

Successful Fat Grafting in a Patient With Thromboangiitis Obliterans

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ABSTRACT

Thromboangiitis obliterans, or Buerger disease, is a rare nonatherosclerotic segmental inflammatory vasculitis that generally affects young tobacco smokers. Although no surgical treatment is available, the most effective way to halt the disease's progress is smoking cessation. In this case report, a 29-year-old smoker showed up to emergency department with gangrene of his fifth left toe and extensive plantar ulceration. After investigative angiography, he was diagnosed with Buerger disease. On November 2017, he underwent fifth left toe amputation and hyperbaric therapy. Five months after amputation, the patient was rehospitalized because of surgical wound dehiscence, wide ulceration, and pain. He was treated with lipofilling using the Coleman technique. Two weeks after the fat grafting procedure, the patient suspended pain control medication, and after 2 months, the surgical wound was almost healed. Fat grafting (lipofilling) is mostly used in plastic surgery; it offers regenerative effects, with minimal discomfort for the patient. This case report demonstrates a successful alternative use of lipofilling for this unique condition and opens up new options for use of this technique in other fields.

KEYWORDS: Buerger disease, fat grafting, lipofilling, plastic surgery, smoking, thromboangiitis obliterans, wound care

ADV SKIN WOUND CARE 2019;32:1–4.

The treatment of Buerger disease is usually conservative, with cycles of prostanoids, antiplatelet drugs, nitric oxide agents, or bosentan.² Surgery is used in rare cases when distal target vessels are available. However, failed bypass occlusion can result in devastating outcomes such as critical limb ischemia; therefore, surgery is not usually recommended. Smoking cessation can slow the progression of symptoms or slightly improve the clinical situation.

Despite general medical advancement, little progress has been made in terms of treatment for patients affected by Buerger disease; few data exist on the use of intra-arterial thrombolytic therapy, prostaglandin therapy, or angiogenesis. That said, there is a growing interest in the use of fat grafting, not only as cosmetic therapy in plastic surgery, but also as a procedure with enormous regenerative potential. Adipose tissue is full of stem cells and, if properly processed, can be used to manage relapsing wounds such as those seen in patients with Buerger disease.^{3,4} Although the true mechanism of recovery is still unknown, many researchers consider fat grafting capable of healing complex wounds via autologous adipose tissue-derived cell (ATDC) fractions.⁵

CASE REPORT

The research described in this report was conducted in accordance with the Declaration of Helsinki. The patient gave informed consent for the study and the publication of this report and associated images.

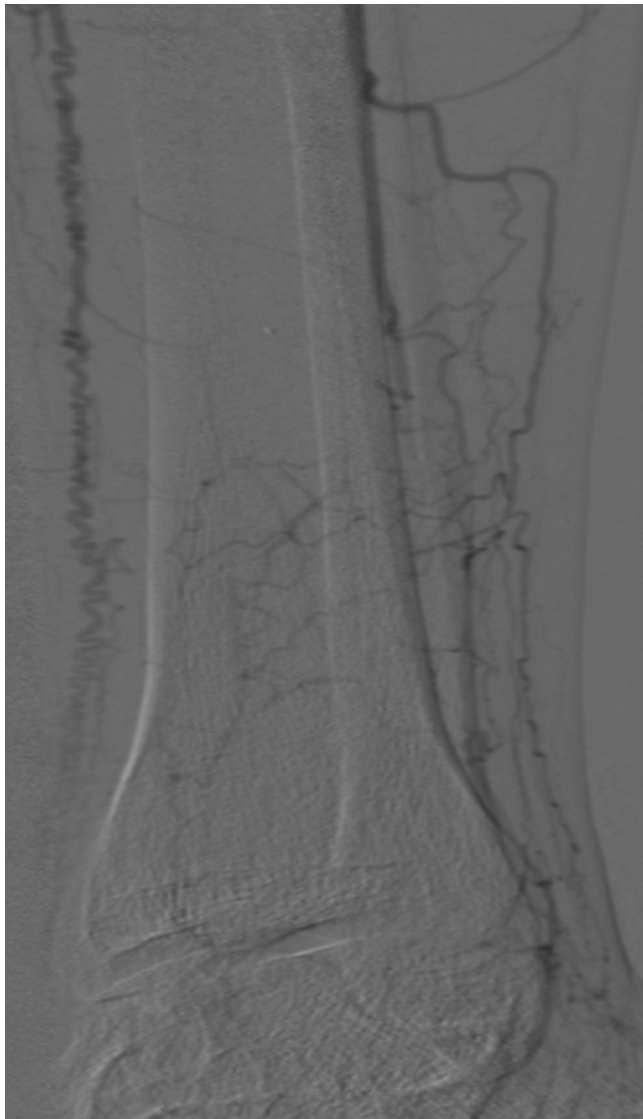
A 29-year-old man with an 8 pack-year smoking history came to the authors' attention in October 2017 because of wet gangrene and necrosis of his fifth left toe and extensive plantar ulceration. He reported a worsening clinical condition during the previous 2 months, with extension of the necrosis/ulceration and an increase in pain. He had previously undergone cycles of antibiotic and antifungal treatment in another clinical department without improvement (Figure 1).

The patient was admitted to the authors' department for a comprehensive clinical and diagnostic study. During his hospitalization, an ultrasound indicated a normal femoropopliteal artery district bilaterally, with triphasic Doppler signals along peripheral

INTRODUCTION

Thromboangiitis obliterans, also known as Buerger disease, is a nonatherosclerotic segmental inflammatory disease of the small and medium arteries that mainly affects males younger than 45 years with a current or recent history of tobacco use. The immune system and inflammation have been implicated in Buerger disease pathogenesis. This condition typically presents with damage to the leg arteries and severe distal ischemia, with the integrity of the proximal part of the femoropopliteal axis and no autoimmune and/or hypercoagulable status.¹

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Figure 1.**PATIENT ANGIOGRAPHY**

Angiography shows typical patterns of thromboangiitis (corkscrew collaterals) and progressive reduction of vascularization.

arteries on his right leg. On his left leg, the Doppler signals were normal for his popliteal artery below the knee and in the proximal tract of anterior and posterior tibial artery. However, no Doppler signals were detected in the distal third of the leg or in his foot.

The patient underwent diagnostic angiography to enhance the clinical picture. Results showed typical patterns of Buerger disease: corkscrew-shaped collateral vessels, cutoff-type vascular occlusions, vessels with smooth-lined lamina in noninvolved

arteries, and discontinuous segmental involvement of affected arteries and veins (Figure 2).⁶

During his hospitalization, the patient underwent immunologic study, but the autoantibody dosage was negative. Cycles of prostanoids and hyperbaric therapy were carried out, but they produced limited benefit. The patient also underwent hyperbaric therapy for 20 days with no significant results. After angiography, he was submitted for fifth left toe amputation; unfortunately, the surgical wound dehisced. The patient was discharged with diagnosis of Buerger disease, materials on smoking cessation, and instructions to take prescribed antiplatelet and pain relief medication.

In March 2018, the patient was rehospitalized for a lack of healing with wide ulceration and the worsening of pain at rest. This time, he was treated with lipofilling using the Coleman technique. His abdominal wall was injected with Klein solution (lidocaine, adrenalin, and saline), and autologous adipose tissue was harvested using nine-hole harvesting cannulas. The adipose tissue was processed (920g for 3 minutes), and only the intermediate layer containing both the adipose-derived stromal/stem cells and stromal/vascular cell component was used.⁵ The terminal branches of the patient's leg arteries were mapped to facilitate graft placement. Multiple injections (1 mL each) of the adipose tissue formulation were inoculated 1 cm above the end of the terminal

Figure 2.**DISEASE EVOLUTION**

The evolution of the patient's thromboangiitis with amputation site necrosis and dehiscence.

branch of the peroneal, anterior, and posterior tibial arteries, respectively (Figure 3).

The day after the procedure, the patient reported a marked resolution of the pain. He was discharged 3 days after the procedure following relief of his pain and stopped painkillers 15 days later. After 30 days, the fifth toe's dehiscence wound showed progressive improvement, and, at 60 days postprocedure, the wound appeared almost healed (Figure 4). The patient was followed up monthly to start and now visits biannually.

DISCUSSION

Fat grafting was used for the first time in 1893 by Gustav Neuber to correct an orbital depression and the sequelae of osteomyelitis.⁷ Today, the Coleman technique is the criterion standard for fat grafting. It was developed in 1994, when a team of plastic surgeons and researchers demonstrated that fat is the greatest reservoir of adult mesenchymal stem cells (MSCs) capable of differentiating into different tissues. Studies³⁻⁵ have demonstrated that ATDC fractions may mediate therapeutic effects through a multitude of mechanisms that include signaling angiogenesis, inflammation, cell homing, and cell survival.

Figure 3.
MAPPING AREAS FOR INJECTION CLOSE TO PRINCIPAL ARTERIES

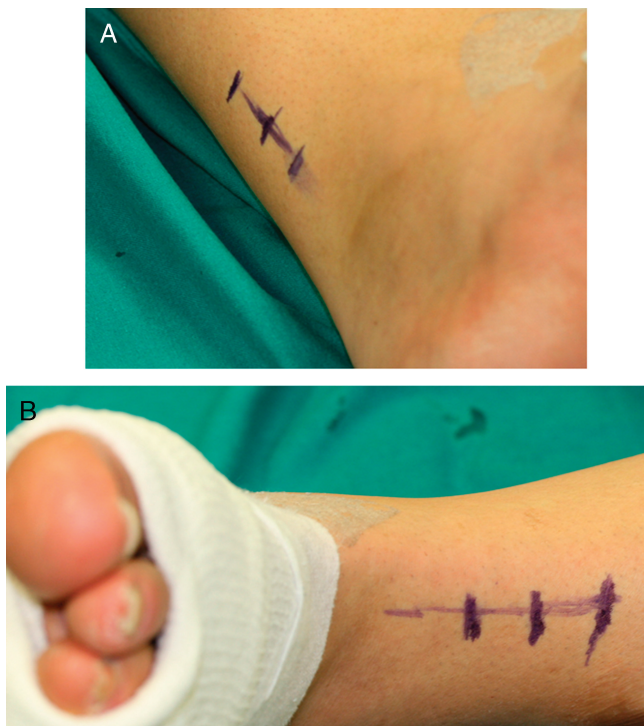


Figure 4.
ULCER HEALING



A, The ulcer at the end of the procedure. B, 3 months postprocedure.

Modern literature describes the use of fat grafting in many fields: in oncologic surgery to reconstruct breast after tumor excision,⁸ in the treatment of scars^{9,10} or burned skin,¹¹ and in patients with scleroderma or Dupuytren disease.¹² Recent studies have demonstrated the utility of adipose-derived stem cells in wound healing, describing their ability to regenerate soft tissues and their remodeling capacity provided by cytokine and growth

factor profiles.¹³ For example, the literature describes local intramuscular injections of autologous or allogeneic MSC that result in significant regression of skin ulcers and improvements in pain at rest, Walking Impairment Questionnaire scores, and patient quality of life.¹⁴

To date, there are no published cases of fat grafting used to treat peripheral arterial disease (PAD) or Buerger disease. Experimental protocols are studying the use of adipose tissue in peripheral arteriopathy that is resistant to medical therapy or not surgically or endovascularly treatable. Other researchers are evaluating the direct injection of processed centrifuged fat into damaged tissue. However, there is no published literature about the stimulation of neoangiogenesis via perivascular stem cell injections.

CONCLUSIONS

The evidence for fat grafting with ATDC or the direct injection of MSCs to treat Buerger disease or PAD is still anecdotal; only meticulous preclinical and clinical studies can provide more certainty. One major issue is the lack of data about the long-term survival of the injected fatty tissue. That said, autologous fat grafting is a promising field of research in both cosmetic and reconstructive surgery. This minimally invasive technique may offer some patients satisfactory clinical results in alleviating signs and symptoms, as well as improving their quality of life and reducing amputations. This case report illustrates the importance of new methods to treat Buerger disease and, more generally, PAD. ●

REFERENCES

1. Dargon PT, Landry GJ. Buerger's disease. *Ann Vasc Surg* 2012;26(6):871-80.
2. De Haro J, Bleda S, Acin F. An open-label study on long-term outcomes of bosentan for treating ulcers in thromboangiitis obliterans (Buerger's disease). *Int J Cardiol* 2014;177(2):529-31.
3. Zuk PA, Zhu M, Ashjian P, et al. Human adipose tissue is a source of multipotent stem cells. Raff M, ed. *Mol Biol Cell* 2002;13(12):4279-95.
4. Moseley TA, Zhu M, Hedrick MH. Adipose-derived stem and progenitor cells as fillers in plastic and reconstructive surgery. *Plast Reconstr Surg* 2006;118(Suppl):121S-8S.
5. Papa N Del, Di Luca G, Sambataro D, et al. Regional implantation of autologous adipose tissue-derived cells induces a prompt healing of long-lasting indolent digital ulcers in patients with systemic sclerosis. *Cell Transplant* 2015;24(11):2297-305.
6. Hagen B, Lohse S. Clinical and radiologic aspects of Buerger's disease. *Cardiovasc Intervent Radiol* 1984;7(6):283-93.
7. Hollander E. über einen Fall von fortschreitenden Schwund des Fettgewebes und seinen kosmetischen Ersatz durch Menschenfett. *Munch med Wochenschr* 1910;57(1794).
8. Debald M, Pech T, Kaiser C, et al. Lipofilling effects after breast cancer surgery in post-radiation patients: an analysis of results and algorithm proposal. *Eur J Plast Surg* 2017;40(5):447-54.
9. Riyat H, Touil LL, Briggs M, Shokrollahi K. Autologous fat grafting for scars, healing and pain: a review. *Scars Burn Heal* 2017;3:205951311772820.
10. Gotland N, Rangatchew F, Khorasani H, Holmgaard R, Kølbe S-F, Bonde C. Treating scars with lipofilling [in Danish]. *Ugeskr Laeger* 2018;180(26).
11. La Padula S, Hersant B, Meningaud JP, D'Andrea F. Use of autologous fat graft and fractional CO₂ laser to optimize the aesthetic and functional results in patients with severe burn outcomes of the face. *J Stomatol Oral Maxillofac Surg* 2018.
12. Hovius SER, Zhou C. Advances in minimally invasive treatment of Dupuytren disease. *Hand Clin* 2018;34(3):417-26.
13. Bellini E, Grieco MP, Rapisio E. The science behind autologous fat grafting. *Ann Med Surg* 2017;24:65-73.
14. Martin-Rufino JD, Lozano FS, Redondo AM, et al. Sequential intravenous allogeneic mesenchymal stromal cells as a potential treatment for thromboangiitis obliterans (Buerger's disease). *Stem Cell Res Ther* 2018;9(1):150.