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Case Report

Mycobacterium Abscessus Infection Following Injections of Botulinum Toxin: A Report of Two Cases

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Abstract

Botulinum Toxin A has become popular worldwide and is considered a safe treatment protocol. The complications are usually transient and minimal. Injection site infections or long-term reactions are rare. Here, we report 2 cases of *Mycobacterium* abscessus infection following injection of botulinum toxin of dramatic clinical repercussions and prolonged treatment. Case 1, a 61-year-old woman after receiving botulinum injections presented papules and nodules in her forehead and periorbital areas and diffuse frontal edema. Papules became erythematous nodules, and purulent drainage occurred. The lesions did not show any alleviation after the prescription of corticosteroids and broad-band antibiotics. The incisional biopsy of skin tissue showed inflammatory cell infiltration. Afterward, the puncture on the abscess was performed and *Mycobacterium* abscessus was successfully isolated. The patient was treated with the strategy of linezolid, cefoxitin, and amikacin, according to the result of the drug sensitivity test. The treatment lasted five months and led to an aesthetic sequel. Case 2, a 31-year-old woman after three days of receiving facial botulinum injections presented violaceous and fibrous nodules. Laboratory tests also showed *Mycobacterium* abscessus. The patient was treated with linezolid, tigecycline, and amikacin and got complete remission of the lesions after four months. The consequences caused by aesthetic procedures are rarely discussed and can significantly impact the patient's self-esteem and physical and psychological status.

Keywords: Botulinum Toxin; Infection; Mycobacterium Abscessus; Nontuberculous Mycobacterium

Abbreviations

BoNTA: Botulinum Toxin A; IV, intravenous; NTM: Non-Tuberculous Mycobacterium; M. abscessus: Mycobacterium Abscessus

Introduction

Botulinum toxin A (BoNTA) injection is one of the most popular non-surgical cosmetic procedures to combat wrinkling [1,2]. In general, the application has been considered a safe treatment protocol due to its reversible, short-term and localized effects. Most injection site reactions are easily managed and not considered serious [3].

Cutaneous infections by *Mycobacterium abscessus (M. abscessus)* after injection of BoNTA are scarce in the literature and considered rare in the world [2-6].

Thus, we report two cases of *M. abscessus* cutaneous infection following injections of BoNTA injection of dramatic clinical repercussions and prolonged treatment.

Case Report/Case Presentation

Two patients had complications after cosmetic application of BoNTA in the forehead and periorbital areas with the same product and performed by the same experienced professional.

Case report 1

A 61-year-old woman was injected with BoNTA. The procedure was aseptically administered, following standardized protocol (100-unit bottle of BoNTA with 2.5 ml of normal saline). Three days after, papules and nodules appeared at all injection sites, accompanied by diffuse edema at the frontal region. After 15 days, the swelling subsided, while papules became erythematous nodules and more evident (Figure 1. A). The patient reported self-administration of prednisone 10 mg/d. When the medication was interrupted, the lesions progressed acutely and severely, resulting in abscess formation and spontaneous suppuration, with local pain and no systemic symptoms (Figure 1. B). Subsequently, an incisional biopsy was performed revealing an inflammatory infiltrate without constituting granuloma. Ziehl-Neelsen staining was negative for

alcohol-acid-resistant bacilli (AARB) and Koch's bacillus culture revealed *Mycobacterium sp*. Broad-band antibiotics for atypical mycobacteria were administered: levofloxacin 750 mg once/daily + clarithromycin 500 mg twice/daily for two months. The lesions did not show alleviation after the prescription of corticosteroids and broad-band antibiotics. Afterward, the polymerase chain reaction (PCR) of the puncture on the abscess was performed and *M. abscessus* was successfully isolated. The antibiogram showed sensitivity to amikacin; cefoxitin; linezolid; tigecycline; and resistance to ciprofloxacin; clarithromycin; doxycycline; moxifloxacin. Thus, the patient was hospitalized for drug administration (amikacin 500 mg five times/week IV + azithromycin 500 mg once/daily + imipenem 500 mg twice/daily IV + levofloxacin 500 mg once/daily). After 30 days, the lesions were milder, decreased in size, crust formation developed, and suppuration was absent (Figure 1. C). Ototoxicity and hepatic and renal alterations were observed. Treatment proceeded at home for another two months (linezolid 600 mg once/daily + cefoxitin 1 g twice/daily IV + amikacin 500 mg five times/week IV). After five months of treatment, absolute infection control, regression of lesions, and skin lightening were observed. No recurrences occurred in 6, 12, and 24 months of follow-up, but deep scars developed (Figure 1. D). The patient was referred for a surgical procedure to repair the scars and a new application of BoNTA. There were no intercurrences.

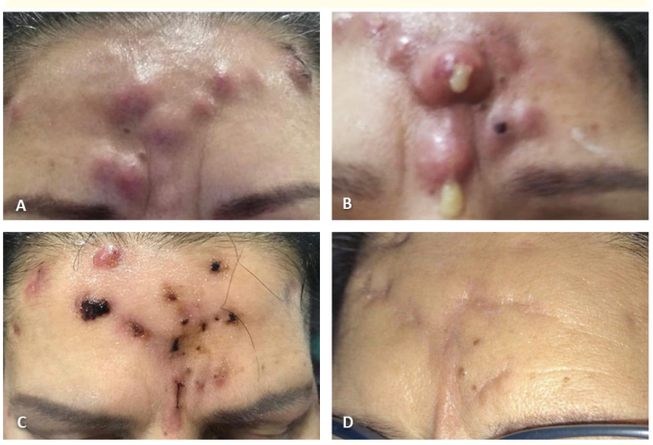

Figure 1: A. Clinical Evolution: erythematous nodules at the BoNTA application sites (15 days). B: abscess development and spontaneous suppuration (30 days). C: lesions were milder, smaller, absence of suppuration and the apparition of crusts (3 months). D: Deep facial scars at the toxin application sites (2 years).

Case report 2

A 31-year-old woman after three days of receiving facial BoNTA injections presented papules and nodules, accompanied by diffuse edema at the frontal region (Figure 2. A). For 15 days, the lesions evolved sub-acutely, and the papules became nodules of fibrous consistency, restricted to the points of application, with no edema and hyperemia (Figure 2. B). As in case 1, the patient reported self-administration of prednisone for 60 days, and after the medication was interrupted, the nodules became violaceous and more expressive (Figure 2. C). There were no local symptoms or systemic repercussions. Laboratory tests also showed *M. abscessus.* The medications administered followed the same pattern as Case 1 until hospital admission. In 30 days, a slight improvement in the lesions was observed. Then, the patient was transferred to the hospital (linezolid 600 mg once/daily + tigecycline 50 mg twice/daily + amikacin 500 mg once/daily). The central catheter was placed in the external jugular vein. There were transient hepatic and renal alterations and side effects such as nausea, diarrhea, and fungal infection. Ototoxicity was not observed. At four months of treatment, there was complete control of infection, complete remission of the lesions, and skin lightening. No recurrences occurred in 6, 12, and 24 months of follow-up. BoNTA injections were applied again in the frontal and periorbital regions with satisfactory effect and no intercurrences (Figure 2. D).

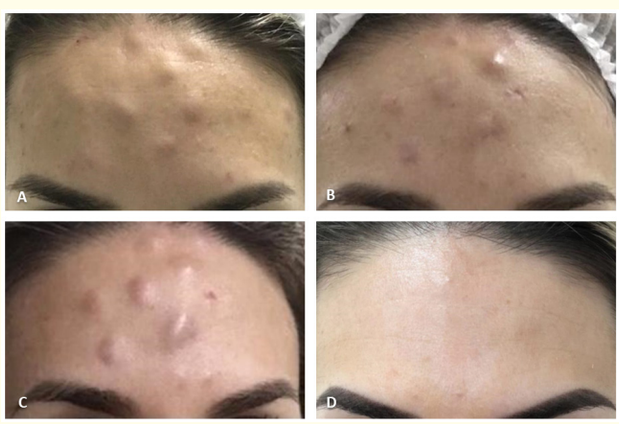

Figure 2: A. Clinical Evolution: papules and nodules without color alteration at the BoNTA application sites, accompanied by generalized edema in the frontal region (3 days). B: papules turned into fibrous nodules (15 days). C: nodular lesions became violaceous and more expressive (80 days). D: remission of lesions without scarring (4 months).

Discussion

BoNTA complications are usually transient and minimal [5]. Injection site infections or long-term reactions are rare [2]. Site infections of *M. abscessus* associated with the application of BoNTA are even rarer in the world [6]. To the best of our knowledge, our cases were the only reports of *M. abscessus* infection associated with BoNTA that had dramatic clinical repercussions, long-lasting hospital treatment with multiple intravenous drugs, and requirement of surgical intervention for correction of aesthetic sequels.

The main mechanisms of *M. abscessus* infection are aerosol route, dust, water, ingestion, and inoculation through the skin [7]. In the cases presented, the *M. abscessus* may have been introduced as a contaminant at any step during the procedure with BoNTA.

Tap water and saline solution exposed to the environment or already opened and antiseptics used to sterilize the injection site may be contaminated can be considered the most plausible source of contamination [8]. Other sources of contamination reported are contaminated needles, metal objects, drug delivery systems, drugs, or marking solutions used in the procedure [8]. In our cases, procedures were performed according to standardized aseptic protocol. The product was registered and commercialized under several branches under strict quality industrial control. No similar cases among other professionals and cosmetic consultancies in the same manufacturer of the BoNTA supplied were identified. Although there is no evidence, we consider that dilution in saline solution may have been the most sensitive step and a possible source of contamination due to greater exposure to the environment. Another hypothesis would be that the contaminated water was transformed into ice, which was in contact with the BoNTA application points for analgesia. Anyway, our understanding is that the cases are not necessarily considered iatrogenic.

Recent speculations attribute the increase in non-tuberculous mycobacterium (NTM) cutaneous infection rates to the exponential increase in cosmetic procedures [5-7]. And more recently, NTM cutaneous infections associated with the application of BoNTA [2,6,7]. Skin infections by NTM may manifest as localized erythematous papules/pustules, nodules, granulomas, ulcers, or abscesses [2,8,9]. In case 1, the clinical course was more severe. That may be justified by the patient's advanced age, delay in seeking medical recourse, and the physical and emotional impact of the changes in daily habits as a result of social isolation. Local factors, in addition to the patient's immune response, may favor the installation of infection [2,8,9]. In case 2, lesions' course was similar to previous reports, regardless of the bacteria involved [2,4,6,10]. However, concerning the treatment, both cases differ due to the specific bacterial sensitivity and need for mainly intravenous therapy in a hospital.

The treatment of *M. abscessus* infection may be challenging due to the bacteria's multidrug resistance and difficult and prolonged diagnosis [8]. According to the summary, macrolide antibiotics, such as clarithromycin combined with other antibiotics according to drug sensitivity testing, are recommended to be the initial therapy for at least four months [6]. Clarithromycin was initially administered without success, and after resistance by the antibiogram, it was replaced and disregarded. Regarding amikacin, it was effective only when associated with sensitive drugs. Sensitivity data are needed to guide treatment, which requires drug association for an extended period. Treatment time varies substantially from weeks to months, not having a standard protocol because there is a lack of data, differences in sensitivity among bacteria, and variation in the clinical course [8]. The treatment was concluded with complete remission of lesions and skin lightening after 4-5 months.

The long period of hospitalization caused systemic alterations such as nausea, diarrhea, nutritional deficit, weight loss, fungal infection, and transient liver and kidney function alterations in both cases. The prolonged use of amikacin provoked ototoxicity in case 1, with mild hearing loss in the left ear. The aesthetic sequel had a meaningful psychological impact when the pursuit of a cosmetic procedure to improve self-esteem resulted in hospitalization, a high load of medications, and all its consequences. The patient of case 1 was referred to psychological treatment for better acceptance of the facts and her own face. Despite the consequences generated by the infectious process, we emphasize that there is no contraindication to a new application of BoNTA.

Conclusion

BoNTA is one of the most popular cosmetic procedures performed worldwide; however, each application involves an operational risk. The consequences caused by aesthetic procedures are rarely discussed and can significantly impact the patient's self-esteem and physical and psychological status. The repercussions can be unpredictable, such as the need for long-term treatments and aesthetic damage of difficult reparation. Therefore procedures must strictly follow the aseptic protocols performed in an appropriate local by experienced professionals, using registered products in order to minimize all risks.

Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Dr. Luisa Barin: supervision; conceptualization; resources; writing-original draft preparation; writing-reviewing and editing. Kathleen Jarmendia-Costa: visualization; data curation; writing-reviewing and editing; writing-original draft preparation. Isabela Reginaldo: data curation; writing- reviewing and editing; writing-original draft preparation.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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