Rehabilitation in Chronic Graft-Versus-Host Disease

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KEYWORDS

- Chronic graft-versus-host disease • GVHD • GVHD rehabilitation
- Bone marrow transplant rehabilitation • Cancer rehabilitation

KEY POINTS

- Both the direct inflammatory effects of graft-versus-host disease (GVHD) and the treatment to suppress the disease can significantly impact function and cause pain.
- Few studies exist to guide management; the authors review the extant literature and discuss approaches that show promise based on their clinical experience.
- GVHD can affect many organ systems; this review addresses the skin/fascia and cardiac/pulmonary systems because these likely are associated with the highest degree of impairment.

INTRODUCTION

Chronic graft-versus-host disease (cGVHD) is the most common and potentially devastating complication of allogeneic (donor) hematopoietic stem cell transplantation (HSCT), often referred to as bone marrow transplantation. cGVHD occurs in 30% to 70% of patients who receive an HSCT for hematologic malignancy, and is caused by the newly donated T cells attacking highly mitotic areas of the transplant recipient's body that are considered foreign to the engrafted immune cells.[1] Most affected by cGVHD are the skin and fascia, gastrointestinal, pulmonary, hepatic, ocular, and oral mucosal organ systems. This inflammatory process can cause significant damage to the tissues affected, directly contributing to functional impairment. The treatment of cGVHD, which typically involves high-dose corticosteroids to suppress the immune system as first-line therapy, also can be destructive and necessitate rehabilitation to restore function and quality of life.[2]

Disclosure Statement: The authors have no relevant financial or commercial interests to disclose.

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Phys Med Rehabil Clin N Am 28 (2017) 143–151
http://dx.doi.org/10.1016/j.pmr.2016.08.009
pmr.theclinics.com

Although the HSCT itself requires special considerations in rehabilitation, recently transplanted patients are often pancytopenic and at increased risk for infection and bleeding events,[3] this article addresses the rehabilitation of specific impairments directly or indirectly caused by cGVHD. Furthermore, autologous HSCT, in which a person's own immune system is retransplanted into their body after myeloablation, is not discussed, as this does not cause cGVHD. Finally, acute GVHD represents a pathologically distinct process, typically occurring within the first 100 days after transplantation and affects the dermal and gastrointestinal systems, and does not impact function in the same way as cGVHD.[4] This is not directly discussed, although glucocorticoids are first-line treatment of acute GVHD, of which the side effects are addressed.

For purposes of simplicity, we have broken down this review into categories of the most physically devastating manifestations in these patients: skin/fascial and cardiopulmonary cGVHD, and the effects of steroids on muscle and bone. Manifestations of cGVHD in other organ systems, is beyond the scope of this review but a brief summary is listed in **Table 1**. For further information on the sequelae and symptomatic treatment of cGVHD beyond the measures discussed herein, the Ancillary and Supportive Care Working Group Report from the 2015 National Institutes of Health Consensus Development Project for cGVHD is recommended reading.[5]

SKIN AND FASCIAL CHRONIC GRAFT-VERSUS-HOST DISEASE

Cutaneous cGVHD is the most common manifestation of the disease, nearly 100% of people with cGVHD will develop this, and can affect one or both of the dermis and fascia.[6,7] Dermal involvement typically results in a maculopapular lichenoid rash and itself does not cause direct physical impairment; however, it is often the first sign of a cGVHD flare,[8] and may indicate that corticosteroids will soon be initiated or the dose increased.

Fascial cGVHD, on the other hand, is similar to eosinophilic fasciitis and can cause edema, fibrosis, and joint contracture.[9] Edema is often the first sign of fascial involvement, and the most common joints affected are the wrists, shoulders, and ankles, with distal joints affected first in a symmetric, bilateral fashion.[2,8] In addition to contracture, patients may develop joint destruction and skin breakdown as the upper layers of the skin become thin from the disease and corticosteroid use, and the deeper layers thicken.

When examining a patient, the progression of skin sclerosis from "moveable," that is, being able to easily compress focal areas of sclerosis, to "nonmoveable," in which

Table 1
Chronic graft-versus host disease organ involvement and common symptoms

Organ System	Symptoms
Skin (dermal)	Erythematous maculopapular rash, pain, desquamation
Skin (fascial)	Contracture, edema
Gastrointestinal	Painful cramping, watery stool
Oral	Painful lichenoid lesions, dryness, thrush, odynophagia, dysphagia
Ocular	Dryness, conjunctivitis
Vulvovaginal	Dryness, sclerosis, dyspareunia
Pulmonary	Bronchiolitis obliterans, airflow obstruction
Neurologic	Myasthenia gravis (rare), polymyositis (rare), Zoster