Cutaneous T-cell lymphoma (CTCL) is a non-Hodgkin lymphoma caused by malignant transformation of "cutaneous T cells," a large subset of normal skin localizing T cells. CTCL most commonly presents as skin plaques, which evolve into cutaneous tumors with systemic dissemination. Allogeneic hematopoietic stem cell transplantation (HSCT) is an effective treatment option for advanced disease, thought to provide durable remissions through its graft-versus-leukemia/lymphoma effect. Donor T cells are thought to kill residual malignant T cells through immunoreactivity against host minor histocompatibility antigens on these malignant cells. Complete donor-derived hematopoiesis is paramount for sustained engraftment of the transplanted stem cells and prevention of disease relapse. Successful engraftment leads to a state of chimerism, which is used as an indicator for disease relapse.

Total skin electron beam therapy involves ionizing radiation to the entire skin surface to treat CTCL and is used either as standalone treatment or in preparation for an HSCT. Radiation damages DNA, proteins, and cell membranes leading to cell death and ultimately resulting in skin ulcerations. Additionally, radiation has long-term effects including microvascular injury resulting in ischemic damage and fibroblast dysfunction leading to poor wound healing and fibrosis—all of which contribute to the persistence of chronic skin ulcers. Fat grafting, with its mesenchymal stem cells and growth factors, is an effective treatment for radiation-induced ulcers. Growing evidence also demonstrates its effectiveness in treating neuropathic pain.

We present a unique case of allogeneic fat grafting between histocompatible brothers in the treatment of painful radiation-induced skin ulcers in a CTCL patient.

**CASE PRESENTATION**

The patient is a 65-year-old man first diagnosed with CTCL in 2007. He was treated with spot radiation therapy, total skin electron beam therapy, and chemotherapy from 2007 to 2012, but these treatments were unable to achieve a durable remission. Therefore, in July 2012, the patient underwent an HSCT from his human leukocyte antigen-matched brother. Engraftment was successful, but the patient went on to develop painful, radiation-induced ulcers. The ulcers were fat-allografted using liposuctioned fat from his brother because of the patient's unique chimeric state. Postprocedure follow-up revealed epithelialization of the ulcer sites and significant improvement in neuropathic pain. Our unique case study supports the use of fat grafting for its restorative purposes and for its ability to alleviate chronic neuropathic pain. Additionally, it appears that our case provides a basis of a general approach to the treatment of radiation-induced ulcers in chimeric patients with lymphoid malignancies.

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The patient remained disease free, but he developed painful, radiation-induced ulcers of his bilateral thighs, left flank, and left axilla for which he was referred to us in 2014. The ulcers were exquisitely painful, requiring high doses of oral and transdermal opioid medication (Fig. 1A). Furthermore, they exhibited constant breakdown, were unresponsive to conservative management, and deemed unsuitable for free-flap reconstruction. Autologous fat grafting of the ulcers was not an option because of the lack of subcutaneous tissue and the necessity of preserving potential flap sites. The possibility of fat allografting the ulcers using liposuctioned fat from his human leukocyte antigen-matched brother was discussed because of the patient’s unique chimeric state. Repeat chimerism testing continued to remain stable. After the risks and benefits of the procedure along with its innovative nature were discussed, the patient and his brother consented to the procedure. The Yale University Human Investigation Committee gave their approval as an innovative procedure.

In August of 2015, fat was harvested using liposuction from the brother’s abdomen and purified using Puregraft (Puregraft LLC, Solana Beach, Calif.). A 50 to 60 cm³ of the purified fat was injected into each of the patient’s ulcer sites subcutaneously for a total of 210 cm³. The procedure was completed without complications, and the patient was discharged home.

Clinical assessment on follow-up revealed new epithelialization of the patient’s ulcer sites (Figs. 1B and 2). Additionally, the patient expressed a dramatic improvement in pain symptoms and was eventually able to stop all his opioid medications. Flow cytometry and chimerism studies showed continued cancer remission and a stable chimerism profile (Fig. 3) (Supplemental Digital Content 2, http://links.lww.com/PRSGO/A255).

**DISCUSSION**

Neuropathic pain is caused by damage to the somatosensory nervous system, which can lead to abnormal processing and sensitization of both peripheral and central neurons. Treatment of neuropathic pain consists of a variety of opioids, antidepressants, anticonvulsants, and lidocaine patches. The difficulty in treating neuropathic pain, however, often leads to the chronic use and abuse of multiple agents. Fat grafting has been shown to improve neuropathic pain from various causes such as postmastectomy pain syndrome, extremity end neuritis, and traumatic and burn scars with sustained responses.8–10

Several hypotheses have been proposed for the mechanism of pain relief with fat grafting. Vaienti et al10 proposed that fat grafts act mechanically as cushions around nerve stumps and act biologically by improving local vascularization and reducing inflammation. Sacerdote et al11 showed in a rodent model that systemic administration of adipose-derived mesenchymal stem cells decreased levels of proinflammatory cytokine interleukin (IL)-1β and increased levels of anti-inflammatory cytokine IL-10. They proposed that adipose-derived mesenchymal stem cells improve neuropathic pain through immunomodulation resulting in decreased inflammation. In a recent study by Huang et al, fat grafts were injected into burn-injured hind paws of rats, which significantly reduced pain symptoms. Furthermore, these fat graft injections reduced levels of inflammatory markers such as IL-1β, tumor necrosis factor–α, COX-2, iNOS, and nNOS in both the spinal cord and burn scars of these rats. The authors concluded that fat grafting had a direct anti-inflammatory effect both peripherally and centrally that reduced neuropathic pain in burn wounds.12

Our concerns during discussions with our patient before allogeneic fat grafting were whether the mesen-
Chymal stem cells from the fat transfer would have any adverse effects such as reactivating our patient’s CTCL or altering his chimeric profile. From our experience, it appears that allogeneic fat grafting does not cause these adverse effects.

Our unique case study supports the use of fat grafting not only for its restorative purposes but also for its ability to alleviate chronic neuropathic pain. Additionally, it appears that our case provides a basis of a general approach to the treatment of radiation-induced ulcers in chimeric patients with lymphoid malignancies.

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