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CASE REPORT

Hyaluronic Acid Filler Injection for Localized Scleroderma – Case Report and Review of Literature on Filler Injections for Localized Scleroderma

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Introduction: Localized scleroderma, also known as Morphea, is a chronic inflammatory condition of connective tissue, the etiology of which is unknown. There is skin thickening with increased quantities of collagen in the indurative lesion. Skin hyperemia is seen in the early inflammatory stage. This is followed by fibrosis, sclerosis, and atrophy with hypopigmentation or hyperpigmentation. Therapeutic options include corticosteroids, oral or subcutaneous methotrexate, calcipotriol, imiquimod, tacrolimus, mycophenolate mofetil, medium-dose UVA1 phototherapy, and CO_2 fractional laser treatment. There is disfigurement in approximately 50% of patients. Surgical excision, autologous bone grafting, and autologous fat grafting have been performed with varying degrees of success in linear morphea. Hyaluronic acid, Calcium hydroxylapatite, Poly L lactic acid, and permanent fillers such as Silicone have been used to correct deformities that occur as a result of morphea. The aim of this case report was to establish hyaluronic acid fillers as an efficacious modality of treating stable localized morphea with facial disfigurement.

Case Report: A 35-year-old lady with stable localized scleroderma had an atrophic scar on the right side of her face extending from the labio-mental crease to the midline of the chin. The contour of the chin was lost leading to facial disfigurement. The atrophic scar was treated with 2 fillers with the same cross-linking polymer but two different G primes with excellent cosmetic outcome. A brief review of literature involving fillers for localized scleroderma is also discussed.

Conclusion: Hyaluronic acid filler can be used safely in cases of stable localized scleroderma with facial atrophies. It is an effective, minimally invasive treatment with minimal downtime. It is extremely important to inject fillers only in stable cases of localized morphea. This modality of treatment should be considered for a larger trial in patients with similar disfigurements.

Keywords: fillers, morphea, stable scleroderma, deformity

Introduction

Localized scleroderma, also known as Morphea, is a chronic inflammatory condition of connective tissue, the aetiology of which is unknown.[1] The disease is rare and is seen more often in young adults.[2]

According to studies, the incidence of localized scleroderma is around 0.3 to 3 cases per 100,000 inhabitants/year.[3] . 90% of children suffering from localized scleroderma are diagnosed between 2 and 14 years of age. In adults, the peak incidence is usually in the fifties. It is more common in Caucasian women, with a ratio of 2–4 women to 1 man.[4–7]

It has a self-limiting course and is always benign. It is usually confined to the skin and/or underlying tissues. There is skin thickening with increased quantities of collagen in the indurative lesion.[8] Skin hyperemia is seen in the early inflammatory stage. This is followed by fibrosis, sclerosis, and atrophy with hypopigmentation or hyperpigmentation.

Localized scleroderma is seen as generalized, guttate, nodular (keloidal), subcutaneous (morphea profunda), and linear scleroderma, including en coup de sabre morphea.[9]

Therapeutic options include corticosteroids, oral or subcutaneous methotrexate, calcipotriol, imiquimod, tacrolimus, mycophenolate mofetil, medium-dose UVA1 phototherapy[10], and CO_2 fractional laser treatment.[11–13]

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Although these modalities help to stop the progression of the disease and the disorder itself is not life-threatening, 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 low self-esteem in the patient.[14] Surgical excision, autologous bone grafting, and autologous fat grafting have been performed with varying degrees of success in linear morphea.[15–18]

More recently, Hyaluronic acid, Calcium hydroxyapatite, Poly L lactic acid, and permanent fillers such as Silicone have been used to correct deformities that occur as a result of morphea.

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 four weeks later, she layered it with a low G' filler to give longer-lasting results and a better cosmetic outcome. The objective was to report a simple and safe technique with minimal downtime and satisfactory results.

Report of a Case

This was an individual case study and a written informed consent was obtained from the patient for publication of her images and case details. . No institutional approval was needed as the patient was treated by the author in her private clinic.

A 35-year-old lady was referred by a dermatologist for treatment of an atrophic scar on her chin. She had been diagnosed with localized scleroderma and was treated for two years. Her active disease resolved, and she was left with an atrophic scar.

The patient was a healthy non-smoker with no other medical disorders. There was no history of herpes simplex infection in the past. She was not on any oral or topical medication for morphea when she visited the author. She had no significant medical problems related to or unrelated to morphea for the past three years . The area of atrophy was asymptomatic. On examination, the patient had an atrophic scar on the right side of her face extending from the labio-mental crease to the midline of the chin. The contour of the chin was lost leading to facial disfigurement. The scar was uneven, indurated, and hyperpigmented. The patient had no difficulty in opening her mouth, eating, chewing, swallowing, or speaking.

The referring dermatologist revealed that the lesion was stable and had not spread for three years. Patient was treated with systemic corticosteroids for 3 months followed by oral methotrexate 15 mg/m^2/week for a year. The disease was then stable for 3 years. The histopathology performed by the referring dermatologist were consistent with that of Scleroderma.

A fresh magnetic resonance imaging (MRI) and laboratory investigations were done when the patient visited the author, 3 years after the scleroderma was found to be stable. Blood investigation which included a complete hemogram, ESR, C Reactive protein, ANA, RNP, dsDNA, liver kidney and thyroid functions were found to be normal. The 3 mm punch biopsy from the deformed part of the chin confirmed that the lesion was of localized inactive scleroderma. Histopathology showed sclerotic collagen bundles infiltrating the entire dermis and extending into subcutaneous fat. The adnexae were replaced by fibrosis . The vessels of the hypodermis show a thickened wall and significantly decreased lumen size.

An orthodontic and maxillofacial evaluation and an ophthalmic evaluation were done, both of which were normal. The patient did not want any surgery. The author chose to inject two fillers with the same cross-linking polymer but with different G primes in two independent sessions (Table 1).

The patient was counselled, and the treatment protocol was discussed. The patient was asked to avoid non-steroidal anti-inflammatory drugs, vitamin E, gingko biloba, essential fatty acids, herbal supplements, green tea for five days before the injection to reduce the chances of bruising. On the day of the treatment, the patient was photographed with a standard power shot camera both in front and a profile view under good lighting. The face was thoroughly cleansed and 2.5% topical 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. One ml of Restylane Lyft® (Galderma, Lausanne, Switzerland) was taken and a non-traumatic 22-gauge, 50 mm long microcannula (Steriglide TSK Laboratory, Japan) was attached to the syringe. A small entry

Table 1 Management of a Case of Localised Scleroderma

Patient Presented With Features of Localised Morphea.
↓
Ophthalmology and dental evaluation normal
↓
MRI normal
↓
Lab investigations and skin biopsy revealed early stages of morphea.
↓
Oral prednisolone given for a period of 3 months
↓
Oral methotrexate 15 mg/m²/week for a year.
↓
Topical pimecrolimus for 6 months
↓
Patient followed up every 6 months. Lesion was found to be stable for 3 years.
↓
After 3 years, patient re-evaluated (blood, MRI, Biopsy) and found to have stable localised morphea
↓
Deformity treated with Hyaluronic acid fillers
↓
Filler lasted even at 1 year follow up

portal was made with a 21-gauge needle at the margin of the atrophic area on the chin to allow easy access to the blunt-tipped microcannula. The 22 gauge, 50mm 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 cannula was moved back and forth in order to be able to subcise few of the tethered bands. The entire deformity was then 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. A second layer was applied in the subcutaneous plane and the remaining 0.4 ml of the product was injected into the areas where the deformity was still visible. Slow injections were administered retrogradely to prevent any compression of the vascular structures and to prevent bruising. The entry point was cleaned with betadine. The injected area was gently massaged to mould the product into the deformity. The patient was advised not to massage on her own to prevent dislodgement of the product. She was asked to avoid strenuous physical activity for 24 hours after injection. She was advised to avoid the use of cosmetic or skincare products for up to 12 hours after the procedure. The patient was also asked to avoid facials or skin treatments for up to four weeks and was advised to follow up after four weeks. When the patient returned in four weeks, the filler settled well, leaving a mild depression in the scar. There were no side effects with the

treatment. The author found the need to inject more filler to give a better result. Since the deformity was now very superficial, the author chose to use Restylane® (Galderma, Lausanne, Switzerland). The product was placed 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, 50mm 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 that was injected four weeks ago. There were no adverse effects. The patient tolerated the procedure well. The patient was followed up after 6 months and then 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 of follow-up (Figures 1–6).

Discussion

Residual atrophy that remains after the inflammatory phase of localized scleroderma has been treated in the past with procedures such as resection of the lesion, implantation of porous polyethylene implants and alloderm tissue matrix. (Table 2) These treatments may have a long downtime or may carry significant risks or perhaps be rather cumbersome. While autologous fat grafts offer good cosmesis, the procedure is lengthy and requires a lot of precision. Grafts must be harvested

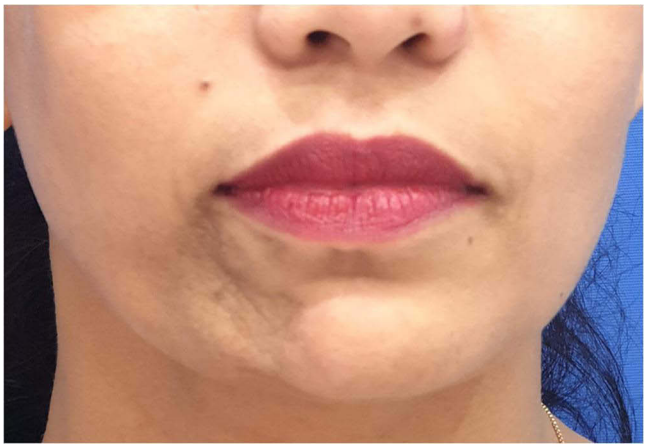

Figure 1 Front view before injecting filler.

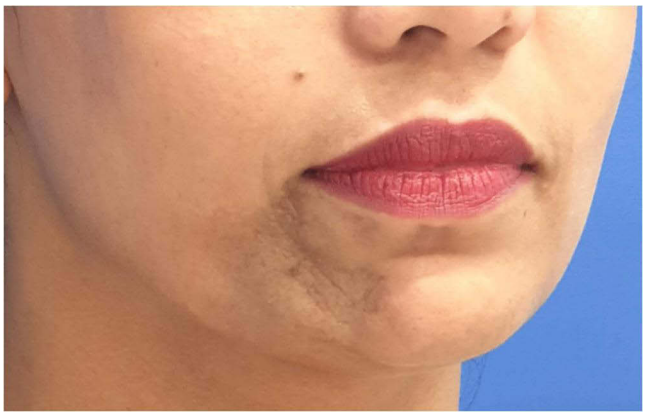

Figure 2 Profile view before injecting filler.

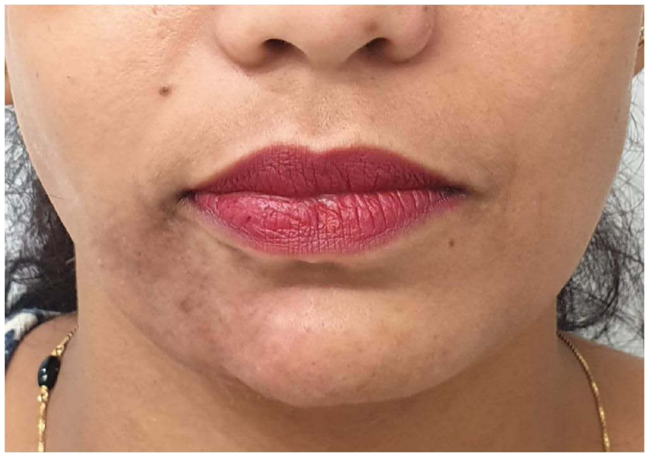

Figure 3 Front view after injecting 1ml of filler.

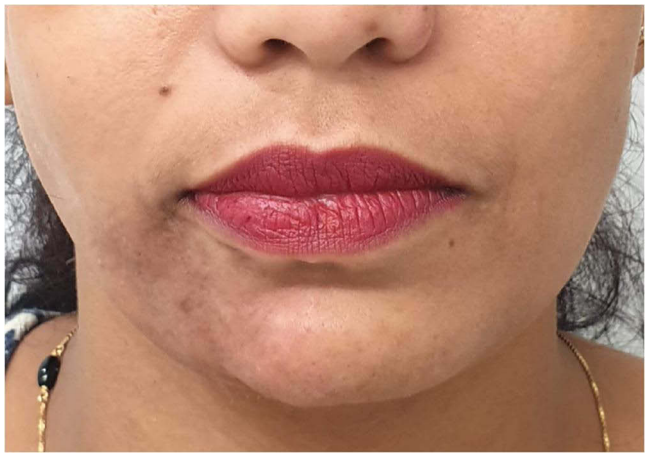

Figure 4 Profile view after injecting 1ml of filler.

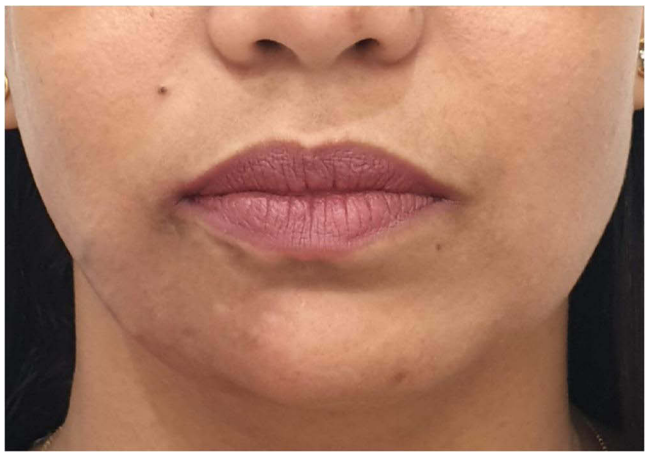

Figure 5 Front view after injecting 2nd ml of filler.

from the donor site and processed well to obtain fat that can be reinjected into atrophic areas. So far there are approximately eleven reports of hyaluronic acid fillers being used in localized 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

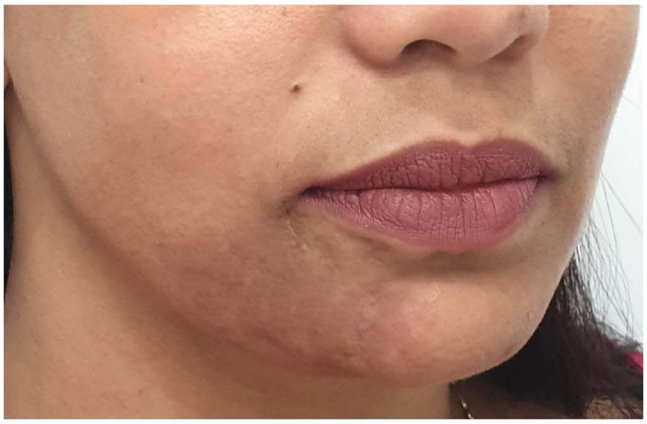

Figure 6 Profile view after injecting 2nd ml of filler.

our country. However, PLLA requires many treatment sessions to obtain optimal cosmetic results and the result is delayed. There have been reports of PMMA-treated nodules and granulomas in cosmetic indications.

Hyaluronic acid filler- is a simple, quick, and minimally invasive option for stable atrophic lesions of localized morphea. Its ease of administration, low immunogenicity, and reversibility with hyaluronidase coupled with excellent patient satisfaction make it one of the best options to provide contour restoration in cases of deformities such as localized 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.[37] 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.[38] Wang et al were able to show that upon injecting HA fillers, fibroblasts take on a more morphologically stretched shape and a more active phenotype, resulting in neocollagenesis.[39]

In cases of stable localized morphea, including en coup the sabre, the skin may be somewhat tethered to underlying structures. Nilforoushzadeh et al described subcision of acne scars with a 22 G microcannula. The author decided to try this in the case of localized morphea too and managed to subcise the fibrous bands in the bound areas using a 22G microcannula with a back and forth movement. The cannula is less traumatic, there is less pain, there are fewer chances of bruises, oedema, and there is an ease of administration of the product with a microcannula.[40] The author's technique of using HA fillers with two different G primes helped to achieve better cosmesis. While the high G prime filler provided support and volume, the low G prime filler cleared the surface irregularities.

Slow injections should be given adding less pressure while injecting. Large volumes should be avoided as a bolus to prevent vascular compromise by direct external pressure on the artery.

Despite the theoretical risk of reactivation of Scleroderma because of trauma from the injection, there are no such evidence-based reports. Most of the patients who underwent filler treatment were not on any immune modifying medication and their disease was stable.[41] It is known that the disease activity lasts around 3 to 5 years and can extend up to 25 years. The progression time is uncertain and filler injections do not prevent a possible relapse to the proliferative phase.

Conclusion

Hyaluronic acid filler can be used safely in cases of stable localized scleroderma with facial atrophies. It is an effective, minimally invasive treatment modality with, minimal downtime. Apart from filling the defect, hyaluronic acid is also known to have bio-stimulatory effects leading to neocollagenesis. There has been no reactivation or exacerbation of the disease for up to 2 years. The outcome of treatment depends on the selection of patients. It is extremely important to inject fillers only in stable cases of localized morphea where there is no growth or alteration in the consistency of the lesion. This modality of treatment should be considered for a larger trial in patients with similar disfigurements.

Table 2 Review of Literature on Filler Injections in Cases of Scleroderma

Authors, Year of Publication	Number of Patients and Diagnosis	Clinical Features	Management of Deformity	Outcome	Follow Up
Roh et al[19] 2008	20, linear scleroderma	Depressed atrophic scars on forehead, infraorbital area, nose, chin	Autologous fat transplantation	Forehead : 51–75% improvement Chin : less than 25% improvement. Infraorbital area : poor correction Nose : poor correction.	Results lasted upto 12 months
Robitscheck et al[20] 2008	1, en coup de sabre	Linear ivory –coloured depression of parital scalp and forehead, furrowing of the forehead	Surgical excision and repair. Combination of implant with alloDerm tissue matrix and filler	Improved contour and symmetry of forehead, graft fullness and excellent overall cosmesis	Cosmetic outcome maintained for the period of 14 months
Lane et al[21] 2008	1, Parry-Romberg syndrome with coexistent morphea	Progressive subcutaneous atrophy on right side of the face.	Hyaluronic acid filler injected into the right side of upper lip.	Improved cosmetic appearance of lip.	Follow up not mentioned
Choksi and Orringer[22] 201	1, Linear morphea	Linear depression on the left side of forehead extending into the scalp	UVA1 therapy for active disease followed by hyaluronic acid filler.	90% improvement in the lesion. No side effects	Sustained cosmetic improvement for 5 months.
Mashiko et al[23] 2013	63, En coup de sabre	concave deformity on the forehead	Onlay injection technique of HA Filler with sharp 30-Gauge needle.	Defect filled until it resulted in overcorrection by 10–20% immediately after treatment.	All patients showed persistent results with over 1 year follow up. 12 patients followed up for more than 3years showed persistent effect.
Thareja et al[24] 2013	1, En coup de sabre	Linear vertical depression on left medial forehead and scalp with a hypo pigmented scar on the lower part associated with alopecia and atrophy of bony skull.	Intradermal Hyaluronic acid filler	Immediate improvement in volume. No side effects.	Sustained results upto 6 months
Arsiwala[25] 2015	1, circumscribed scleroderma	Volume defect on left chin with loss of chin contour and visible indentation at mandibular bone. Focal circumscribed pigmentation and sclerosis on neck.	1ml HA Filler, bolus technique with 30-G Needle	Satisfactory correction in the volume loss of chin. No side effects.	Result maintained upto 9 months
Andrew Walls et al[26] 2012	2, En coup de sabre	Permanent, disfiguring induration and depression over affected area. Depressed linear plaque from glabella to the frontal hairline	1ml Hyaluronic acid filler	Contour deformity was well corrected in both patients. No side effects.	Full correction maintained after 6 months in 1 patient.

(*Continued*)

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Table 2 (Continued).

Authors, Year of Publication	Number of Patients and Diagnosis	Clinical Features	Management of Deformity	Outcome	Follow Up
Sivek and Emer[27] 2014	1, En coup de sabre	Linear atrophy on forehead	Use of 25 G Blunt-tipped micro cannula for soft tissue filler injection with retrograde linear threading technique by using 24mg/ml cross linked HA injectable gel premixed with anesthetic.	Immediate results, excellent improvement, less traumatic, no side effects	Result maintained for more than 9 months.
M. Jo et al[28] 2018	1, Parry-Romberg Syndrome	Facial hemi atrophy and hyperpigmentation on right side of the face.	4ml HA filler injected into the cheek and remaining 3ml injected into mandibular area. After 1 month 1.5ml of HA by using fanning technique on the chin.	Two months later, no signs of atrophy. No adverse events	3ml of HA filler was injected after 1 year to maintain results.
Sharique et al[29] 2019	16, Patients (10 patient with inflammatory stage morphea and 6 patients with burnt out morphea)	Morphea	Intralesional injections of 26mg/ml hyaluronic acid once a month for 2 months in patients with inflammatory stage morphea. Single injection in patients with burnt-out morphea sclerosis.	Excellent results were obtained. No side effects.	Good result after 2 months; one patient maintained full correction even after 4 years.
Pirrello et al[30] 2019	10	Fibrosis, atrophy of the skin.	Three filler injections of hyaluronic acid and platelet-rich plasma at an interval of 15 to 20 days.	Good results after the first injection and improvement was maintained in the following months, up to 2years.	Result maintained 24 months after the end of the treatment.
Owczarczyk-Saczonek et al[31] 2020	3	Facial morphea Case 1-A linear induration of the skin with subcutaneous tissue on forehead from eyebrows to the scalp and accompanying scarring alopecia and partial hair loss within the eyebrows and the eyelashes. Case 2- linear, bifocal dyspigmentation with a discrete depression alongside, seen on the forehead Case 3- Extensive atrophic scar on left side of the chin.	Case 1–0.5ml HA injected into stable morphea lesion. After a week 0.5ml HA injected again. 0.5ml HA injected after 1.5 years. Case 2 - Correction of morphea lesion on forehead with HA filler. Case 3- correction of morphea with 1ml bolus of Ha. One of them was also treated with a fractional CO_2 laser monthly, three times in total in addition to HA fillers.	Good improvement in all 3.	Best result was seen in the case where both HA & fractional carbon dioxide laser treatment were done.

Carruthers and Carruthers.[32] 2008	30	Facial lipoatrophy associated with HIV	Calcium hydroxylapatite injected	All patients were rated as improved or better on the GAIS. Temporary adverse events were edema (93%), ecchymosis (83%) and erythema (77%)	\Results were maintained even at 12 months.
Onesti et al[33] 332009	6 patients (4 with linear scleroderma, 2 with Parry Romberg Syndrome)	Case1-Homogenous subcutaneous atrophy on right side of face. Case2-Depressed area, rough area of left chin.	Case1-Atrophic areas injected with Poly L lactic acid reconstituted with 6ml sterile water every 4 weeks for total five sessions	Patients with PRS showed good restoration of facial volume and symmetry and an improvement in skin quality. No improvement in hyperpigmentation. Side effects : temporary erythema, edema, bruising.	Result were found to be permanent at 18 months in patients with PRS and 12 months in patients with scleroderma. Side effects: Case 2 LS - Subcutaneous nodule Case 4 LS - Palpable but not visible nodule.
Sue Ellen Cox et al[34] 2010	1	Facial hemiatrophy, areas of atrophic hyperpigmented depressed plaques.	Series of five CaHA gel injected subcutaneously at 4 week intervals. 1ml of HA to correct the volume depletion under the right lower eyelid.	Significant improvement in volume depletion. No side effects	Over Six months filler effect has diminished only by approximately 10% and repeat injection anticipated in the next several months
Franco et al[35] 2016	1	Atrophic, depressed lesion from forehead to the scalp	PMMA fillers injected in 3 sessions, with a 3-month interval between sessions.	Correction of deformity	Good result obtained after third session
Jemin kim et al[36] 2021	1 case of linear morphea	Linear vertical depression on the left medial forehead that extended to the scalp.	1ml of a micronized acellular dermal matrix filler along two different planes: the periosteum and dermal-subcutaneous junction.	Immediate improvement of the surface contour. No early or late complications developed postoperatively.	Six months following the injections, the depressed lesion was adequately augmented with a favourable aesthetic outcome.

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Disclosure

The author reports no conflicts of interest in this work.

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