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Case Report

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Late Onset of Multiples Nodules and Edema after the Injection of Poly-D,L-Lactic Acid (PDLLA) Treated with Intralesional Triamcinolone and Collagenase

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Abstract

Biostimulators are the latest trend in aesthetic procedures, utilizing substances like PDLLA (Poly-D, L-Lactic Acid) to stimulate collagen by inducing a controlled, subclinical inflammatory response. This subtle inflammatory reaction triggers the body's natural healing process, promoting the synthesis of new collagen fibers and enhancing skin texture and appearance. In this report, we describe a case of a 26-year-old female without any history of allergies or immune disorders. She developed multiple nodules and swelling three months after receiving PDLLA injections (Aesthefill, Regen Biotech, Seoul, South Korea) in the temporal, cheek, and mandibular regions. Upon examination, we prescribed an oral dose of prednisone at 20 mg daily for three days and administered intralesional Triamcinolone (Triamcicort) 40 mg /ml injections for each nodule. After three treatments of Triamcinolone, the size of the nodules decreased, prompting us to proceed with intralesional collagens (Inbiogenase, Inbiotec, Spain) injections, which led to the complete resolution of the nodules.

Keywords: *Poly-D,L-Lactic Acid, Triamcinolone, Collagenase, Granuloma, Treatment Outcome.*

1. Introduction

For many years, dermal fillers such as hyaluronic acid have been commonly used in cosmetic procedures; However, more recently, patients have opted for biostimulants as an alternative to hyaluronic acid fillers. They are attracted to biostimulants for their ability to naturally stimulate collagen production, rather than simply filling the area, as hyaluronic acid products do [1, 2]. Biostimulants such as poly-L-lactic acid (PLLA) and poly-D, L-lactic acid (PDLLA) promote collagen synthesis by stimulating fibroblasts through a subclinical inflammatory response [3, 4, 5]. These substances are designed to be absorbed into body tissue, but side effects associated with collagen inducers, specifically nodules, and granulomas, have occasionally been reported.

It is crucial to distinguish between these reactions, as they have different origins and clinical manifestations [3, 6]. A granuloma typically results from an excessive inflammatory response by the body. It presents clinically with significant swelling, a large, hard mass that can be felt and palpated at the injection sites. The presence of a granuloma should be verified by histopathological examination [4, 6]. The onset of this reaction can occur between 6 and 24 months after the injection and can be the size of a bean or larger and may be accompanied by skin discoloration and swelling. This condition generally responds well to treatment with intralesional steroids [4, 6].

On the other hand, a nodule results primarily from an unusual accumulation of the product, often due to incorrect application techniques or accumulation in active facial muscles (orbicularis oris muscle). Clinically, these nodules are well-defined, and their visibility may vary depending on their location, such as the neck, hands, or forehead, which are visible regions [4, 5]. Nodules mostly begin to appear between 1 and 2 months after application and are usually solitary, located near dynamic muscles. Their size can vary from that of a lentil to that of a pea or larger. They may or may not respond effectively to intralesional steroids. In rare cases, surgical removal may be necessary [6].

When administering a biostimulant, we cannot predict our patients' immune response, and it is crucial to follow a protocol that guides us in the management of these types of reactions. Therefore, this case report aims to demonstrate the clinical management of the appearance of nodules and swelling in a patient 3 months after application of PDLLA to the temporal region, cheek, and jaw.

2. Case Report

A 26-year-old woman without any history of allergies or immune diseases visited our Aesthetic Department three months after receiving a PDLLA (Aesthefill 200 mg/vial, Regen Biotech, Seoul, South Korea) treatment. As a care protocol, a photographic record was made prior to the application of the PDLLA, which has been used in this report to observe the comparisons (Figure 1A, 1B, 1C).

In the history record, it was observed that the Aesthefill was prepared with the back-and-forth method with 8cc of sterile water and 2cc of lidocaine without epinephrine, in total 10cc (5cc per side) administered using a 22G x 50mm cannula in the subcutaneous plane. It used the back-and-forth technique to achieve a uniform reconstitution of the PDLLA as suggested in the reconstitution protocol [7, 8].

After reviewing her medical history, it was confirmed she had no infection or trauma in that area. Additionally, she had not undergone any dental or medical procedures following the PDLLA treatment and had no medical history of a recent COVID-19 vaccination.

She reported experiencing facial swelling and multiple nodules at the injection sites. Physical examination revealed multiple nodules, three on the left cheek and six on the right, with a stony firmness to palpation, scattered throughout the PDLLA injection site (temporal region, cheek, and jaw), and swelling was also detected throughout the aforementioned area (Figure 1D, 1E, 1F). After evaluating the patient, we made a presumptive diagnosis of multiple nodules and edema. This clinical presentation is called "hot nodules or inflammatory nodules" due to the presence of two clinical signs (edema and nodules). The nodules were easily palpable during physical examination, measuring approximately 3 to 5 cm in diameter. A biopsy of the lesions could not be performed due to the risk of scarring, and no imaging studies were performed; The diagnosis was exclusively clinical, based on the patient's signs and symptoms.

It was decided to prescribe oral prednisone at a dose of 20 mg daily for three days and intralesional triamcinolone (40 mg/ml, Triamcicort Brand), the amount of triamcinolone injected was approximately 0.15 cc per nodule.

Twelve days after treatment, the nodules had become softer and smaller, measuring approximately 1 to 3 cm, and the swelling had completely subsided, becoming "cold nodules or noninflammatory nodules".

Following this improvement, we decided to inject 0.10 cc of triamcinolone into each remaining nodule. Fifteen days after the second intralesional triamcinolone injection, the nodules had further reduced in size, reaching approximately 1 cm in diameter. Since intralesional injections are more difficult in such small nodules and to prevent skin atrophy, collagenase 1500 UI (Inbiogenase, Inbiotec, Spain) was decided to be a safer option. This was diluted in 3.5 cc of sodium chloride and 0.5 cc of lidocaine without epinephrine; the amount of collagenase applied to each nodule was approximately 0.25cc to 0.35cc. Twenty days after collagenase application, the nodules completely resolved, and no side effects were reported after the application (Figure 1G, 1H, 1I). The patient was asked if she experienced any discomfort during the following month of her recovery. She reported that she had no discomfort and that the nodules had not recurred. The last evaluation was performed 12 months later, and it was verified that she had not had any recurrence.

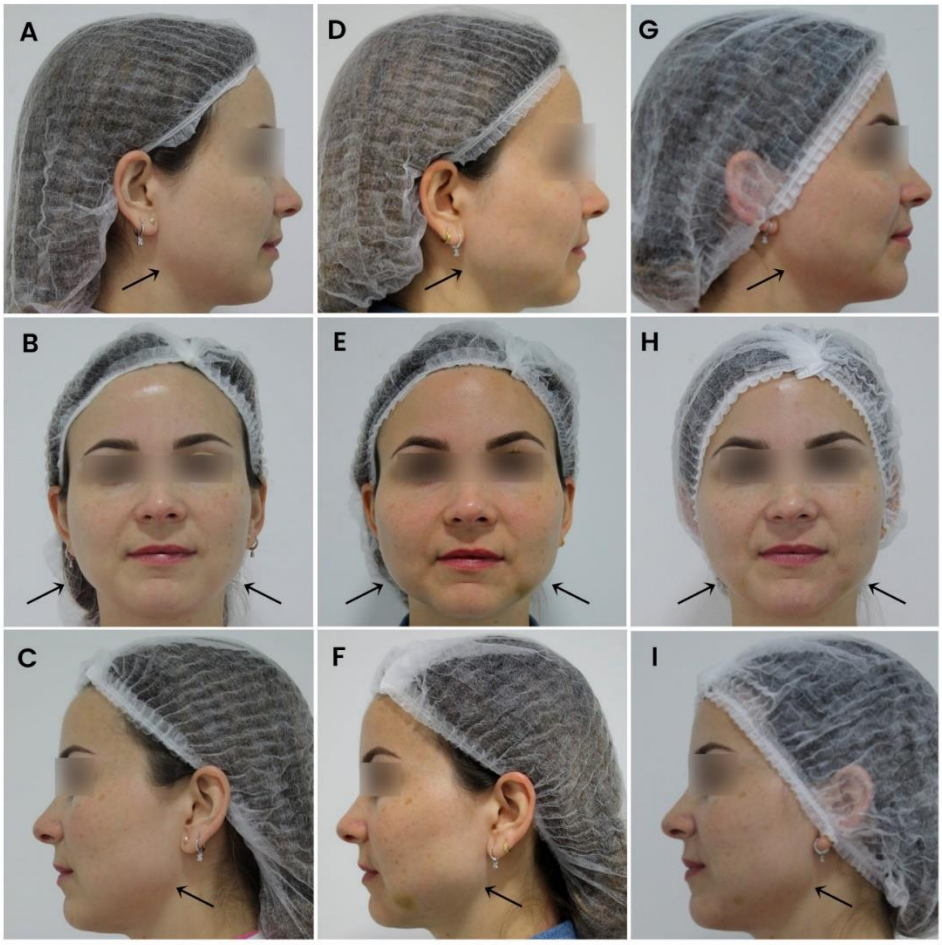

Figure 1. *A, B, C.* Photographic record before PDLLA application. No swelling or nodules were observed. *D, E, F.* Three months after application, bilateral edema, swelling around the face, and multiple bilateral nodules. *G, H, I.* After treatment, twenty days after, there was no swelling, and the facial contour was clear due to decreased swelling and resolution of the nodules.

3. Discussion

Collagen stimulation is a widely used and increasingly popular cosmetic procedure that is generally safe, although in rare cases it can lead to adverse reactions such as nodules or granulomas. PDLLA is a new molecule that, due to the high porosity of its microspheres, has a total volume several times greater than that of PLLA microparticles, allowing not only for the stimulation of new tissue formation but also the provision of structural support [1, 9, 3].

Initially, tissue grows on the surface of the microspheres and gradually expands to occupy the spaces between them, while the porous microspheres slowly degrade and are replaced by newly formed tissue, maintaining the initial volume for several months. Although PDLLA and PLLA are comparable molecules, they are not without complications (1, 9, 3).

The molecule Aesthefill (PDLLA) is considered safer than PLLA because its perfectly defined and uniform spheres reduce the risk of nodule or granuloma formation, unlike other PLLA molecules with sharp edges that are more likely to promote fibroblast accumulation and, consequently, a higher risk of such complications. Short-term adverse reactions to PLLA injections reported in the literature include pain, swelling, bleeding, bruising, skin discoloration, and overcorrection, which typically appear within a few days of the injection and usually resolve spontaneously within one to two weeks [6].

In addition, more severe complications such as embolism and localized cellulitis have been documented and require specific management depending on the case. Late-onset reactions like granulomas and nodules induced by PLLA are particularly concerning, as they may be disfiguring, appear months after the procedure without an apparent cause, and often demand prolonged and targeted treatment [10].

Similar complications have been observed more frequently with hyaluronic acid following COVID-19 vaccination, underscoring the need for further research to determine the mechanisms that trigger the formation of nodules and granulomas associated with various substances commonly used in cosmetic facial and body rejuvenation procedures. Although numerous case reports describe the appearance of these adverse reactions with different types of biostimulants, there is still no specific management protocol tailored to each substance. Treatment options for late-onset subcutaneous nodules and granulomas include intralesional and systemic steroids, systemic antibiotics, intense pulsed light, 5-fluorouracil, allopurinol, and surgical excision [4]. Despite the consistent use of steroids across therapeutic approaches, outcomes vary—while some cases resolve successfully, others remain unresponsive to steroid treatment [11].

In this specific case, intralesional injections of triamcinolone at a concentration of 40 mg/ml were effective, and at the end of the protocol, collagenase injections were considered a safer option to dissolve the remaining collagen capsule. This approach helped minimize the remaining nodules and avoided the risk of skin atrophy. Only a few cases of delayed foreign body reactions induced by PLLA filler have been reported in Europe and America [12, 13] and one case of PDLLA [14].

Given the potential for early and late complications, it is strongly recommended that practitioners using biostimulators and other injectables implement standardized protocols for complication management to ensure timely and effective patient care. Although PDLLA is considered safer than PLLA due to its molecular isomerization, no scientific evidence or comparative studies currently support this claim. In the present case, despite the absence of histopathological or imaging confirmation, clinical evaluation guided the diagnosis and treatment plan. The patient responded favorably to steroid therapy, with complete resolution of nodules and no recurrence after five months of follow-up.

Ianhez M et al. reported 55 complications associated with the use of biostimulants such as poly-L-lactic acid (PLLA), calcium hydroxyapatite (CaHa), and polycaprolactone (PCL), with 38 cases linked to PLLA—27 of which were related to the newer brand Elleva and the rest to Sculptra. These complications, mostly nodules, typically occurred within a month and were associated with the use of more than one vial per patient; notably, most Elleva-related nodules did not resolve completely with intralesional steroids, unlike our case where triamcinolone proved effective, possibly due to the spherical structure of poly-D,L-lactic acid (PDLLA), which may facilitate resolution.

While Vleggaar D et al. suggested that intralesional steroids are generally ineffective for PLLA-related nodules, our case involved PDLLA (Aesthefill), which may explain the favorable response [6]. Similarly, Pérez KM and Ramírez Gálvez R. reported a granuloma four months after Aesthefill application that responded well to steroid treatment, underscoring the potential role of the biostimulant's composition in treatment outcomes [14]. Aguilera SB et al. described the resolution of a CaHa-induced nodule with a single intralesional injection combining 5-FU, dexamethasone, and triamcinolone, suggesting that CaHa complications may also be more manageable than those associated with PLLA [11]. Furthermore, McCarthy AD et al. reported a non-inflammatory nodule post-CaHa injection that resolved with mechanical vibration, contrasting with our case of inflammatory nodules and edema, highlighting that different biostimulant compositions result in distinct clinical presentations and management protocols [15].

Nodules or granulomas after biostimulant injections persist as an unwanted complication. The type of complications will vary depending on the type of biostimulant. CaHa and PDLLA nodules or granulomas appear to respond to oral and intralesional steroids; however, PLLA nodules or granulomas may sometimes respond to steroids and in other cases must be excised. In conclusion, we could suggest that steroids should be considered first-line therapy in these cases, as they work by modulating the exaggerated fibroblast response, and intralesional collagenase should be considered in the final stage of treatment, when the nodules or granulomas are already regressing, as collagenase may play a role in the degradation of the collagen that holds the particles in place.

A limitation of this clinical case was the lack of complementary studies, such as ultrasound or MRI, which would have allowed for better characterization of the nodules. Although these tests were suggested, the patient preferred not to request them at other centers. Furthermore, histopathological analysis was not performed due to the impossibility of obtaining tissue from the

lesion, given that the patient received conservative treatment in the outpatient clinic. These limitations limit the possibility of establishing a more precise differential diagnosis, especially in the case of noninflammatory lesions such as foreign body granulomas. Consequently, the clinical diagnosis was made based on the semiological findings and the relevant clinical history, which should be considered when interpreting the scope of this report.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data is not publicly available due to privacy or ethical restrictions.

Consent

Written informed consent was obtained for the use of photographs and data related to medical history and for the preparation of this manuscript, understanding that this information may be publicly available.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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