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## Donor lymphocyte infusion for post-transplant relapse of Hodgkin's lymphoma

We report the case of a patient with poor prognosis Hodgkin's disease who received an allogeneic transplant, relapsed after a few months, and was rescued by salvage treatment followed by donor lymphocyte infusion.

Sir,

A 25-year old male was diagnosed as having mixed cellularity, stage IV Hodgkin's disease (HD) in 1995. Since chemotherapy (VEBEP,[1] an ABVD-like regimen) induced only a partial remission, in 1996 he underwent allogeneic bone marrow transplantation (BMT) from his HLA-identical sister with major blood group incompatibility (donor B, recipient A). The conditioning regimen was BuCy2 and graft-versus-host disease (GvHD) prophylaxis was a short course of methotrexate and cyclosporin A (CSA). The number of mononuclear cells (MNC) infused was $0.5\times10^8$/kg. Hematologic recovery was delayed and transfusional support was considerable. Six months later mediastinal relapse occurred. Salvage chemotherapy (C-MOPP) was ineffective, producing only a partial response. At +10 months, a persistent mixed chimerism (blood group: mixed fields) prompted us to try adoptive immunotherapy by donor lymphocyte infusion (DLI). The first infusion consisted of $0.4\times10^8$/kg MNC. To prevent myelosuppression and potentiate engraftment,[2,3] a second infusion was enriched in $CD34^+$ cells by donor mobilization with rhG-CSF (MNC infused $1.6\times10^8$/kg). One month after the second DLI, a grade IV acute cutaneous and hepatic GvHD occurred, successfully treated by CSA and prednisone. Unfortunately, cerebral toxoplasmosis occurred three months later, which required prolonged administration of pyrimethamine and spiramycin. Complete conversion of the blood group from A to B and a progressive increase of allogeneic hematopoiesis was documented cytogenetically (100% XX mitoses). CT and $^{67}$gallium scans repeated every three months showed a gradual and almost complete disappearance of the mediastinal nodes.

The role of allogeneic bone marrow transplant (BMT) in Hodgkin's disease (HD) is still uncertain.[4] In particular, a graft versus lymphoma effect has not been clearly demonstrated in this setting. Very few HD patients have been treated by donor lymphocyte infusion (DLI) for a post -transplant relapse.[5,6] At +31 months after DLI, our patient has chronic GvHD involving the skin and liver, and residual central nervous system damage due to the previous cerebral toxoplasmosis, but no evidence of HD activity (Figure 1). Thus, it seems that DLI may be effective even in HD patients. If this is the case, more intensely immunosuppressive and less intensely myeloablative conditioning regimens can be envisaged in the allogeneic setting also for HD.

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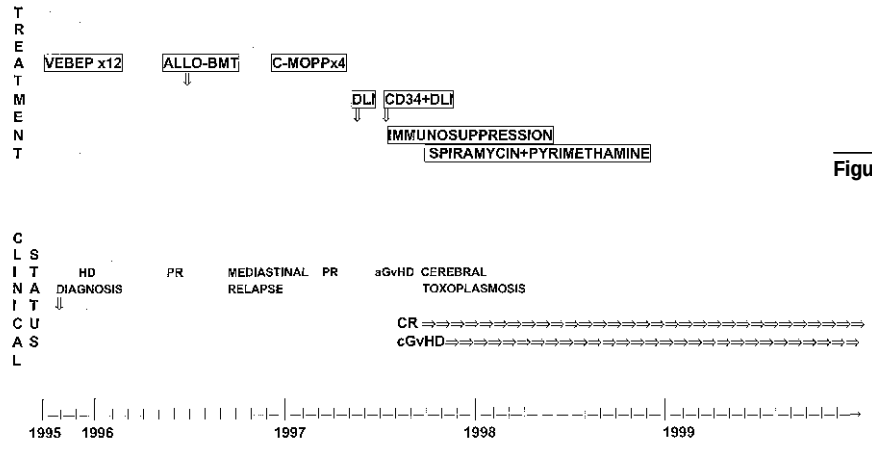


**Figure 1. Disease course summary.**

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## Severe disseminated toxoplasmosis after unrelated bone marrow transplantation: a case report

We report on a case of disseminated toxoplasmosis that occurred 39 days after unrelated bone marrow transplantation in a patient in good clinical and hematologic condition. The clinical course was characterized by presentation of septic shock and the evolution of sudden and rapidly overwhelming respiratory failure which was unresponsive to emergency and anti-shock therapy. Disseminated toxoplasmosis was diagnosed at autopsy.

Sir,

A 16-year old boy with myelodysplastic syndrome which developed into refractory anemia with excess blasts in transformation (RAEB-t), underwent HLA identical bone marrow transplantation from an unrelated donor. Pre-transplant recipient anti-toxoplasma IgG was 240 IU/mL and anti-toxoplasma IgM was negative. No information on toxoplasma donor serology was available. The conditioning regimen included busulfan, cyclophosphamide and melphalan. Graft-versus-host disease (GVHD) prophylaxis consisted of cyclosporin A, antilymphocyte globulin and a short course of methotrexate. Polymorphonuclear cell engraftment occurred on day +13, whereas the patient never became platelet transfusion independent. The boy developed acute GVHD grade I-II which was treated with methylprednisolone up to a dose of 10 mg/kg/die i.v.

**Figure 1. Myocardial tissue: evidence of tachyzoites and bradyzoites.**

On day +39 the patient developed fever and a blood culture showed *Pseudomonas aeruginosa* which was treated with cephtazidime i.v. On day +44, signs of septic shock syndrome abruptly appeared, with high grade fever (>39.5°C), sudden dyspnea, severe hypoxemia and renal dysfunction. Seizures and a dramatic worsening of the boy's general condition led to severe lethargy. As a result of progressive hypoxemia, the patient was put on life-support where breathing was mechanically assisted. Despite an initial improvement, nitric oxide had to be administered, 3 hours later. Notwithstanding the administration of norepinephrine 2 µg/kg/min, 4L of crystalloids and 1L of plasma expander, the boy's blood pressure was 80/30 and heart rate 156 bpm. An echocardiogram showed reduced myocardial function with an ejection fraction of 40%. His blood pressure fell to 60/20 and methylene-blue was infused, with no improvement. Further increments in vasoactive drugs failed to provide hemodynamic improvement and the patient died 8 hours later.

Post-mortem histologic examination was carried out with the parents' consent. Liver, lung, heart and brain specimens revealed multiple *Toxoplasma gondii* cysts. Bacterial, fungal and viral cultures were negative. There were no signs of GVHD.

This report outlines an interesting case of a severe systemic infection due to *Toxoplasma gondii* which presented with septic shock features in a BMT recipient and was diagnosed at autopsy. Toxoplasmosis is an unusual opportunistic infection which can be life-threatening in immunocompromised patients such as BMT recipients.[1-3] The etiologic diagnosis is usually made post-mortem.[3,4] In all such cases, profound immunosuppression results in reactivation of latent *Toxoplasma gondii*[5] and the most frequently presenting features are: isolated pneumonitis,[4,6] isolated ocular disease[5,7] and disseminated encephalitis.[2,5,8,9] Since any one of these complications[4,6] can be life-threatening in spite of prophylaxis[3,5,7] and standard treatment, Foot has suggested including pyrimethamine-sulfadoxine in the BMT setting.[10]