Case Report/Case Series

Narrowband UV-B Phototherapy for Steroid-Refractory Sclerotic Chronic Cutaneous Graft-vs-Host Disease

Eric Sorenson, AB; Rachel McAndrew, BS; Viraat Patel, BS; Aaron C. Logan, MD, PhD; John Koo, MD; Ethan Levin, MD

**IMPORTANCE** Chronic graft-vs-host disease (GVHD) affects 50% to 70% of patients who receive allogeneic hematopoietic cell transplants (HCTs), and the skin is the most common site of involvement. Chronic cutaneous GVHD can present with sclerotic or nonsclerotic changes of the skin and often requires treatment with systemic immunosuppressants, extracorporeal photopheresis, or phototherapy. We describe the first reported case, to our knowledge, of the effective treatment of sclerotic chronic cutaneous GVHD with narrowband UV-B (NB UV-B) phototherapy.

**OBSERVATIONS** A woman in her 40s presented with sclerotic chronic GVHD of the skin 6 years after HCT for treatment of chronic myelogenous leukemia. The patient’s cutaneous disease progressed despite treatment with prednisone and oral tacrolimus. The patient was initiated on NB UV-B phototherapy 3 times per week, resulting in clinically significant improvement of cutaneous lesions over the first 2 months. The NB UV-B regimen allowed for a reduction of prednisone dose and continued control of cutaneous GVHD over 6 months of therapy.

**CONCLUSIONS AND RELEVANCE** Our case report describes the successful use of NB UV-B phototherapy for the treatment of sclerotic chronic cutaneous GVHD. Further study should be performed to evaluate the effectiveness of this therapeutic modality for patients with sclerotic chronic cutaneous GVHD.

Published online March 25, 2015. Corrected on April 10, 2015.

Report of a Case

A woman in her 40s developed sclerotic cutaneous lesions in the setting of chronic graft-vs-host disease (GVHD). Six years previously, the patient received a myeloablative hematopoietic cell transplant (HCT) using a 10/10 HLA-matched unrelated donor for the treatment of chronic myelogenous leukemia resistant to tyrosine kinase inhibitor therapy.

Early in the posttransplant course, the patient developed acute GVHD limited to the gastrointestinal (GI) tract, which was treated with prednisone and oral tacrolimus therapy. Approximately 1 year post-HCT, the patient developed a severe extensive GVHD overlap syndrome characterized by morbilliform eruptions, oral mucosal ulcerations, xerophthalmia, anorexia, and waxing-waning lower GI tract symptoms. Intermittent prednisone tapers were administered to control disease flares, and tacrolimus was continued but eventually tapered to subtherapeutic serum troughs.

In an attempt to reduce the use of oral corticosteroids following a chronic GVHD flare roughly 4 years after transplantation, the patient was initiated on therapy with extracorporeal photopheresis (ECP) with initial good response of GI tract and cutaneous GVHD. After 13 months, ECP was tapered and discontinued owing to symptom improvement and successful reduction of other immune suppression. The patient was receiving low-dose prednisone at 10 mg daily and using a topical dexamethasone with tacrolimus mouth rinse. A small sclerodermatous plaque on her hand (<1% body surface area [BSA]) was treated with topical fluocinonide.

Shortly after the discontinuation of ECP, the patient developed severe thrombocytopenia most consistent with immune-mediated thrombocytopenic purpura. The dose of prednisone was increased, and rituximab was administered. Although this regimen resulted in a recovery of the platelet count and improved control of mucosal lesions, 4 months later the patient began to develop sclerotic, hyperpigmented cutaneous lesions at the abdomen and presacral area. The lesions progressed over the following 4 months despite continuation of prednisone, 20 mg daily, and oral tacrolimus dosed to therapeutic serum trough levels. On physical examination, hyperpigmented, waxy, indurated plaques were noted at the bilateral anterior inferior costal margins, flanks, and presacral area (Figure, A). Early sclerotic changes characterized by skin dim-
pling, tightness, and underlying induration were noted diffusely across the abdomen and lower back, affecting approximately 15% of the BSA. The lesions were not responsive to potent topical corticosteroids. Owing to the occurrence of intercurrent infections thought likely to be related to the use of systemic corticosteroids, including pneumonia and recurrent thrush, as well as a history of avascular necrosis of the right hip, efforts were made to avoid increasing the systemic corticosteroid dose.

To this end, the patient was initiated on narrowband UV-B (NB UV-B) phototherapy at the University of California, San Francisco, 3 times per week for the treatment of sclerotic chronic cutaneous GVHD. A starting dose of 130 mJ/cm² was selected based on Fitzpatrick skin type, and the dosage was increased as tolerated at subsequent sessions based on a standard protocol. Over the first 2 months of therapy, the patient received a cumulative NB UV-B dose of 11.5 J/cm² and demonstrated a clinically significant response with marked flattening, softening, and lightening of hyperpigmented plaques and a reduction of diffuse skin tightness. At 3 months of therapy, the patient had received a total NB UV-B dose of 21.9 J/cm², and cutaneous lesions continued to improve, with clinically significant improvement of hyperpigmented plaques and skin tightness and a slower but appreciable response at areas of skin dimpling (Figure, B). The prednisonone dose was tapered to 10 mg daily, oral tacrolimus was reduced but maintained at therapeutic levels owing to past flares of noncutaneous GVHD on discontinuation, and topical therapy was continued for oral mucosal GVHD. To date, control of the patient’s sclerotic cutaneous GVHD has been maintained over 6 months of NB UV-B phototherapy.

Discussion

Chronic GVHD is a major complication affecting 50% to 70% of patients following allogeneic HCT, and approximately 75% of patients who develop chronic GVHD demonstrate cutaneous involvement.1,2 Chronic cutaneous GVHD may manifest as sclerotic or nonsclerotic changes of the epidermis, dermis, subcutaneous tissues, and/or fascia. Our patient developed morphea-like sclerosis following HCT, a finding that according to the National Institutes of Health Consensus Development Project is diagnostic of chronic GVHD without the need for further testing.3

Although a variety of phototherapeutic modalities have been used for the treatment of chronic cutaneous GVHD, the current literature is limited to small case series and case reports. Past reports have described effective treatment of sclerotic chronic cutaneous GVHD with systemic psoralen plus UV-A (PUVA), bath PUVA, or UV-A1.4-8 However, reports of the use of NB UV-B for the treatment of chronic cutaneous GVHD are scarce.9,10 Brazelli et al9 described a series of 10 pediatric patients with nonsclerotic chronic cutaneous GVHD treated with NB UV-B in which 8 patients achieved a complete response and 2 demonstrated partial response. Enk et al10 reported a series in which 1 patient with nonsclerotic chronic cutaneous GVHD achieved full remission with NB UV-B phototherapy, while 2 patients with sclerotic chronic GVHD achieved reduction of pruritus but not improvement of skin lesions.

Our patient’s sclerotic chronic cutaneous GVHD demonstrated remarkable improvement in response to NB UV-B phototherapy. This response permitted a reduction of oral corticosteroid dose and a minimization of the risk of future corticosteroid-related infections and other complications. NB UV-B therapy is often overlooked as a potential therapy for sclerotic chronic cutaneous GVHD. However, NB UV-B produces immunomodulatory effects in the dermis, a principal site of fibrosis in morphea-like sclerosis.11 It may also induce systemic effects, as a recent study12 in patients with acute cutaneous GVHD demonstrated a significant increase in peripheral Foxp3+ regulatory T cells in response to NB UV-B therapy. Furthermore, NB UV-B therapy has achieved clinically significant reduction of severity in localized autoimmune scleroderma.13

NB UV-B phototherapy has a number of advantages compared with PUVA and UV-A1 for the treatment of GVHD. NB UV-B does not require the administration of oral psoralen, which causes nausea in some patients and may lead to decreased adherence. In rare cases, psoralen may be hepatotox-
Carcinogenic potential is unknown. Not widely available in the United States, and its long-term toxic, complicating the assessment of causality in GVHD patients who may develop elevated liver enzymes secondary to GVHD involvement of the liver, viral infections, or other medications. In addition, PUVA may be associated with a higher risk of cutaneous malignant neoplasms compared with NB UV-B, and this risk may be further increased in patients receiving chronic systemic immunosuppression.\textsuperscript{14,15} UV-A1, however, is not widely available in the United States, and its long-term carcinogenic potential is unknown.

Conclusions

Based on our patient's response, NB UV-B phototherapy should undergo further study for the treatment of sclerotic chronic cutaneous GVHD. Larger studies could determine optimal treatment regimens for induction and maintenance therapy and may identify patient or lesion characteristics that predict response to therapy.