

Autologous lipotransfer can improve the outcomes of localised scleroderma

Sir,

Localised scleroderma, also known as morphea, presents heterogeneously, from small plaques to extensive linear morphea that can cause joint contracture, limb length discrepancy and significant functional impairment (1). Morphea further impacts patient quality of life through cosmetic disfigurement, with patients reporting embarrassment, stigmatisation, along with high rates of anxiety and depression (2).

Treatment options for morphea target the underlying disease process, however, treatments for established disfigurement are extremely limited (3). Autologous fat grafting (AFG), also known as autologous lipotransfer, is an increasingly popular reconstructive technique with demonstrated utility in the treatment of fibrotic conditions such as systemic sclerosis and radiation-induced fibrosis (4, 5). AFG is useful for reconstructing soft-tissue volumetric defects, however, recent research has also demonstrated regenerative and antifibrotic properties, putatively through the presence of Adipose Derived Stem Cells (ADSCs) (6).

Literature reporting the use of AFG in morphea is sparse (3).

We report our experience with two patients presenting with morphea predominantly affecting the lower limb. We performed AFG through the technique described by Coleman; in short, fat is harvested from the abdomen using a cannula connected to a 20ml Luer-Lock syringe, the lipos aspirate is centrifuged at 3000rpm for 3 minutes, with the blood and free oil being discarded before grafting (6).

The first patient was a 22-year-old female with linear morphea of the left lower leg, including the groin, posterior knee, dorsum of foot from the age of 11. After successful treatment with methotrexate, she relapsed following the birth of her first child. Despite increased methotrexate and the addition of multiple systemic and topical treatments, her morphea worsened. She required physiotherapy, cognitive behavioural therapy and cosmetic camouflage. 48ml of fat was harvested from the abdomen and both thighs and transferred into the left leg using the Coleman technique (6). Despite incomplete graft retention, the patient was able to stop all systemic treatment for her second pregnancy, with her morphea remaining stable.

The second patient was a 29-year-old female

with morphea of the left leg, abdomen and arm that started from the age of 17. She was treated with intravenous steroids, topical therapy and phototherapy as she did not tolerate further systemic therapy.

Extensive fibroatrophic changes to her left leg and foot resulted in difficulty walking or standing, the need for orthotics, with progressively limited movement of her ankle and knee. AFG was harvested from the abdomen and grafted to the thigh, tibial border, heel and plantar surface of the foot. Despite incomplete graft retention, the patient experienced improvement in joint mobility which persisted at long-term follow-up (Fig. 1). AFG is a minimally invasive, safe technique that utilises a readily available autologous substrate with minimal donor site morbidity. Its ability to produce long-term symptomatic improvements has been demonstrated in other fibrotic conditions (4, 5). The cases we report here demonstrate its potential utility as a treatment for morphea, including in severe cases causing functional deficit.

The mechanism by which AFG reverses tissue fibrosis is not well understood, however, graft ADSCs are implicated through enhancing angiogenesis, localised immunomodulation and inhibition of transforming growth factor beta1 (TGF- β 1) signalling (7). ADSCs are thought to promote tissue angiogenesis indirectly through vascular endothelial growth factor (VEGF) expression and directly through differentiation into endothelial cells (8). TGF- β 1 is a potent inducer of collagen synthesis and plays a key role in tissue fibrosis; the mechanism by which AFG reduces its expression is poorly understood, but thought to be the result of paracrine signalling between ADSCs and fibroblasts (4).

AFG has shown significant promise in the

treatment of fibrotic conditions. Utilising AFG in the treatment of morphea has, so far, been limited, but promising early results warrant further investigation of this innovative treatment modality and its underlying mechanisms.

B.J. Langridge¹, MBBS, MA(Cantab.), MRCS, FHEA

F.H.K. Jeon¹, MBBS, MSc

A. Almadori¹, MBChB, MSc

M.F. Griffin¹, MBChB, MSc, MRes, MRCS, PhD

C.P. Denton², PhD, FRCP

P.E.M. Butler¹, MD, FRCS (Plast)

¹Department of Plastic Surgery, Royal Free Hospital, London, Charles Wolfson Centre for Reconstructive Surgery, Royal Free Hospital, London, and Division of Surgery & Interventional Science, University College London;

²Centre for Rheumatology, UCL Division of Medicine and Royal Free London NHS Foundation Trust Hospital, London, UK.

Please address correspondence to: Dr Benjamin J. Langridge, Department of Plastic and Reconstructive Surgery, Royal Free Hospital, Pond Street, Hampstead, NW3 2QG London, UK. E-mail: b.langridge1@nhs.net

Competing interests: none declared.

References

1. MERTENS JS, SEYGER MMB, THURLINGS RM, RADSTAKE TRDJ, DE JONG EMGJ: Morphea and Eosinophilic Fasciitis: An Update. *Am J Clin Dermatol* 2017; 18: 491-512.
2. KLIMAS NK, SHEDD AD, BERNSTEIN IH, JACOBHEH: Health-related quality of life in morphea. *Br J Dermatol* 2015; 172: 1329-37.
3. DE ALBUQUERQUE JV, ANDRIOLO BN, VAS- CONCELLOS MR, CIVILE VT, LYDDIATT A, TRE- VISANI VF: Interventions for morphea. *Cochrane Database Syst Rev* 2019; 7: CD005027.
4. ALMADORI A, GRIFFIN M, RYAN CM *et al.*: Stem cell enriched lipotransfer reverses the effects of fibrosis in systemic sclerosis. *PLoS One* 2019; 14: e0218068.
5. RIGOTTI G, MARCHI A, GALIÈ M *et al.*: Clinical treatment of radiotherapy tissue damage by lipoaspirate transplant: A healing process mediated by adipose-derived adult stem cells. *Plast Reconstr Surg* 2007; 119: 1409-22.
6. COLEMAN SR: Structural fat grafting: More than a permanent filler. *Plast Reconstr Surg* 2006; 118 (Suppl.): 108S-120S.
7. RIGOTTI G, MARCHI A, SBARBATI A: Adipose- Derived mesenchymal stem cells: Past, present, and future. *Aesthetic Plast Surg* 2009; 33: 271-3.
8. HONG KY, YIM S, KIM HJ *et al.*: The Fate of the Adipose-Derived Stromal Cells during Angiogenesis and Adipogenesis after Cell-Assisted Lipotransfer. *Plast Reconstr Surg* 2018; 141: 365-75.

Fig. 1. Patient 2 pre- operatively (left) and 5 years post-Autologous Fat Grafting (right), demonstrating sustained improvement in her joint contracture.

