

Management of Chronic Graft-Versus-Host Disease

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Chronic graft-versus-host disease (GVHD) is an immune-mediated disorder that adversely affects quality of life and clinical outcomes in patients following hematopoietic stem cell transplantation. Conventional treatment of GVHD includes prolonged and high-dose corticosteroids; however, those drugs are associated with multiple side effects. This article describes the ability of extracorporeal photopheresis therapy to exhibit a steroid-sparing effect, which can reduce long-term complications as a consequence of steroid treatment.

Allogeneic hematopoietic stem cell transplantation (HSCT) is an effective therapeutic modality used to treat a variety of hematologic and nonhematologic conditions (Saria & Gosselin-Acomb, 2007). Although mortality related to allogeneic HSCT has improved since 2000, the management of serious complications after transplantation remains a formidable challenge (Gooley et al., 2010).

Graft-Versus-Host Disease

Graft-versus-host disease (GVHD), a complex complication following allogeneic HSCT, adversely affects the quality of life and clinical outcomes for HSCT survivors (Barton-Burke et al., 2008). The incidence of acute and chronic GVHD is about 30%-60% and carries a mortality rate of 50% (Anders & Barton-Burke, 2007). Acute GVHD occurs within the first 100 days after HSCT in response to activation of donor-derived T cells that mediate a cytotoxic response against specific target host cells, leading to cellular damage and subsequent clinical manifestations (Ferrara & Antin, 2009). The target organs of acute GVHD are the skin, liver, and gastrointestinal tract (Pavletic et al., 2005). In contrast to acute GVHD, the pathophysiology of chronic GVHD is not well defined. Chronic GVHD is believed to involve both alloreactive donor-derived T cells as well as recipient T cells that have been educated by the thymus and become

autoreactive (Woltz, Castro, & Park, 2006). The variable clinical manifestations of chronic GVHD resemble an autoimmune syndrome and are most commonly seen in the skin and mouth, although ocular, gastrointestinal, hepatic, pulmonary, vaginal, musculoskeletal, and hematopoietic involvement may be evident (Horwitz & Sullivan, 2006; Mattson, 2007; Pavletic et al., 2005). In human leukocyte antigen-matched marrow grafting, the incidence of chronic GVHD with liver involvement is estimated as 40%-73%, skin involvement as 65%-80%, eye involvement as 18%-47%, and oral involvement as 48%-72% (Higman & Vogelsang, 2004).

Glucksberg et al. (1974) proposed the first grading system for acute GVHD using time of onset to distinguish between acute and chronic disease (less or more than 100 days after transplantation) based on the degree of skin, liver, and gut involvement. Criteria to establish a chronic GVHD diagnosis include the presence of at least one diagnostic clinical manifestation or at least one distinct manifestation confirmed by biopsy and exclusion of other possible etiologies (Joseph, Couriel, & Komanduri, 2008;

Lee & Flowers, 2008). Histologic confirmation may be used to corroborate a clinical diagnosis. Specific to liver GVHD, a biopsy is necessary to confirm GVHD, along with distinctive manifestations of the complication in at least one other organ system (Joseph et al., 2008; Lee & Flowers, 2008).

Treatment

Corticosteroids are the mainstay of treatment in acute and chronic GVHD (Mattson, 2007). In chronic GVHD, prolonged immunosuppressive therapy is required, averaging two to three years, with 10% of patients continuing treatment longer than five years (Lee & Flowers, 2008). Potential adverse effects of prolonged steroid treatment include hypertension, body habitus changes, osteoporosis, insomnia, emotional lability, cataracts, diabetes mellitus, and life-threatening infections (Knobler et al., 2009) (see Figure 1). Complications of steroid treatment have led to the development of steroid-sparing regimens and use of alternative immunosuppressive agents (Greinix & Antin, 2009; Knobler et al., 2009). Treatment

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