Hyaluronic acid fillers and SARS CoV-2 vaccination. Potential mechanisms associated with delayed inflammatory reactions

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It has come to our attention that some cases of delayed inflammatory reactions (DIR) have been reported in patients with history of treatment with soft tissue fillers (mainly hyaluronic acid fillers) after SARS-CoV-2 vaccination.[1,2] A wide range of symptoms have been reported, including edema, erythema, induration and swelling, among others. The reactions are typically present in the area where the filler has been administered, most commonly involving the zygomatic area, lips, tear troughs and temples. Although the reported adverse reactions are self-limiting, they can be quite stressful for both the patient and the physician.

While a thorough review of the treatment of DIR is beyond the scope of this letter, it is important to remember that the unique clinical picture and presentation of a given patient, must ultimately guide treatment. Nevertheless, we emphasise that several medications have been used by colleagues, such as lisinopril, an angiotensin converting enzyme inhibitor (ACE-1), and recombinant hyaluronidase. While still anecdotal in nature, they have been beneficial in a specific set of patients.[1] We therefore briefly present three potential mechanisms underlying DIR in patients with hyaluronic acid fillers in the setting of SARS-CoV-2 vaccination. First, we should consider the role of the major histocompatibility complex. A study performed recently by a group of multidisciplinary experts, demonstrated that patients bearing HLA subtypes B*08 and HLA DRB1*03 are at greater risk of developing a late-onset cutaneous inflammatory event to dermal fillers.[3] While this study was performed before vaccination programs were available, it is judicious to believe that specific haplotypes involved in antigen presentation and complement activation pathways, may confer susceptibility to DIR after SARS-CoV-2 vaccination. Polyethylene glycol, a polymer used as a stabiliser in certain vaccines, has been proposed as a possible and potential factor involved in anaphylactic reactions to COVID19 nano-vaccines, although there is still an ongoing debate in the scientifical community worldwide.[4] We hypothesise that individuals with known hypersensitivity reactions to polyethylene glycol may be at increased risk of a DIR in a patient with history of hyaluronic acid fillers administration in the setting of vaccination. The CD44 antigen (a cell-surface glycoprotein), participates in a wide variety of physiological functions. It is also the main ligand for hyaluronic acid and can be expressed on fibroblasts. Hyaluronic acid fragments of low to intermediate molecular weight have been shown to activate macrophages, dendritic cells, and deliver costimulatory signals to T cells.[5] It could be the case that the vaccination process acts as a trigger contributing to the local pro-inflammatory environment present in patients with fillers. Any foreign body elicits an immune response and care should be taken in patients with predisposing conditions. We must remember that adherence to dosing schedules is critical for providing maximum effectiveness against any vaccine-preventable diseases. Providers should consider deferring this type of elective aesthetic procedure in cases of recent vaccination administration.

CONFLICT OF INTEREST

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