

En Coupe de Sabre Morphea Treated with Hyaluronic Acid Filler While Maintained on Systemic Therapy: A Case Presentation and Discussion

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Abstract

Linear morphea in an en coupe de sabre pattern is a variant of localized scleroderma. It is limited to the paramedian forehead or frontoparietal scalp and may extend to underlying structures. Although identified as a self-limited disorder, linear morphea may result in extensive atrophy and disfigurement. Previous treatments have focused on the stabilization of active disease or correcting disease sequelae. We report a case of a 42-year-old female treated with hyaluronic acid filler while maintained on systemic therapy to prevent disease progression. Dermal fillers provide a cosmetic option that can be used in conjunction with systemic therapies.

Introduction

En coup de sabre is a subtype of linear morphea (localized scleroderma) localized to the paramedian forehead or frontoparietal scalp and may involve subcutaneous tissue, muscle, and bone.¹ Characterized by excessive collagen deposition, the disease leads to sclerosis and subsequent atrophy.² This form of localized morphea is most commonly seen as a solitary, perpendicular, atrophic plaque near the midline, with a second plaque at the lateral forehead.³ The pathophysiological mechanism of localized morphea remains unclear, but it is considered an autoimmune disorder based on associated autoantibodies. An increased prevalence of positive antinuclear antibody (ANA) levels has been reported in patients with morphea. A case-control study of 187 patients showed ANA positivity in 34% of the morphea patients compared with 11% of 651 matched controls. In patients with linear morphea, presence of single-stranded DNA antibodies was associated with both extensive body surface area (BSA) involvement and functional limitation.⁴

Linear morphea is a self-limiting disorder that begins with an inflammatory stage, which clinically appears as a pruritic, edematous plaque. The linear lesion is usually indented and colorless with a violaceous, hyperpigmented periphery.⁵ En coup de sabre may result in extensive atrophy and disfigurement, leading to discomfort and psychological distress.⁶ Furthermore, manifestations in severe cases include neurological impairment, presenting as complex partial seizures, headaches, and facial paralysis.⁷ En coup de sabre is not to be confused with Parry-Romberg syndrome, which is characterized as hemifacial atrophy of the skin and subcutaneous tissue below the forehead, also associated with neurological abnormalities.⁸

Although regression and softening of lesions may occur in 50% of patients with morphea over a period of two and a half years, treatment of active lesions has proved difficult.⁹ Treatment of morphea includes topical steroids, calcineurin inhibitors, low-dose methotrexate, systemic steroids, and ultraviolet A1 (UVA1) phototherapy.¹⁰ Systemic therapies have been found most efficacious in active disease states, and early onset of treatment is most beneficial. Active disease is characterized by new lesions of less than six months' duration, disease extension, inflammation (erythema or edema), or the presence of a sclerotic/indurated periphery.² Depth of lesions and involvement of subdermal structures are also important factors in considering the use of systemic therapies. Treatments including D-penicillamine, cyclosporine, antimalarials, ultraviolet light therapy and vitamin D analogues have been used with varied success. Moreover, in a systematic review of morphea treatment, it was noted that methotrexate alone or in combination with pulsed corticosteroids provided the greatest evidence (level 2) of disease response in deep lesions.¹⁰ Mycophenolate mofetil (MMF) has shown promise in patients who don't respond to standard treatments.

Most treatments to improve cosmesis once the disease has been stabilized have been found to achieve unsatisfactory results. Fat and bone grafting, synthetic tissue inserts, and surgical excision have all been reported in the literature with mixed results.¹² Recently, dermal fillers, especially hyaluronic acid (HA), have been used as monotherapy in patients with localized morphea with positive results.¹³⁻¹⁵ Herein, we report a case of en coup de sabre treated successfully with hyaluronic acid filler while the disease was being maintained with mycophenolate mofetil and hydroxychloroquine sulfate.

Case Report

A 42-year-old female was referred by her primary care physician for a linear lesion on her left forehead for an unknown duration. The patient was unaware of the exact onset time of the lesion but noted a clinical progression in size and depth over the past five years. The patient had not been treated in the past but had been using topical clobetasol solution to the area for two months prior to being evaluated. She denied any previous cosmetic procedure to the area and admitted to using concealer makeup to camouflage the lesion.

Physical exam revealed a linear, atrophic plaque with peripheral hyperpigmentation measuring 8 cm, located 2 cm lateral to midline on the forehead (Figure 1). Subcutaneous tissue and underlying bone was involved, leaving a slight depression at the center of the lesion. At initial evaluation, a 3-mm punch biopsy was performed and was consistent with morphea in an en coupe de sabre pattern. The patient was referred to ophthalmology to initiate treatment with hydroxychloroquine sulfate 200 mg twice daily.

After two months of mild worsening of disease, the patient was started on mycophenolate mofetil (MMF) 1 gm twice daily in addition to hydroxychloroquine. After two months of treatment, the patient's lesion was clinically stable, and it was decided to decrease the MMF to 500 mg twice daily with concomitant hydroxychloroquine at 200 mg twice daily. The patient was clinically stable after several months of therapy but showed intermittent clinical flares upon attempting to decrease both systemic medications. After several months of therapy, the patient's lesion showed apparent softening, and there was improvement of surrounding pigmentation (Figure 2).

Figure 1

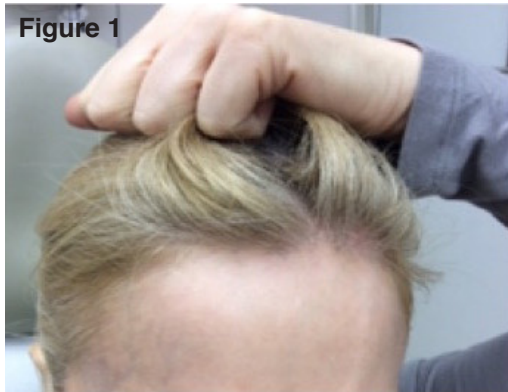


Figure 2



At this point, the patient was given the option to improve the overall cosmesis of her condition by injecting a hyaluronic acid filler into the lesion. Benefits, risks, alternative options, and off-label use of hyaluronic acid fillers were discussed prior to treatment. Topical lidocaine 10% cream was liberally applied 30 minutes prior to the procedure. Juvederm Ultra Plus XC was injected above the periosteum and throughout the linear defect using a 27-gauge needle in aliquots of 0.05 cc to 0.1 cc. A total of 0.7 cc was used at the initial treatment session with moderate improvement. Injections were well tolerated, and the patient returned for a second treatment session six weeks later, at which point an additional 0.5 cc was injected for full correction. At six months post treatment, the patient had maintained a significant cosmetic improvement and was extremely pleased with her results.

Discussion

Treatment of the en coup de sabre variant of linear morphea has proved challenging in regard to obtaining disease remission and improving clinical appearance. As discussed by Zwischenberger and Jacobe, the depth of involvement of morphea plays a vital role in determining treatment options.¹⁰ In the case of deep involvement, defined as sclerosis or inflammation of the reticular dermis, subcutis, fascia or muscle, topical corticosteroids, calcineurin inhibitors and phototherapy are likely to be ineffective and should not be considered as first-line treatments. There has been notable success with both low-dose methotrexate and systemic corticosteroids in treating linear morphea. In a small clinical trial of nine patients given methotrexate (MTX) at 15 mg per week, six patients showed clinical response in the form of improved tissue texture.¹⁷ In addition, the administration of pulse corticosteroids (1,000 mg for three days monthly) with concomitant low-dose methotrexate at 15 mg per week for six months was found to be beneficial and safe in severe forms of localized scleroderma.¹⁸

Of cases that are recalcitrant to conventional therapies, there have been various case reports showing improvement with mycophenolate mofetil (MMF). As a selective inhibitor to de novo purine synthesis, MMF has been shown not only to inhibit lymphocytes but also to down-regulate fibroblast and smooth muscle cell proliferation.¹⁹ In a retrospective chart review by Martini et al., 10 juvenile patients with various subtypes of morphea who showed disease activity despite four months of treatment with MTX and pulse corticosteroids were administered MMF in doses ranging from 600 mg/m²/day to 1,200 mg/m²/day, twice daily. All 10 patients showed a favorable response, defined as "absence of extension of the lesions and improvement in at least one of the following: signs of inflammation, softening and/or lightening of the skin by clinical examination and/or absence of activity by thermography." Substantial clinical response was noted at three to six months after initiation of therapy, and mean duration of treatment was 20 months. MMF was well tolerated and allowed for decreases or discontinuations in corticosteroid and MTX doses.¹¹ In a separate case series by Mertens et al., seven patients with localized scleroderma were treated with MMF due to MTX ineffectiveness or MTX intolerance. Of these patients, five remained on oral prednisone at the onset of therapy with MMF. The starting dose of MMF was 500 mg daily to 2,000 mg daily, and mean duration of treatment was 15 months.

A favorable response was noted in six patients, and complete disease remission was seen in four patients. In one patient, treatment was discontinued due to elevated liver enzymes.²⁰ Overall, the study substantiated the possible benefit of MMF in the treatment of advanced localized scleroderma or cases recalcitrant to standard therapies.

In stabilized lesions, cosmetic correction of defects has been attempted with various techniques including fat allograft transfer, surgical excision, prosthetic implants, and synthetic tissue matrix. The use of hyaluronic acid dermal filler has been documented in a few case reports in recent literature.¹³⁻¹⁵ Hyaluronic acid (HA) filler is an excellent alternative to invasive procedures for restoring the defect in en coup de sabre. As a non-sulfated glycosaminoglycan that naturally occurs in the body, HA has been shown to hydrate, volumize, and stimulate collagen synthesis.²¹ Initially introduced for intra-articular joint injection, HA fillers have become the most commonly used facial fillers over the past several years. They exhibit an excellent safety profile and are simple to use, allergy free, and temporary. In cases of poor results or complications, the enzyme hyaluronidase can be used to catalyze the degradation of hyaluronic acid.²² In our case, Juvederm Ultra Plus XC was injected due to its viscosity and indication for deep dermal augmentation. In addition, hyaluronic acid filler proved the most cost-effective approach for maintaining volume and is noted to last one year.

Conclusion

Our case demonstrates a significant cosmetic correction to an en coup de sabre defect using hyaluronic acid filler while the patient was clinically stable on mycophenolate mofetil 1 gm twice daily and hydroxychloroquine sulfate 200 mg twice daily. She had two sessions of injections with Juvederm Ultra Plus XC six weeks apart with no complications or change in disease activity. Systemic therapy was continued during the cosmetic procedures in part because it has been suggested that morphea may be induced or exacerbated by trauma.

References

1. Katz K. Frontal linear scleroderma (en coup de sabre). *Dermatol Online J*. 2003;9:10.
2. Zulian F, Athreya BH, Laxer R, et al. Juvenile Scleroderma Working Group of the Pediatric Rheumatology European Society (PRES). Juvenile localized scleroderma: clinical and epidemiological features in 750 children: an international study. *Rheumatology*. 2006;45(5):614-20.
3. Eubanks LE, McBurney EI, Galen W, Reed R. Linear scleroderma in children. *Int J Dermatol*. 1996 May;35(5):330-6.
4. Dharamsi JW, Victor S, Aguwa N, Ahn C, Arnett F, Mayes MD, Jacobe H. Morphea in adults and children cohort III: nested case-control study--the clinical significance of autoantibodies in morphea. *JAMA Dermatol*. 2013 Oct;149(10):1159-65.
5. Laxer RM, Zulian F. Localized scleroderma. *Curr Opin Rheumatol*. 2006;18:606.
6. Kroft EB, de Jong EM, Evers AW. Psychological distress in patients with morphea and eosinophilic fasciitis. *Arch Dermatol*. 2009;145:1017-22.
7. Holland KE, Steffes B, Nocton JJ, et al. Linear scleroderma en coup de sabre with associated neurologic abnormalities. *Pediatrics*. 2006;117:e132.
8. Blaszczyk M, Jablonska S. Linear scleroderma en Coup de Sabre. Relationship with progressive facial hemiatrophy (PFH). *Adv Exp Med Biol*. 1999;455:101.
9. Peterson LS, Nelson AM, Su WP, Mason T, O'Fallon WM, Gabriel SE. The epidemiology of morphea (localized scleroderma) in Olmsted County 1960-1993. *J Rheumatol*. 1997;24:73-80.
10. Zwischenberger BA, Jacobe HT. A systematic review of morphea treatments and therapeutic algorithm. *J Am Acad Dermatol*. 2011;65:925-41.
11. Martini G, Ramanan AV, Falcini F, Girschick H, Goldsmith DP, Zulian F. Successful treatment of severe or methotrexate-resistant juvenile localized scleroderma with mycophenolate mofetil. *Rheumatology*. 2009 Nov;48(11):1410-3.
12. Park SW, Wang HY. Survival of grafts in coup de sabre. *Dermatol Surg*. 2002;28:763-6.
13. Thareja SK, Sadhwani D, Alan Fenske N. En coup de sabre morphea treated with hyaluronic acid filler. Report of a case and review of the literature. *Int J Dermatol*. 2015 Jul;54(7):823-6.
14. Mashiko T, Mori H, Kato H, Doi K, Kuno S, Kinoshita K, Kunitatsu A, Ohtomo K, Yoshimura K. Semipermanent volumization by an absorbable filler: onlay injection technique to the bone. *Plast Reconstr Surg Glob Open*. 2013 May 7;1(1). pii: e4-e14. doi: 10.1097/GOX.0b013e31828c66b0. eCollection 2013 Apr.
15. Choksi AN, Orringer JS. Linear morphea-induced atrophy treated with hyaluronic acid filler injections. *Dermatol Surg*. 2011 Jun;37(6):880-3.
16. Vierra E, Cunningham BB. Morphea and localized scleroderma in children. *Semin Cutan Med Surg*. 1999;18:210-25.

17. Seyger MM, van den Hoogen FH, de Boo T, de Jong EM. Low-dose methotrexate in the treatment of widespread morphea. J Am Acad Dermatol. 1998 Aug;39(2 Pt 1):220-5.
18. Kreuter A, Gambichler T, Breuckmann F, Rotterdam S, Freitag M, Stuecker M, et al. Pulsed high-dose corticosteroids combined with low-dose methotrexate in severe localized scleroderma. Arch Dermatol. 2005;141:847-52.
19. Roos N, Poulalhon N, Farge D, Madelaine I, Mauviel A, Verrecchia F. In vitro evidence for a direct anti-fibrotic role of the immunosuppressive drug mycophenolate mofetil. J Pharmacol Exp Ther. 2007;321:583-9.
20. Mertens JS, Marsman D, van de Kerkhof PC, Hoppenreijs EP, Knaapen HK, Radstake TR, de Jong EM, Seyger MM. Use of Mycophenolate Mofetil in Patients with Severe Localized Scleroderma Resistant or Intolerant to Methotrexate. Acta Derm Venereol. 2016 May;96(4):510-3.
21. Wang F, Garza L, Kang S, et al. In vivo stimulation of de novo collagen production caused by cross-linked hyaluronic acid dermal filler injections in photodamaged human skin. Arch Dermatol. 2007;143:155-63.
22. Goa KL, Benfield P. Hyaluronic acid. A review of its pharmacology and use as a surgical aid in ophthalmology, and its therapeutic potential in joint disease and wound healing. Drugs. 1994;47:536-66.