



*Case report*

## **Mycobacterium chelonae-induced granulomatous nodules following botulinum toxin injections: A case report and literature review**

**Joe Khodeir<sup>1,\*</sup>, Paul Ohanian<sup>2</sup> and Ali Awwad<sup>3</sup>**

<sup>1</sup> University of Balamand, Faculty of Medicine and Medical Sciences, Department of Dermatology, Saint Georges Hospital University Medical Center, Lebanon

<sup>2</sup> University of Balamand, Faculty of Medicine and Medical Sciences, Department of Family medicine, Saint Georges Hospital University Medical Center, Lebanon

<sup>3</sup> Wayne state University, Faculty of Medicine, Department of Internal Medicine, Detroit Medical Center, USA

\* **Correspondence:** Email: [joe.khodeir@std.balamand.edu.lb](mailto:joe.khodeir@std.balamand.edu.lb); Tel: +96171610580; Fax: +9611562110.

**Abstract:** Background: Non-tuberculous mycobacteria (NTM)-induced nodules following botulinum toxin injections are increasingly being reported. These infections can present as persistent nodules or abscesses, posing significant diagnostic and therapeutic challenges. Case Presentation: We report a case of a 35-year-old healthy male who developed multiple tender and painful nodules localized at injection sites on the forehead and periorbital areas three weeks after receiving Onabotulinum toxin injections from an untrusted provider. Initial treatment with oral steroids and empiric antibiotics was ineffective. Biopsy and NTM PCR confirmed the presence of *Mycobacterium chelonae*. The patient was successfully treated with a six-month regimen of oral clarithromycin, levofloxacin, and trimethoprim/sulfamethoxazole, resulting in complete remission without relapse at the eight-month follow-up. Discussion: A comprehensive review of the literature revealed eight reported cases of NTM-induced granulomatous nodules following botulinum toxin injections. These cases predominantly involved female patients and were associated with *Mycobacterium abscessus*, *Mycobacterium immunogenum*, and unidentified NTM species. This case is the first reported instance of *Mycobacterium chelonae* as an etiological agent in such a context. Effective management involves early biopsy, accurate microbiological diagnosis, and tailored antimicrobial therapy. Conclusion: This case emphasizes the need for clinicians to consider NTM infections in patients with persistent nodules post-botulinum toxin injections, especially when initial treatments fail. To prevent such infections, it

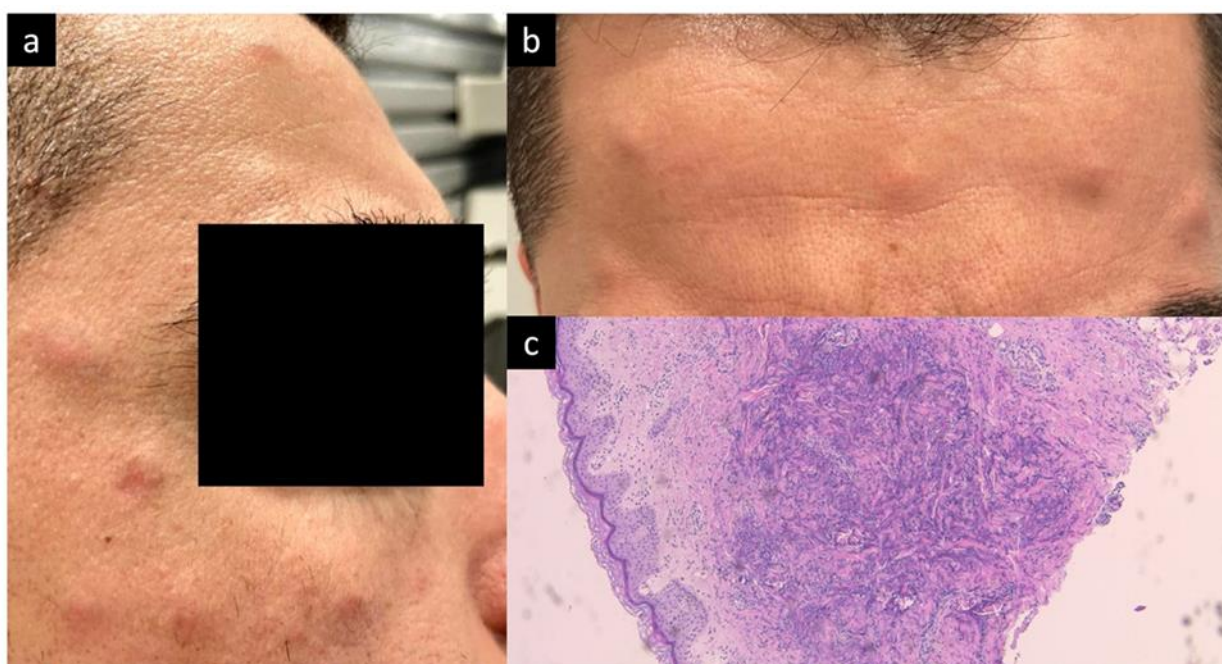
is crucial for patients to seek treatment from trusted and licensed providers who use authentic products and maintain sterile environments during procedures.

**Keywords:** botox; botulinum toxin; NTM skin infection; botox induced nodules; botox induced granulomas; treatment

## 1. Introduction

Non-tuberculous mycobacteria (NTM)-induced nodules following botulinum toxin injections are increasingly being reported [1–3]. These infections often present as persistent nodules, which can be challenging to diagnose and manage [3–5]. This report presents a rare case of *Mycobacterium chelonae*-induced granulomatous nodules following botulinum toxin injections and includes a comprehensive review of the literature on NTM infections specifically related to botulinum toxin procedures. The aim is to highlight the importance of accurate diagnosis, appropriate antimicrobial therapy, and to provide an overview of reported cases to inform clinical practice.

## 2. Case presentation



**Figure 1.** Erythematous inflamed nodule seen on the injection sites on the periorbital region (a) and forehead (b). c) H&E stain x 20, showing interstitial granulomatous inflammation with moderate mixed inflammatory infiltrates in favor of a suppurative granuloma.

A 35-year-old healthy male presented with multiple tender and painful nodules localized at injection sites on the forehead and periorbital areas. These nodules appeared three weeks after receiving Onabotulinum toxin injections from an untrusted provider. Initially, the patient was treated with oral

steroids by his initial provider without any improvement. On examination, the nodules were tender and erythematous, confined to the injection sites, and no lymphadenopathy was observed (Figure 1a,b). Empiric antibiotic therapy with oral ciprofloxacin 500 mg twice daily and clindamycin 900 mg daily was initiated to cover potential bacterial infections. However, there was no improvement after three days of treatment. A biopsy was performed on the largest nodule. The specimen was sent for histopathology to rule out mycobacterial infection or sarcoidosis. Additional samples were sent for mycobacterial, bacterial, and fungal cultures, along with NTM PCR testing. Histopathological analysis revealed interstitial granulomatous inflammation with mild necrosis, indicative of a suppurative granuloma (Figure 1c). NTM PCR confirmed the presence of *Mycobacterium chelonae*. Antimicrobial susceptibility testing was performed, showing no resistance. Based on the diagnosis of NTM-induced granulomatous nodules, the patient was started on a combination therapy of oral clarithromycin 500 mg, levofloxacin 500 mg, and trimethoprim/sulfamethoxazole 160 mg/800 mg, all administered twice daily for six months. Significant improvement was noted six weeks into the therapy, with total remission observed at four months. At an eight-month follow-up, the patient showed no signs of relapse.

### 3. Discussion

A comprehensive review of the literature identified eight reported cases of botulinum toxin-induced granulomatous nodules attributed to NTM infection. The key characteristics of these cases are summarized in Table 1.

#### 3.1. Demographics and clinical presentation

The eight cases involved female patients with a mean age of 38 years. Six cases were associated with botulinum toxin injections for wrinkle treatment, while two cases were related to injections for masseter hypertrophy. The nodules typically appeared an average of 20 days post-injection and were characterized by painful, erythematous, and violaceous lesions, with some cases progressing to abscess formation [1–7].

#### 3.2. Histopathological and microbiological findings

Of the eight cases, six underwent biopsy, which revealed suppurative granulomas [1–4,6,7]. In the remaining two cases, a biopsy was not performed due to positive culture results [1,2]. All isolated organisms were identified as NTM. Specifically, five cases were caused by *Mycobacterium abscessus* [2–5], one case by *Mycobacterium immunogenum* [7], and one case was culture and PCR-negative but treated empirically based on strong clinical and histological suspicion [6]. One case presented with acid-fast positive bacilli on histology, but the specific NTM species was not identified [1]. Notably, nodules caused by *M. abscessus* appeared between 4 to 10 days post-injection, while the nodule due to *M. immunogenum* emerged 3.5 months after the procedure [2–5,7].

To date, no previous cases of *M. chelonae* associated with botulinum toxin-induced granulomatous nodules have been reported in the literature. The identification of this organism in our case thus represents the first documented instance of *M. chelonae* as an etiological agent in such a context.

**Table 1.** Summary of all reported botulinum toxin-induced nodules attributed to NTM infection.

| Study                  | Age & Sex | Toxin Source       | Clinical Presentation  | Histology   | Organism                         | Treatment   | Outcome  |
|------------------------|-----------|--------------------|--|---|----------------------------------|---|--|
| Li et al.              | 39/F      | NA                 | Painful nodules at injection sites 1 week later                                  | Necrotic granuloma                                    | <i>M. abscessus</i> (PCR)        | Levofloxacin 500 mg BID, clarithromycin 500 mg BID (stopped in 1 week), surgical excision   | NA   |
| Thanasarnaksorn et al. | 42/F      | Neuronox®          | Tender nodules at all sites of injection 4 days later                            | Suppurative granuloma                                 | Negative culture and PCR for NTM | Clarithromycin 500 mg/day, levofloxacin 500 mg/day for 6 months (empirically)   | Major improvement at 6 weeks, full resolution at 6 months  |
| Deng et al.            | 53/F      | NA                 | Painful nodules and abscesses at injection sites 10 days later                   | Suppurative granuloma                                 | <i>M. abscessus</i> (culture)    | Amikacin 200 mg, clarithromycin 500 mg, moxifloxacin 400 mg for 7 months  | Full resolution after 7 months                             |
| Chen et al.            | 32/F      | Non-trusted source | Painful papules and nodules on all injection sites 1 week later                  | Suppurative granuloma                                 | <i>M. abscessus</i> (culture)    | Prednisone 30 mg/d, intravenous azithromycin, clarithromycin 250 mg BID, rifampicin 450 mg daily, ethambutol 250 mg TID for 3 months            | Full resolution after 3 months with atrophic scars and PIH |
| Chen et al.            | 34/F      | Non-trusted source | Painful papules and nodules on lower jaw, malar, and temple region 10 days later | Biopsy not done                                       | <i>M. abscessus</i> (culture)    | Intralesional corticosteroids, oral penicillin, gentamicin, debridement, clarithromycin 250 mg BID, rifampicin 450 mg daily for nearly 6 months | Full resolution after 6 months with scarring and PIH       |
| Yeon et al.            | 34/F      | Unknown source     | Tender nodule over the left mandible after 3.5 months                            | Suppurative granuloma                                 | <i>M. immunogenum</i> (culture)  | Phenoxymethylpenicillin, clindamycin, clarithromycin 500 mg BID for 6 months  | Full resolution  |
| Saeb-Lima et al.       | 45/F      | NA                 | Tender nodules at points of injection 1 week later                               | Suppurative granuloma with acid-fast positive bacilli | Culture not done                 | Rifampicin, clarithromycin, azithromycin for 40 days  | Full resolution with PIH                                   |
| Ou et al.              | 25/F      | Unknown source     | Painful nodules on cheeks 10 days later  | Biopsy not done                                       | <i>M. abscessus</i> (culture)    | Azithromycin for 2 weeks, surgical excision, clarithromycin 300 mg for 6 months   | Full resolution with dog-ear deformity after excision      |

### 3.3. Management

In patients presenting with nodules after botulinum toxin injections, initial management can include oral antibiotics and topical treatments [8,9]. It is crucial to avoid starting oral steroids empirically due to the high risk of infectious nodules compared to non-infectious ones. Biopsy remains the gold standard for determining the etiology of the nodule. If the nodule is found to be inflammatory, such as in sarcoidal nodules, systemic steroids along with immunosuppressive agents may be administered [8,10–14]. However, if the histology shows suppurative or necrotic features, NTM infection should be ruled out using special stains, cultures, and PCR [9].

### 3.4. Treatment

For infectious granulomas with positive NTM PCR or culture results, treatment should be tailored according to antibiotic sensitivity profiles. Since *M. abscessus* is the most frequently isolated organism and is known for its rapid growth and high resistance rates, combination therapy involving at least two antimicrobial agents is recommended for a duration of 4 to 6 months. Preferred treatments include a macrolide, such as clarithromycin, paired with agents like amikacin, levofloxacin, cefoxitin or tigecycline [15–17].

In the single case involving *M. immunogenum*, successful treatment was achieved with clarithromycin 500 mg twice daily for six months [7]. Antimicrobial therapy alone led to complete remission in five cases, though post-inflammatory hyperpigmentation (PIH) was noted in three instances [1,2]. When antimicrobial therapy proved insufficient, surgical excision or debridement was performed in three cases, despite the higher risk of scarring associated with these procedures [2,4,5].

Given that negative cultures and PCR results are not uncommon in NTM infections, it is crucial to consider NTM infection as a potential cause of suppurative granulomas with negative test results. For cases with strong clinical and histological suspicion, multiple specimens should be tested through culture and PCR if initial tests are negative. Alternatively, empirical treatment can be initiated based on clinical and histological findings [15,16]. This approach was exemplified by Thanasarnakorn et al., who achieved full remission with a six-month regimen of clarithromycin and levofloxacin despite initial negative test results [6].

## 4. Conclusion

This case, along with the review of the literature on NTM infections following botulinum toxin injections, underscores the necessity for clinicians to consider NTM infections in patients presenting with persistent nodules post-procedure, particularly when initial treatments fail. This is the first reported case of *M. chelonae* as the etiological agent in such a context. To prevent such infections, it is crucial for patients to seek treatment from trusted and licensed providers who use authentic products and perform procedures in sterile environments.

### Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

## Conflict of interest

The authors declare no conflict of interest.

## Author contributions

Joe khodeir conceived the study, diagnosed and managed the patient, and drafted the manuscript. Paul ohanian conducted the literature review and contributed to the manuscript writing. Ali Awwad contributed to the diagnosis and treatment discussion with overall supervision. All authors critically reviewed and approved the final manuscript.

## Ethics approval of research

The patient in this manuscript has given written informed consent to the publication of their case details.

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