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EDITORIAL

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Methotrexate as a game-changer for COVID-19 vaccine-related dermal nodules

Patrick Joseph Treacy

Department of Dermatology, Medical Director, Cork, Ireland

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During the COVID-19 pandemic, an unexpected issue emerged among patients who had previously received cosmetic dermal fillers. Reports surfaced of delayed-onset swelling, nodules, and other inflammatory reactions following mRNA-based vaccines like Moderna and Pfizer and the viral vector AstraZeneca vaccine. Although rare, these side effects raised concerns within the medical and cosmetic industries. Initially, the complications were thought to result from a Type IV hypersensitivity reaction an immune system response to what it recognized as foreign material, such as fillers [1]. While treatments such as antihistamines, hyaluronidase, and intralesional steroids were attempted, many patients experienced only limited or temporary relief. Some presented with severe cases, including clusters of multiple hard nodules in areas treated with fillers, causing significant cosmetic and psychological distress [2]. These challenges have left healthcare providers and dermatologists questioning: How should these vaccine-associated filler reactions be managed effectively? Are current treatment protocols enough to address these complications?

With more patients receiving booster doses, the problem has grown, highlighting the need for better solutions. In this context, methotrexate, a chemotherapy agent with immunosuppressive properties has emerged as a potential treatment option. Could methotrexate be the answer to managing these stubborn complications? This editorial explores the implications and potential of this novel approach, urging the medical community to consider newer, evidence-based strategies for patient care [3].

Discussion of the Issue

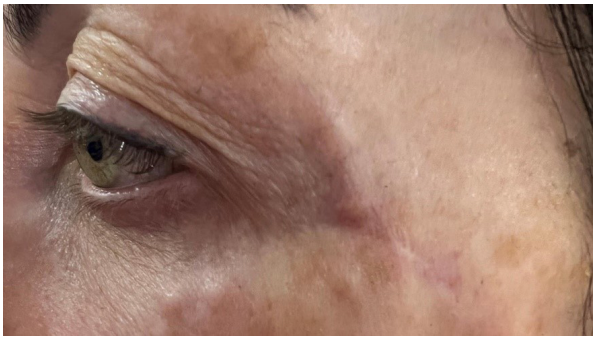
The COVID-19 pandemic revealed unexpected complications in patients with dermal fillers, particularly following vaccination. Reactions were reported with both mRNA vaccines (e.g., Moderna, Pfizer/BioNTech) and viral vector vaccines (AstraZeneca), suggesting that different vaccine technologies could trigger immune responses [4] (Figures 1-3).

This raised concerns among clinicians about managing these unforeseen complications. Managing these nodules has been challenging, with many patients unresponsive to treatments like antihistamines, hyaluronidase, steroids, and 5-fluorouracil (5-FU) [5]. In severe cases, excision of the filler material was considered, though it was reserved as a last resort. Some patients developed persistent nodules that resisted all established protocols, presenting with multiple nodules weeks after their vaccinations (Figures 4 and 5).

Figure 1,2, and 3. Swelling, nodule formation, and immune responses post-vaccination in dermal filler patients (Source: Images are taken by author)

Figures 4 and 5. Clinical examination showing filler-induced swelling resistant to conventional treatment protocols (Source: Images are taken by author).

The immune system's hypersensitivity to filler materials plays a crucial role in these cases. The complications are driven by two types of immune overreactions: Type I hypersensitivity, where IgE antibodies trigger immediate allergic reactions, and Type IV delayed hypersensitivity, where immune cells respond weeks later (Figure 6) [6].



Figures 6. Hypersensitivity reactions varying by filler type, highlighting immune-related complications (Source: Image is taken by author).

***Correspondence:** Professor Patrick Joseph Treacy, Department of Dermatology, Medical Director, Ailesbury Clinics, Ireland, e-mail: ptreacy@gmail.com

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This unpredictability makes it difficult to manage these cases effectively and points to gaps in existing treatment protocols. In pre-pandemic times, dermal filler complications were rare and generally manageable. However, COVID-19 vaccines have introduced an unexpected dimension to these complications. The overlap between aesthetic procedures and immunology is becoming increasingly clear, highlighting the need for updated clinical guidelines to address these emerging challenges. Moving forward, a more comprehensive approach involving both dermatologists and immunologists will be essential to improve patient care and develop standardized treatment protocols [7].

Methotrexate as a New Solution

Methotrexate, a well-known immunosuppressant often used for conditions like rheumatoid arthritis and psoriasis, is now offering new hope for patients struggling with vaccine-related filler complications. In many cases, conventional treatments like steroids and antihistamines provided little relief, leaving patients with lingering swelling and discomfort. This is where methotrexate works when other treatments fall short. Given these promising outcomes, methotrexate opens a new avenue for managing immune-related complications [8]. Over a three-month period, patients experiencing significant facial disfigurement reported notable improvement, with their nodules gradually disappearing. Its ability to fine-tune immune responses makes it especially effective in these situations. Although traditionally used for autoimmune diseases, methotrexate's role in treating post-vaccine filler nodules presents an exciting, underexplored opportunity. With its potential to calm immune overreactions, it may become a valuable tool for clinicians addressing rare but distressing side effects linked to vaccinations. As ongoing vaccine efforts continue, methotrexate offers hope for improved patient care and a smoother path forward for those experiencing complications [9].

Reflections on Future Direction

Should dermatologists monitor filler patients more closely after vaccination? This study highlights how dermal fillers, typically considered safe, triggered immunological responses post-vaccination, including both IgE-mediated and delayed hypersensitivity reactions. These immune reactions led to nodule formation, causing discomfort and disfigurement in patients. Notably, the variations in filler types, such as hyaluronic acid and poly-L-lactic acid, can influence their interaction with the immune system, suggesting a need for more cautious use and individualized patient assessments [10].

Given the complex immune dynamics involved, a collaborative effort between immunologists and dermatologists could foster the development of standardized protocols for managing such cases. This would ensure prompt recognition and treatment of adverse reactions, enhancing patient safety. Future research could explore how different vaccines interact with fillers and whether specific vaccine formulations might carry a lower risk of inducing such reactions [11]. The success of the methotrexate protocol in resolving nodules unresponsive to other treatments demonstrates the importance of considering immunosuppressive therapies in similar scenarios. However, further studies are needed to assess long-term outcomes and refine dosage regimens to minimize potential side effects. The growing recognition of this protocol at prominent conferences, such as AIDA and IMCAS, underscores the importance of broadening awareness and advancing clinical practices in dermatology. With this approach gaining international attention, ongoing research and clinical monitoring will be pivotal in optimizing care for patients undergoing both dermal filler treatments and vaccinations [12].

Conclusions

The use of methotrexate has delivered promising results in managing delayed onset nodules linked to COVID-19 vaccinations. Patients who did not respond to traditional treatments like steroids and antihistamines found significant relief. Within three months of starting methotrexate, most nodules dissipated, greatly improving patients' quality of life. Necessity gives rise to invention as discussed by Prof. Patrick Treacy in his published article "Non-responsive Covid-19 vaccine nodules". His methotrexate method, originally published to address non-responsive Covid-19 vaccine nodules, demonstrated how necessity sparks innovation, and now this method is being used in patients with dermal filler nodules unrelated to the Covid vaccine. Just as penicillin did during World War II. Fleming's discovery became a lifesaver under pressure, much like the need for adaptable treatments today. It's this blend of urgent need and scientific ingenuity that keeps pushing medical progress forward.

Disclosure Statement

No potential conflict of interest was reported by the author.

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