with an interval of approximately 10 months:

- **First Session (08/27/2024)**: A total of 69 u was administered, distributed in the following muscles: frontalis (14 u), procerus (5 u), corrugator supercilii (5 u/side), orbicularis oculi (4 u/side), nasalis (6 u), mentalis (4 u) and platysma (10 u/side), infraorbital region (1 u/side). (**Figure 1A**).
- **Second Session (06/12/2025):** A total of 84 u was administered, distributed in the following muscles: frontalis (12 u), procerus (5 u), corrugator supercilii (5 u/side), orbicularis oculi (4 u/side), nasalis (5 u), depressor anguli oris (2 u/side), mentalis (6 u) and platysma (16 u/side), infraorbital region (1 u/side). (**Figure 1B).**

The evaluation of the results was conducted with standardized clinical photography and the patient's subjective assessment.

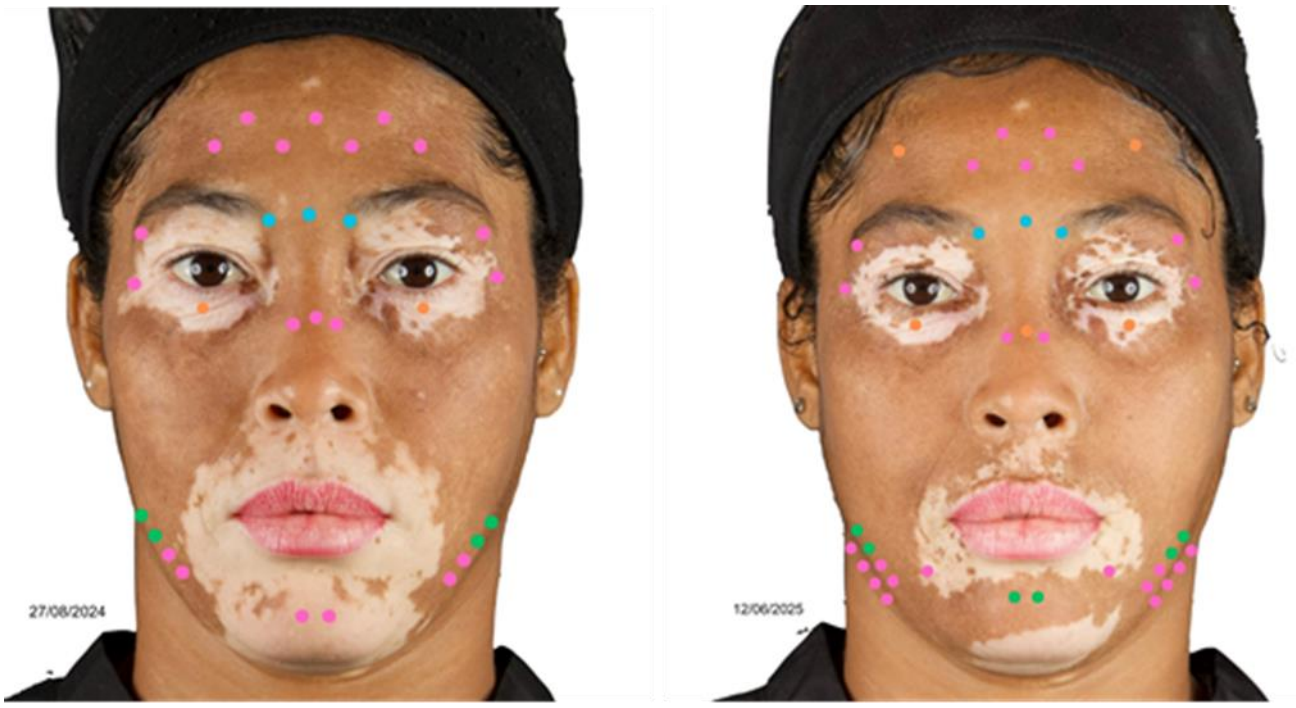

Figure 1 A and B - Markings A (06/27/2024) and B (06/12/2025) are shown. The doses were identified by colors: Blue (5u), Green (3u), Pink (2u), and Orange (1u).

Following the completed protocol, partial skin repigmentation was observed, especially in the perioral and periorbital regions, which coincided with the main application points of the botulinum toxin.

After the first session, the patient reported a significant improvement in facial tone and the softening of dynamic rhytides, as expected in the aesthetic context. However, an additional finding was noteworthy: discrete, but evident, repigmentation was observed in areas adjacent to the application points, especially in the perioral, periorbital, and mental regions. The coloration evolved from achromic areas to a slightly hypochromic tone, with less defined margins, suggesting initial melanocytic activity.

During the interval between sessions, the repigmentation remained stable, with no new lesions appearing or expansion of existing macules. After the second application, performed 10 months later, an intensification of the previously described repigmentation was observed, with an expansion of the pigmented areas and better chromatic integration with the surrounding skin.

Standardized photographic analysis demonstrated a reduction in the achromic area of approximately 30% when comparing the initial record (Figure 2) to the intermediate record (Figure 3), with an even greater reduction observed in the final records (Figure 4). The regions that showed the greatest clinical response were those with the highest density of toxin application points, suggesting a possible relationship between the local concentration of the drug and the degree of repigmentation.

Figure 2. Initial records (08/27/024).

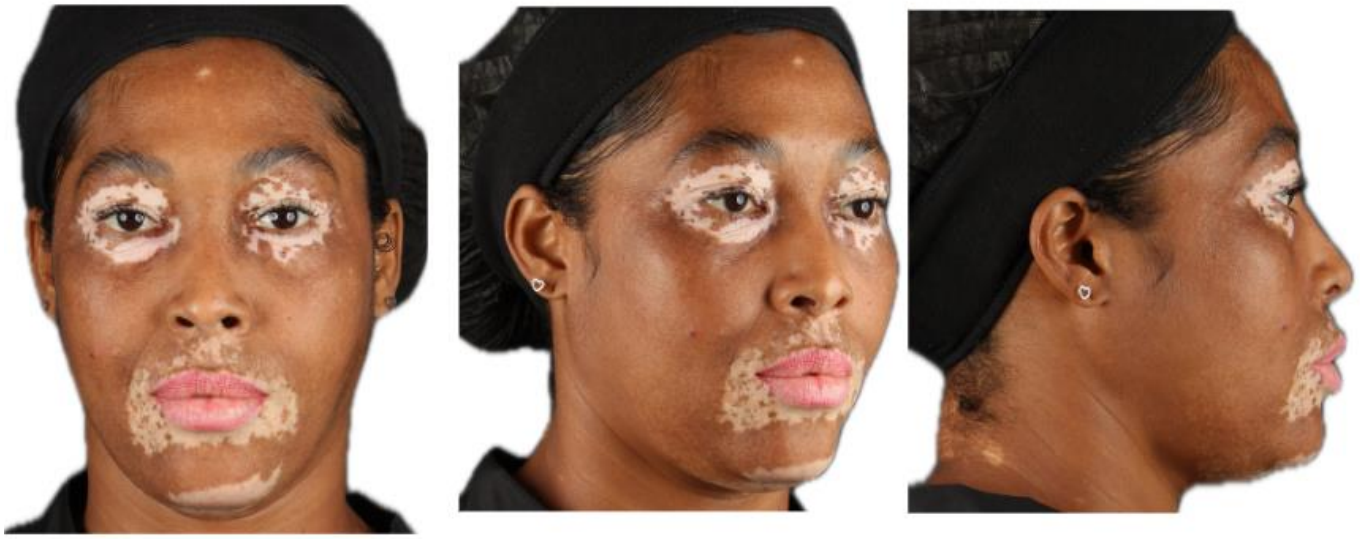

Figure 3. Records from 07/04/2025

Figure 4. Final records (08/26/2025).

DISCUSSION

This case report describes a result of repigmentation in facial vitiligo lesions after the application of BoNT-A for aesthetic purposes, a finding that contrasts with the published literature. It is important to emphasize that, to exclude confounding factors, the patient was extensively investigated for the concomitant use of any topical or systemic medications that could impact the repigmentation process, with no reports of such use. Notably, the study by BinSaif et al. (2010) specifically evaluated the use of BoNT-A for localized vitiligo and did not observe any clinical response, leading the authors to conclude the therapy's failure[7]. The divergence between the results may be attributed to methodological differences, such as the type and dose of the toxin used, the patient's vitiligo subtype (universal vs. localized), or the frequency of the applications.

Vitiligo can be described as a chronic skin condition characterized by the progressive loss of melanocytes, resulting in depigmented areas on the skin. Its etiology involves autoimmune, neurogenic, and oxidative factors[1,2]. Although the autoimmune process is central to its pathophysiology, growing evidence indicates that neurogenic mechanisms and oxidative stress play fundamental roles in the maintenance and progression of the disease[2,9]. In this context, the interaction between the peripheral nervous system and the inflammatory skin microenvironment emerges as a potential target for new therapeutic approaches.

The current therapeutic approach to vitiligo is stratified according to the disease's activity and extent. For localized and unstable forms, first-line treatments include high-potency topical corticosteroids and calcineurin inhibitors. In cases of extensive disease, narrow-band UVB (NB-UVB) phototherapy is considered the gold standard, while mini-pulse therapy with systemic corticosteroids is an option for controlling rapidly progressing cases. Surgical techniques, in turn, are reserved for stable lesions that are refractory to clinical treatments[12].

Topical ruxolitinib, by modulating the IFN-γ pathway, became the first treatment specifically approved by the FDA for non-segmental vitiligo, demonstrating significant results in phase 3 clinical trials[13]. Recent advances have expanded the therapeutic arsenal, with Janus Kinase (JAK) inhibitors standing out as effective and safe for repigmentation. Besides the topical route, oral JAK inhibitors, such as tofacitinib, are emerging as a promising frontier, especially when combined with phototherapy to enhance the results[14].

In this report, applying Botulinum Toxin Type A (BoNT-A) to facial regions with vitiligo lesions resulted in partial repigmentation, a finding that may be explained by the local neurochemical modulation the toxin promotes. BoNT-A works by blocking the release of neurotransmitters and neuropeptides, such as acetylcholine, substance P, and CGRP, thereby reducing neurogenic inflammation and oxidative toxicity, both of which are implicated in melanocyte destruction[6,10]. Studies suggest that this intervention can help restore the neurocutaneous balance, favoring the survival and proliferation of melanocytes in the affected area[5,10].

The theoretical basis for using BoNT-A in vitiligo lies in the cholinergic hypothesis of the disease. As reviewed by Enkhtaivan & Lee (2021), vitiligo lesions have a microenvironment with high concentrations of acetylcholine (ACh) and low activity of the acetylcholinesterase (AChE) enzyme[5]. ACh, in turn, appears to have an inhibitory effect on melanogenesis. Therefore, it is biologically plausible that blocking the release of ACh by BoNT-A at cutaneous nerve endings could remove this inhibitory signaling, restoring an environment conducive to melanocyte function and subsequent repigmentation[5,6].

In addition to its direct effect on ACh, BoNT-A also inhibits the release of other neuropeptides, such as Substance P and CGRP, which have pro-inflammatory properties and may be involved in the pathogenesis of vitiligo[1,9]. The modulation of these factors by BoNT-A could further contribute to disease stabilization and the stimulation of repigmentation through a local anti-inflammatory effect[10].

The potential of botulinum toxin in treating localized vitiligo was previously explored by El-Zawahry et al. (2010), who observed clinical improvement in facial and cervical lesions after applying BoNT-A. The authors hypothesized that areas with high neuromuscular activity, such as the upper third of the face, may benefit from an environment less prone to the release of pro-inflammatory mediators when neurosensory conduction is blocked. This phenomenon may explain the clinical response observed in the present case.

In addition to the observed cutaneous benefits, it's essential to consider the psychosocial impact of vitiligo, especially in visible areas like the face. The literature highlights that patients with vitiligo frequently experience emotional distress, low self-esteem, social anxiety, and a compromised quality of life.[4] Facial manifestations, with even partial areas of depigmentation, can significantly affect an individual's sense of identity and self-image. In this sense, aesthetic treatment can promote therapeutic effects beyond the dermatological aspect, restoring a patient's confidence and psychological well-being.

The connection between clinical improvement and self-esteem was evidenced in this case, where the patient reported increased self-confidence and a reduction in anxiety associated with her appearance. This result aligns with a patient-centered approach, where subjective outcomes such as satisfaction and quality of life hold a value comparable to objective clinical parameters. It's also worth noting that the result remained consistent, even during a period of significant emotional distress experienced by the patient. This would have previously led to an exacerbation of hypopigmentation areas due to the emotional nature of her condition. Therefore, using botulinum toxin, even outside its traditional scope, may represent a relevant adjuvant tool for the integrated care of vitiligo patients, particularly in areas with significant aesthetic implications.

Although this isolated case can't establish a cause-and-effect relationship, it raises the hypothesis that BoNT-A, by acting on the neuro-immuno-cutaneous pathway, may represent a new therapeutic approach, especially in areas like the face where aesthetic and therapeutic treatment can be combined.

Despite these encouraging results, it's important to emphasize that the use of BoNT-A for vitiligo remains outside conventional clinical guidelines[3]. The scarcity of controlled, long-term studies limits the extrapolation of these findings, requiring caution in its indication. Future research with robust methodology and an evaluation of psychosocial impacts is essential to validate this approach and better understand the neuro-immune mechanisms involved.

CONCLUSION

In the present case report, the application of Botulinum Toxin Type A (BoNT-A) in a patient with facial vitiligo resulted in partial repigmentation of the lesions, suggesting a possible modulating effect on the neuro-immuno-cutaneous axis. In addition to the clinical improvement, a positive impact on the patient's self-esteem was observed, reinforcing the value of approaches that integrate aesthetic and psychosocial benefits. Despite these promising findings, this is an isolated report, and additional studies are therefore necessary to clarify the mechanisms involved and to evaluate the efficacy of BoNT-A as an adjuvant option in the management of vitiligo.

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