

To find out the co-relation between Nodule formation after Botox and Covid-19 vaccination.

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Abstract:

This case series examines the rare phenomenon of nodular formation following botulinum toxin injections, focusing on patient demographics, clinical presentations, and treatment approaches. The study includes diverse cases from various geographic regions to illustrate the complexity and variability in patient responses and outcomes. Following the COVID-19 pandemic and vaccination, there has been an increase in various adverse effects (AEs) and serious adverse effects (SAEs), including blood clotting and elevated stroke rates among vaccinated individuals.

The first case involves a woman in her mid-40s, a frequent Botox user with a history of back and muscle pain, who contracted COVID-19 shortly before her injection. Post-injection, she developed painful nodules on her forehead and neck, initially treated with oral and intravenous steroids, antibiotics, and antihistamines. While she experienced some early improvement, noncompliance led to further complications, requiring additional interventions like massage and heat application. Ultimately, after sustained steroid therapy and surgical drainage, the nodules resolved.

The second case focuses on a mid-50s woman with hypertension and hypothyroidism who also developed similar nodules after botulinum toxin injections but did not seek follow-up care. After receiving treatment from another physician involving steroids and antibiotics, she recovered after more than a year.

This paper highlights a recurring pattern of nodular issues post-COVID-19 across various regions. Treatment approaches varied, including intralesional injections,

steroids, and other topical and systemic therapies, with resolution times ranging from one week to several months.

The findings underscore the importance of patient compliance and thorough pre-procedure discussions. Factors such as COVID-19 history, saline dilution types, and injection techniques may contribute to nodular formation. The study calls for further research to establish standardized management practices and address the underlying causes of these rare but significant complications.

Here's a rephrased version of your introduction, streamlined for clarity and conciseness:

Introduction:

Botulinum toxin injections remain the most popular nonsurgical cosmetic procedure worldwide, achieving high patient satisfaction and efficacy rates. Generally, botulinum toxin demonstrates an excellent safety profile and is well-tolerated therapeutically. When adverse effects do occur, they are often moderate, transient, and self-limiting. The demand for nonsurgical cosmetic procedures has surged in recent years, with the Aesthetic Surgery Report (2022) noting that 28% of the \$11.8 billion revenue in the sector comes from this area, primarily driven by dermal fillers, skin treatments, and neuromodulators. These options are favored for their ability to enhance confidence, reduce signs of aging, and rejuvenate appearances with minimal recovery time, distinguishing them from surgical alternatives.

Despite the transformative impact of minimally invasive procedures on cosmetic surgery and medicine, challenges and potential drawbacks remain. Nodular formations and lumps, although rarely reported after botulinum toxin treatment, can lead to significant distress for both patients and clinicians due to the unclear etiology and lack of consensus on management strategies. This paper examines cases of patients who developed nodular eruptions shortly after receiving botulinum toxin type A injections. We detail the clinical presentation and management of this rare side effect and review the existing literature to compare similarities and differences in reported cases.

Notably, the majority of these nodules were observed in patients who had previously contracted COVID-19 and received COVID-19 vaccinations or boosters. Our primary objective is to investigate the relationship between nodular formation following Botox treatment and COVID-19 vaccination or booster administration.

pt no	Patients having Nodules formation	pt who had covid	pt who had vaccine and booster
1	yes	yes	yes
2	yes	yes	yes
3	yes	no	yes
4	yes	yes	yes
5	yes	no	yes
6	yes	no	yes
7	yes	no	yes
8	yes	no	yes
9	yes	no	yes
10	yes	no	yes
11	yes	no	yes
12	yes	no	yes
13	yes	no	yes
14	yes	no	yes
15	yes	no	yes
16	yes	yes	yes
17	yes	yes	yes
18	yes	yes	yes
19	yes	no	yes
20	yes	No	No
21	yes	yes	yes
22	yes	no	yes
23	yes	no	yes
24	yes	no	yes
25	yes	no	yes
26	yes	no	yes

Data Overview

- **Total Patients:** 26
- **Nodule Formation:** All 26 patients (100%) experienced nodule formation.
- **COVID-19 History:**
 - **Yes:** 7 patients
 - **No:** 19 patients
- **Vaccination and Booster Status:**
 - **Yes:** 25 patients
 - **No:** 1 patient

Findings

1. **Nodules and COVID-19 History:**
 - Among the 7 patients with a history of COVID-19, all received vaccines or boosters and experienced nodule formation.
 - The 19 patients without COVID-19 history also developed nodules, with 16 of these patients having received vaccines/boosters.
2. **Nodules and Vaccination Status:**
 - Of the 25 patients who were vaccinated, all had nodule formation regardless of their COVID-19 history.
 - Among the 1 unvaccinated patient, also developed nodules, and had no history of COVID-19.

Insights

- There is a high prevalence of nodule formation across all groups, regardless of COVID-19 infection history or vaccination status, although the majority were vaccinated.
- This suggests that while there may be a trend of nodule formation in vaccinated patients, further analysis is needed to determine if COVID-19 or vaccination directly impacts the risk.

Data Analysis:

To analyze the data thoroughly, let's look into the correlation between nodules formation and the variables—COVID-19 history and vaccination/booster status. I'll summarize key findings, calculate correlation metrics, and highlight any patterns or trends that emerge from the data.

Summary of Data

Category	Count (out of 26)	Percentage
Patients with Nodules	26	100%
Patients with COVID-19 History	7	26.9%
Patients without COVID-19 History	19	73.1%
Patients with Vaccination and Booster	25	96.1%
Patients without Vaccination and Booster	1	3.8%

Key Observations

1. **Nodule Formation in All Patients:** Every patient in the dataset (100%) developed nodules following botulinum toxin injections, indicating that nodule formation was common across all groups in this study.
2. **COVID-19 History and Nodules:** Among patients who had COVID-19 (7 out of 26), all were vaccinated, and all developed nodules. This suggests a

possible association between COVID-19 history and the occurrence of nodules in the vaccinated population.

3. **Vaccination and Nodules:** Of the 25 vaccinated patients, all had nodules. The one patient who did not receive vaccination or boosters also developed nodules. This indicates that, in this dataset, vaccination alone does not fully account for the nodules since the unvaccinated patient also developed them.

Potential Statistical Analysis

To understand if there is a statistically significant correlation between COVID-19 history, vaccination status, and nodule formation, we could perform a few analyses (if the sample size were larger and more diverse):

1. **Chi-Square Test for Independence:**
 - This test could help determine if there is a statistically significant relationship between COVID-19 history and vaccination status with nodule formation. However, since every patient in the dataset developed nodules, this test might not yield meaningful results due to a lack of variability in the outcome (nodule formation).
2. **Correlation Coefficient:**
 - Calculating a correlation coefficient between variables (e.g., COVID-19 history and vaccination status) might give insights into the strength of relationships between these factors.
3. **Logistic Regression:**
 - With a larger sample, logistic regression could help predict the probability of nodule formation based on COVID-19 history and vaccination status.

Insights and Implications

1. **High Nodule Formation Rate Across All Groups:**
 - The data reveals that nodules formed in all cases, regardless of COVID-19 or vaccination status. This might suggest that other factors not included in the dataset—such as injection technique, type of botulinum toxin used, or individual patient characteristics—could be significant contributors.
2. **COVID-19 and Vaccination Overlap:**
 - The majority of patients with a history of COVID-19 (100%) were also vaccinated. This could indicate an additive or interacting effect between COVID-19 and vaccination on the risk of nodule formation. However, this cannot be confirmed without a larger sample size and more data variability.
3. **Further Investigation Needed:**
 - While this case series provides interesting preliminary data, the sample is limited, and other variables may need to be considered to clarify any causal relationships. Future studies could incorporate factors like injection technique, botulinum toxin brand, and patient immune response profiles.

1. Nodule Formation Observed in All Patients (100%)

- **Result:** Every patient in the case series (26 out of 26) developed nodules following botulinum toxin injections, irrespective of COVID-19 history or vaccination status.
- **Interpretation:** This high incidence of nodules suggests that other, possibly uncontrolled factors (such as injection technique, patient immune response, or toxin type) may be contributing to this outcome. The common occurrence of nodules across all groups raises questions about the role of botulinum toxin in the context of post-COVID-19 vaccination.

2. Correlation Between COVID-19 History and Nodule Formation

- **Result:** 7 patients (26.9%) had a history of COVID-19, and all of them were vaccinated. They all developed nodules.
- **Interpretation:** Although the dataset suggests a link between COVID-19 infection, vaccination, and nodule formation, the data does not confirm causation. Given the small sample and lack of variability (all cases had nodules), we cannot conclusively determine if COVID-19 history directly influences nodule formation after Botox.

3. Vaccination and Nodule Formation

- **Result:** Out of 26 patients, 25 (96.1%) were vaccinated, and all developed nodules. The 1 unvaccinated patient also developed nodules.
- **Interpretation:** Vaccination does not appear to be the sole factor linked to nodule formation, as nodules were observed in both vaccinated and unvaccinated patients. However, the high percentage of vaccinated individuals with nodules could hint at an immune response interplay in vaccinated individuals, potentially influencing nodule formation.

4. Lack of Clear Association Due to Uniform Outcome

- **Result:** Since all patients developed nodules, there is no variation in the outcome to analyze a difference in nodule formation based on COVID-19 or vaccination status.
- **Interpretation:** The lack of a control group (i.e., patients who received Botox but did not develop nodules) limits the ability to discern clear associations or risk factors. A larger and more diverse sample size with both affected and unaffected patients would be required to identify any meaningful patterns or causative factors.

Final Interpretation

This case series reveals a potential trend in nodule formation following botulinum toxin injections, particularly in patients with recent COVID-19 infection or vaccination history. However, the universal outcome of nodules across all patients

prevents us from establishing a definitive relationship between COVID-19, vaccination status, and nodule formation. These findings suggest the need for further research with a larger, more varied sample to understand the role of post-COVID-19 immune responses or other factors in nodule development.

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2. A study reviewed cosmetic filler reactions post-COVID-19 vaccination, noting inflammatory nodules and hypersensitivity responses, which may share mechanisms with post-botulinum toxin nodule formation in vaccinated individuals ([Guelinckx et al., Journal of Cosmetic Dermatology, 2021](#)).
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