A Case Report of Hyaluronic Acid Filler Injection used for Localized Scleroderma with a Review of Fillers for Localized Scleroderma

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Abstract

Localised scleroderma also known as Morphea is chronic inflammatory condition of the connective tissue, the aetiology of which is unknown. Skin hyperemia is seen in the early inflammatory stage. This is followed by fibrosis, sclerosis, and atrophy with hypopigmentation or hyperpigmentation. The disease is rare and is seen more often in young adults. Localized scleroderma is seen as generalized, guttate, nodular (keloidal), subcutaneous (morphea profunda), and linear scleroderma, including en coup de sabre morphea. Therapeutic options include corticosteroids, methotrexate, calcipotriol, imiquimod, tacrolimus, ultraviolet A and CO_2 fractional laser treatment. Although these modalities help to stop the progression of the disease and the disorder itself is not life threating, atrophic scars and hyperpigmentation or hypopigmentation that are seen are permanent. There is disfigurement in approximately 50% of patients and this disfigurement can have a huge negative impact and even cause a low self-esteem in the patient.

Keywords: Morphea profunda • Skin hyperemia • Linear morphea

Introduction

Surgical excision, autologous bone grafting, and autologous fat grafting have been performed with varying degrees of success in linear morphea [1-5]. More recently, hyaluronic acid, calcium hydroxylapetite, poly L lactic acid and permanent fillers such as silicone have been used to correct the deformities that result as an aftermath of morphea [6,7]. The author reports a case of Morphea treated with two Hyaluronic acid fillers, where she first injected the deformity with a high G′ filler and 2 weeks later, she layered it with a lower G′ filler to give longer lasting results and a better cosmetic outcome [8-11].

Case Presentation

A 35 year old lady was referred by a dermatologist for treatment of an atrophic scar on her chin. She had been diagnosed as a case of localized scleroderma and was treated for it medically for two years. Her active disease resolved and she was left with an atrophic scar. The referring doctor revealed that the lesion was stable and had not shown any spread for three years. The MRI and histopathology done by the referring dermatologist were consistent with that of Scleroderma. On history, the patient was healthy nonsmoker with no medical disorders. There was no history of herpes simplex infection in the past. She was not on any oral or topical medication for her morphea. She had no significant medical complaints related or unrelated to morphea for 3 years preceding her visit to our clinic. The area of atrophy was asymptomatic. On examination, the patient had an atrophic scar on the right side of her face extending from the labiomental crease to the midline of the chin. The contour of the chin was lost leading to a facial disfigurement. The scar was uneven, indurated, and hyperpigmented. The patient had no difficulty in opening her mouth, eating, chewing, swallowing or speaking. Blood investigation which included a complete hemogram, ANA, RNP, and dsDNA were found to be normal. The 3 mm punch biopsy from the deformed part of the chin confirmed that the lesion was inactive. The patient did not want any surgery and had already been counselled by the referring dermatologist regarding a non-surgical approach with fillers. The author also shared the same opinion as her colleague as far the treatment modality was concerned. The author chose to inject two fillers with the same crosslinking polymer but with different G primes in two independent sessions. The patient was counselled and the treatment protocol was discussed. The patient was asked to avoid Non-Steroidal Anti-inflammatory Drugs (NSAIDS), vitamin E, Gingko biloba, essential fatty acids, herbal supplements, and green tea for five days before the injection in order to reduce the chances of bruising. On the day of the treatment, the patient was photographed with a standard power shot camera. Written informed consent was taken. The face was thoroughly cleansed and topical 2.5% lidocaine/prilocaine was applied to the affected part. After 30 minutes, the topical anaesthesia was removed. The patient's face was again thoroughly cleansed with chlorhexidine, alcohol and normal saline. 1 ml of Restylane lyft was taken and a non-traumatic, 22 gauge and 50 mm long cannula was attached to it. (Steriglide, TSK Laboratory, Japan). A small entry point was made with a 21 gauge needle at the margin of the atrophic area on the chin (Figure 1). To allow an easy access for the blunt tipped microcannula. A 22 gauge, 50 mm long blunt tipped cannula was then inserted through this opening and obliquely advanced towards the angle of the mandible, gliding the cannula gently over the periosteum. The entire deformity was filled with 0.6 ml of Restylane lyft using a fan shaped technique, placing the filler in a retrograde linear threading manner just above the periosteum and then turning the direction like a fan to cover the entire defect. Care was taken not to place any product near the mental foramen. The tethered bands were subcised with the cannula. A second layering was done in the subcutaneous plane and the remaining 0.4 ml of product was injected in the areas where the deformity was still visible. Slow injections were given in a retrograde manner to prevent any compression on vascular structures and to prevent bruising. The entry point was cleaned with betadine. The area injected was gently massaged to mould the product into the deformity. The patients were advised not to massage on her own in order to prevent dislodging of the product where it is not desired. She was asked to avoid strenuous physical activity for 24 hours after the injection. She was also advised to avoid the use of cosmetics or skin care products for up to 12 hours after the procedure. The patient was also asked to avoid any facials or skin treatments for upto 4 weeks and was advised to follow up after 4 weeks. When the patient returned in 4 weeks, the filler had settled well leaving a mild depression in the scar. Though the patient was happy with the result, the author found the need to inject more filler in order to give a better result. Since the deformity was now very superficial, the author chose to use Restylane and inject it with a cannula in the deep dermis to correct the visible irregularities on the skin surface. The same protocol for filler injection was followed which included taking photographs and consent, cleaning the area , applying topical anaesthesia and finally injecting the filler with a 22 gauge, 50 mm long blunt tipped cannula. The scar was barely visible after injecting 0.5 ml of the low G prime filler more superficially, layering it over the high G prime filler which was injected 4 weeks ago. There were no adverse effects. The patient

followed up after 6 months and after 1 year. It was seen that after 1 year, the patient retained the filler and there was no deterioration in its effect. The skin looked smooth and the deformity was barely visible except for mild Post Inflammatory Hyperpigmentation (PIH). It was interesting to note that this PIH was much less as compared to the PIH which was seen before injecting the filler the first time. There were no signs of reactivation of the disease at the 1 year follow up (Figure 2 and 3).

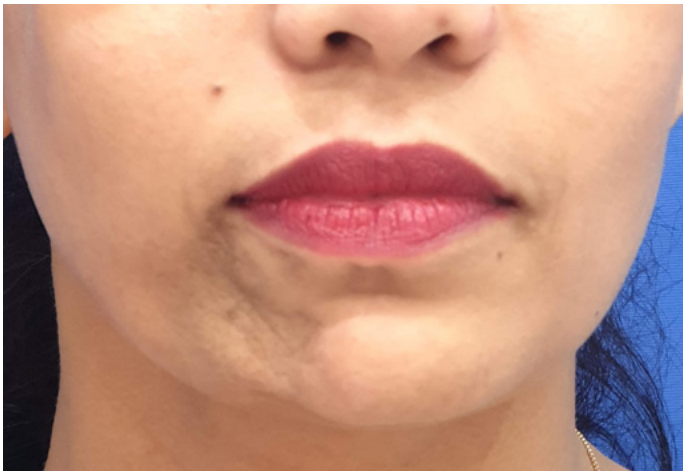

Figure 1. Localised morphea before injecting HA filler.

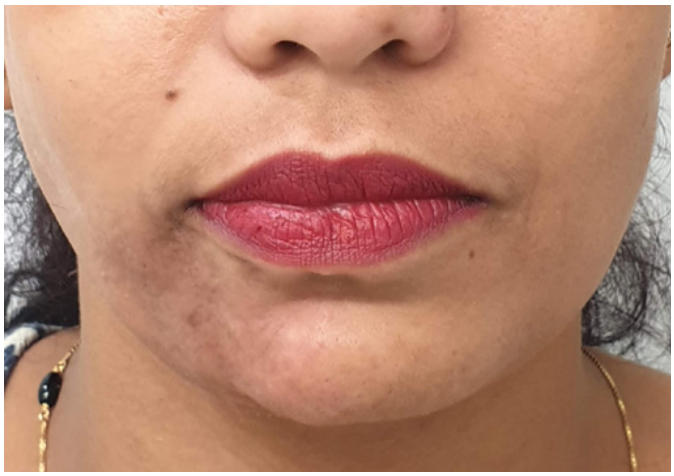

Figure 2. Localised morphea after injecting 1 ml of high G prime HA filler

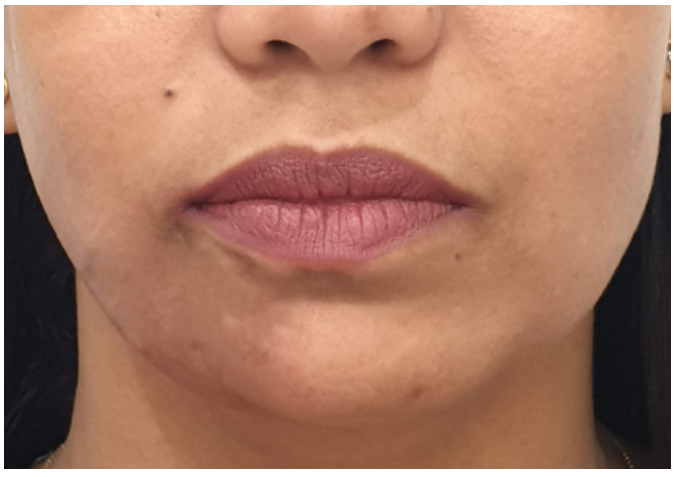

Figure 3. Localised morphea after second session with low G prime HA filler

Results and Discussion

Residual atrophy that remains after the inflammatory phase of localised scleroderma has been treated in the past with procedures such as resection of the lesion, implantation of porous polyethelene implants and alloderm tissue matrix. These treatments may have a long downtime or may carry significant risks or may be rather cumbersome. While autologous fat grafts offer good cosmesis, the procedure is lengthy and requires a lot of precision. One has to harvest grafts from donor site and process it well to be able to obtain fat which can be reinjected into the areas of atrophy. Roh and colleagues published their findings of 20 patients with facial linear scleroderma. They found that, although autologous fat transplantation was effective for the correction of atrophic scars on the forehead, it was less effective for other affected areas such as the nose, infraorbital area, and chin [12]. There are a few reports on fillers being injected to correct the residual disfigurement of morphea. A 53-year-old female with linear scleroderma en coup de sabre on the forehead was treated with a combination of an implant and filler by Robitschek et al [13]. The patient underwent alloplastic implantation with AlloDerm tissue matrix, which was placed in a subgaleal plane. This improved the contour and symmetry of the forehead. Four months after surgery, hyaluronic acid filler was injected along the borders of the implant in an effort to smooth the forehead contour. Follow-up at 8 months and 14 months revealed maintained graft fullness and excellent overall cosmesis. In a case of Parry-Romberg syndrome, Lane, et al. injected hyaluronic acid filler in the upper lip [14]. This filler improved the cosmetic appearance of the lip and was used as a guide before they planned autologous fat transfer for the lip. Choksi and Orringer treated a 20 year old man with linear morphea, en coup de sabre , on the forehead with UVA1 therapy [15]. The patient was asymptomatic for 3 years. However, he had a residual cosmetically disfiguring atrophic lesion on the forehead. This atrophic lesion was injected with 1 ml of hyaluronic acid filler in a linear threading technique in order to improve the disfigurement. Excellent results were seen immediately after the treatment and the contour defect improved by about 75%. The residual contour defect was injected with 1 ml of Perlane five months after the first injection. This resulted in 90% improvement in the lesion and there were no side effects. Mashiko, et al. treated a 29-year-old Japanese woman with localized scleroderma (morphea; en coup de sabre) with 1 ml of HA [16]. They injected Restylane on the frontal bone with a sharp 30-gauge needle to elevate the overlying tissue and skin of the defect until the filler resulted in overcorrection by 10%-20%. They found that even after 12 months, this volumization was well preserved. They hypothesised that periosteal stem cells may be activated by HA injection and may contribute to persistent volumizing effects. This treatment may be a much less invasive alternative to fat or bone grafting. A 34 year old female with linear scleroderma on the left medial forehead was treated with 2 vials of hyaluronic acid by Thareja, et al. [17]. They injected the filler intradermally and found satisfactory results. The injections were repeated after six months and the patient was very satisfied with the results. However, since the skin was tethered to the underlying structures at both the inferior and superior aspects of the lesion, the improvement was primarily noted in the central portion of the lesion. Arsiwala injected 1 ml of Perlane in a stable circumscribed morphea on the chin, using a bolus technique with a 30-G needle with satisfactory results. Perlane with its large particle size of 1000 microns and 20 mg/ml concentration was found to be safe and effective even at 9 months follow up [18]. Walls, et al. reported two cases of en coup de sabre being treated effectively with HA fillers, one patient with Juvederm Ultra and the other with Restylane and both lasted for at least 6 months [19]. Sivek and Emer used a 25 G blunt-tipped microcannula to inject a 24 mg/mL cross- linked HA injectable gel into the forehead of a young girl with En Coup De Sabre. They reported excellent results, no side effects and a maintenance of the improvement for more than 9 months [20]. A study by Sharique, et al. conducted from 2008 to 2019, showed excellent results with intralesional infiltration of sclerosis with hyaluronic acid 26 mg/ml , carried out once monthly for 2 months to ten patients with inflammatory stage morphea; and single injection to six patients with burnt out morphea sclerosis [21]. HA filler was injected deep into dermis including the scarred area using cannula for sclerosis and fine needle for the inflammatory lesions. There were no complications of the procedure. Contour deformity was well corrected in all patients with good patient satisfaction at the time of injection. Follow up was done every 2 weeks for 2 months to 4 years after injection. All the patients with inflammatory lesions had a relapse but none of them had a relapse in the same area that the HA was injected. The outcome in one of the patients persisted for 4 years after the procedure. reported three cases of morphea treated with high G prime HA fillers with excellent results [22] Saczonek, OA, et al. One of them was also treated with fractional

CO_2 laser monthly, three times in total (power 23 W, microbeam spacing 1400 µm, energy density 28 mJ/cm^2) in addition to HA fillers before and after the laser sessions. The combination of HA and FAL therapy produced significantly better aesthetic results than use of one method only. In a study done by Carruthers, 30 patients with HIV-associated facial lipoatrophy, were injected with Calcium Hydroxyapatite (CaHa) [23]. 80% of the patients achieved "very much improved" status on the Global Aesthetic Improvement Scale at 3 months and 59% at 6 months. Because of these volumizing effects and the efficacy observed with HIV-associated facial lipoatrophy, Cox and Soderberg chose to study the efficacy of CaHa in a patient with Parry-Romberg syndrome [24]. Thee patient had extensive subcutaneous tissue loss involving the temple, lateral cheek region, and submalar area and across the mandible. Autologous fat transplantation was not a viable option since the patient had an overall lack of adiposity. The patient was treated with five injections of calcium hydroxylapatite at approximately four week intervals. A supra-periosteal injection of Restylane was also given under the right lower eyelid where there was volume depletion. There was a significant improvement in the deformity and the patient was very satisfied with the result. Onesti et all used Poly L Lactic Acid (PLLA) to treat four patients with linear scleroderma (1 man, 3 women) and two with Parry Romberg Syndrome (2 women) in the age group of 23 to 65 yrs [25]. The atrophic areas were injected with PLLA every 4 weeks for a total of five sessions. The overall results with PLLA were seen after 12 months and were permanent according to the author. All patients with PRS showed good restoration of facial volume and symmetry and an improvement in skin quality. There was improvement in the hyperpigmentation as well. The patients were satisfied with the results even after 18 months. In patients with linear Scleroderma, there was improvement both in contour and skin quality but there was no improvement in hyperpigmentation. There was transient erythema and oedema at the injection site. One patient who suffered from linear scleroderma on the chin developed a submucous nodule which had to be surgically removed. Histology of this nodule revealed PLLA microparticles surrounded by a granular reaction.

Franco, et al. chose to inject Poly Methyl Methaacrylate (PMMA) in a 14-year-old male, with stable scleroderma en coup de sabre [26]. The lesion was filled with PMMA in 3 sessions, with a 3-month interval between sessions. The results were satisfactory and the patient gave an improvement score of 9 out of 10. However, no long term results have been reported. So far there are approximately ten reports of hyaluronic acid fillers being used in localised morphea, and one each of PLLA, PMMA and CaHa. While PLLA, PMMA and CaHa may be good treatment options, we could not explore their usage because of their non-availability in our country. However, PLLA requires many treatment sessions to obtain optimal cosmetic results and the result is delayed. There have been reports of nodules and granulomas with PMMA in cosmetic indications. Hyaluronic acid fillers are a simple, quick, minimally invasive option for stable atrophic lesions of localised morphea. Its ease of administration, low immunogenicity and reversibility with hyaluronidase couple with excellent patient satisfaction makes it one of the better options to provide contour restoration in cases of deformities such as localised morphea. Hyaluronic acid volumizes, softens, and hydrates the skin by potently binding to water. It is said to play a role in cell growth, membrane receptor function, and adhesion [28]. It has also been shown to stimulate collagen production which explains the longer lasting results of HA filler when injected two or three times for the same indication [29]. Andrew, et al. were able to prove that upon injecting HA fillers, fibroblasts take on a more morphologically stretched shape and a more active phenotype resulting in neocollagenesis [30]. In cases of stable localised morphea including en coup the sabre, the skin may be somewhat tethered to underlying structures. Hence, the author chose to use a 22 G microcannula to subcise the fibrous bands in the bound down areas. It is also less traumatic, there is less pain, lesser chances of bruising, oedema and there is an ease of administration of the product with a microcannula. The author's technique of using HA fillers with two different G primes helped to achieve better cosmesis. While the filler with high G prime gave support and volume, the filler with low G prime cleared the surface irregularities. Slow injections should be given adding less pressure while injecting and large volumes should be avoided as a bolus to prevent a vascular compromise by direct external pressure on the artery.

Despite the theoretical risk of disease reactivation of Scleroderma because of trauma from injection, there are no reports of disease reactivation after. The majority of patients with documented morphea who underwent cosmetic injectable treatment had inactive disease at the time of injection and was not taking immune-modifying medications [30].

Conclusion

However, the patient should be also be warned that the treatment does not prevent from a possible relapse to the proliferative phase, since disease activity lasts around 3 to 5 years and may extend up to 25 years, with an uncertain progression time. To summarise, hyaluronic acid filler is a safe treatment option for temporary cosmetic improvement for upto 2 years. Subsequent injections may improve the longevity of the filler. Treatment outcome depends on the selection of patients. It is extremely important to inject fillers only in stable cases of localised morphea where there is no growth or alteration in consistency of the lesion.

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