A Case of Chronic Graft-Versus-Host Disease Treated With Photopheresis

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To the Editor:

We present the case of a 12-year-old boy with T-cell lymphoblastic lymphoma that was treated with an allogenic bone marrow transplant from a related donor.

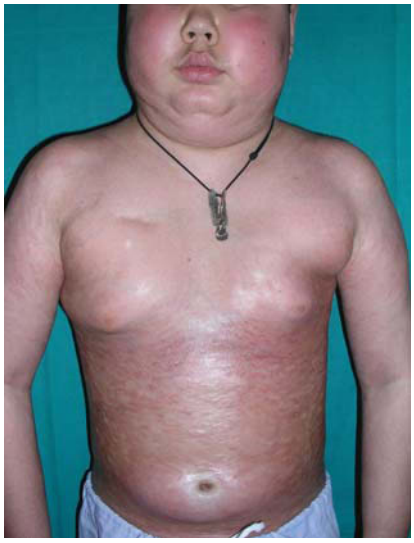

Figure 1. Patient before treatment with extracorporeal photopheresis.

The patient developed acute graft-versus-host disease (GVHD) that was brought under control with cyclosporin and systemic corticosteroids.

Approximately 100 days after the transplant, the patient began to develop indurated plaques on the torso. These plaques progressed to cause diffuse cutaneous sclerosis, with marked joint contracture and inability to perform normal functions (Figure 1). He also presented dyspnea that progressed until it occurred even on minimal effort.

The patient was diagnosed with chronic sclerodermiform GVHD with cutaneous and lung involvement and treatment was initiated with oral cyclosporin (50 mg/12 h) and oral methylprednisolone (20 mg/d).

The patient did not respond to the treatment and was referred to our department for extracorporeal photopheresis. Treatment was performed in 2 sessions on consecutive days every 3 to 4 weeks; 34 sessions were performed and treatment lasted approximately 1 year.

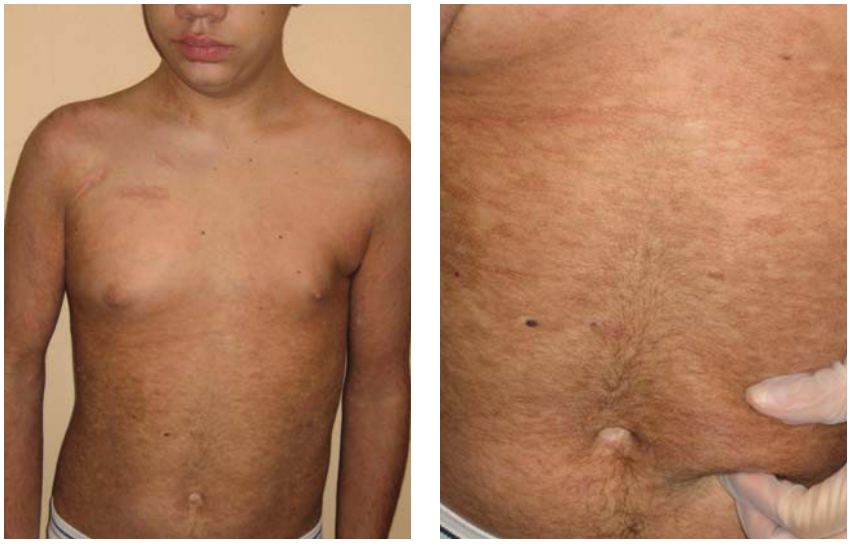

Figure 2. Patient 1 year after suspension of treatment with extracorporeal photopheresis, with immunosuppressant treatment suspended. The absence of cutaneous sclerosis can be observed.

Symptoms improved during the course of the treatment, with clear reduction of cutaneous induration and a marked improvement in joint mobility (Figure 2). On completion of the extracorporeal photopheresis therapy, we were able to reduce the dosage of methylprednisolone to 8 mg per day on alternate days, and the dosage of cyclosporin to 59 mg per day. A year later, the patient required no immunosuppressant treatment.

Chronic GVHD is believed to be the continuation of acute GVHD or the result of dysfunctional regeneration of the immune system, causing it to produce autoantibodies and autoreactive T lymphocytes.[1] Current theories implicate an imbalance between T helper (T_H) 1 and T_H2 responses, with increased T_H2 activity, and an important role of dendritic cells in inducing chronic GVHD.[2,3]

Systemic corticosteroids are the treatment of choice for chronic GVHD, though only a small proportion of patients continue to respond to this treatment indefinitely.[4] Other immunosuppressant therapies have been used with varying results: cyclosporin, thalidomide, tacrolimus, methotrexate, azathioprine, etretinate, clofazimine, and total lymphoid irradiation. These therapies have a high risk of adverse effects.

In 2001, Salvaneschi et al[4] published a series of 14 children with chronic GVHD refractory to immunosuppressant therapy who were treated with extracorporeal photopheresis. Partial or complete responses were obtained in 9 subjects and it was possible to suspend immunosuppressant therapy in 7 of them.

Dall'Amico and Messina[5] carried out a review of 20 published studies that contained 204 cases of resistant GVHD treated with extracorporeal photopheresis. Those authors observed regression of the skin lesions in 76% of cases, with a complete response in 35%. They also found that skin lesions responded slowly and required more than a year to disappear. According to the authors, patients with liver and bronchial involvement appear to have a poorer response to this treatment.

Couriel et al[6] recently performed a retrospective study of 43 patients treated with extracorporeal photopheresis, 61% of whom showed some response and 32% of whom showed a complete response. A year after commencing treatment, 22% of subjects were able to suspend treatment with corticosteroids.

Extracorporeal photopheresis consists of exposing mononuclear cells previously photosensitized with 8-methoxypsoralen to UV-A light outside the body. The cells are then returned to the patient. The mechanism of action of extracorporeal photopheresis is not fully understood. Fimiani et al[1] described 2 apparently opposite effects: activation of the immune system against cancer cells (useful for cutaneous T-cell lymphoma[7]) and reduction of the activity of T-cell clones in autoimmune diseases and allogeneic immune responses (GVHD).

Antigen-presenting cells and T lymphocytes are inactivated by photopheresis, though the cell death caused by this mechanism does not appear to be sufficient to explain the efficacy of the treatment as only between 5 and 10 × 10^6 of the circulating leukocytes are damaged. Phagocytosis of these apoptotic cells appears to activate the dendritic cells and increase levels of immunosuppressant cytokines. Furthermore, photopheresis restores the T_H1/T_H2 balance in the long term.

The frequency of treatment with photopheresis has not been clearly established and treatment cycles currently range between 1 and 4 weeks, depending on the hospital. Until randomized trials have been performed, it would seem appropriate to adapt the treatment regimen to each case according to the severity of symptoms and patient response. Commencing treatment early has been found to improve outcome.[4] Extracorporeal photopheresis has been shown to be effective in both adults and children.[5,8]

We present the case of a boy with chronic GVHD who showed an excellent response to extracorporeal photopheresis, enabling his immunosuppressant treatment to be stopped. Extracorporeal photopheresis is currently an effective option for treating chronic GVHD. Many series of patients treated with this therapy have shown that extracorporeal photopheresis can help to reduce the dosage of immunosuppressants required and even lead to their suspension, thus reducing the risk of complications in these patients.

References

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