Autologous stem cell transplantation for HIV-associated lymphoma


Is peripheral stem cell mobilization followed by autologous stem cell transplantation (ASCT) feasible in patients with human immunodeficiency virus (HIV)–associated lymphoma (HIV-L)? Studies have demonstrated that, in the HIV-negative (HIV−) setting, ASCT may improve lymphoma-free survival in high-risk non-Hodgkin lymphoma (NHL) or relapsed Hodgkin disease (HD). Given the poor prognosis of HIV-L with conventional chemotherapy, this dose-intensive approach was explored. Nine patients with HIV-HD or NHL mobilized a median of $10^6$ CD34+ cells/kg and engrafted after ASCT. CD4 counts recovered to pretransplantation levels and HIV viral loads were controlled in patients compliant with antiretroviral therapy. Seven of 9 patients remain in remission from their lymphoma at a median of 19 months after transplantation. Thus, patients with HIV-L on antiretroviral therapy can engraft following ASCT. Prolonged lymphoma remissions, without significant compromise of immune function, can be seen, suggesting that ASCT can be used in selected patients with HIV-L.

**Introduction**

Highly active antiretroviral therapy (HAART) has changed the natural history of human immunodeficiency virus (HIV) infection by improving immune function in HIV-infected individuals. However, multiple studies have shown no impact of HAART on the incidence of acquired immunodeficiency syndrome (AIDS)–related non-Hodgkin lymphoma (NHL) or Hodgkin disease (HD).

Earlier therapeutic approaches to HIV-associated lymphoma (HIV-L) focused on reduction of chemotherapy dose intensity due to fears of further worsening the immune function in these patients. In the era of HAART, more aggressive approaches are being explored. In HIV-negative (HIV−) patients with relapsed aggressive NHL and HD, high-dose chemotherapy with autologous stem cell transplantation (ASCT) is the optimal therapy. This modality has also been explored in patients with NHL in first remission who are considered to be at increased risk for relapse with conventional-dose chemotherapy. We report here on our initial experience using ASCT in patients with HIV-L receiving HAART.

**Study design**

Between March 1998 and May 2000, 9 HIV-L patients on HAART received myeloablative chemotherapy followed by ASCT at our institution. Informed consent was obtained from all patients in accordance with the City of Hope Medical Center institutional review board guidelines. The median age was 41.6 years (range, 11.4–54.3 years). Seven patients had NHL and 2 had HD (Table 1). The NHL patients who were in first remission had high-risk features as defined by the international prognostic index (IPI).

**Results and discussion**

Engraftment occurred in all 9 patients. White cell engraftment, defined as an absolute neutrophil count greater than 500/μL, occurred at a median of 11 days (range, 9–12). Platelet engraftment, defined as platelet transfusion independence and a platelet count greater than $20 \times 10^3/\mu L$, occurred at a median of 10 days (range, 7–15).

Infectious complications during the period of neutropenia up to

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The CD4 counts gradually decreased after transplantation in all 9 patients and reached a nadir of 138/µL (range, 25–411) at a median of 2 months in 7 evaluable patients (Figure 1). Two nonevaluable patients died at approximately 4 months after transplantation with relapsed lymphoma. Six of these 7 evaluable patients recovered CD4 counts to pretransplantation levels by a median of 14 months (range, 2–28). One patient (UPN 209) had the highest CD4 counts before transplantation (>1000/µL), which may account for the failure to return to this baseline.

Six patients had a rise in their HIV VL in the first month following the transplantation, whereas 3 patients maintained an undetectable VL (Figure 2). In 5 of the 7 patients evaluable at 12 months, the VL was at undetectable levels (b-DNA assay or RNA polymerase chain reaction Roche Amplicor assay). One patient (UPN202), had a significant rise at 18 months and one (UPN406) at 36 months due to noncompliance with HAART. Two patients (UPN203, UPN407) had a persistently high VL after transplantation. UPN203 required multiple changes in his regimen. He was compliant with HAART, hence his high VL may reflect the inability of HAART to eradicate the latent HIV reservoir. Patient UPN407 stopped all antiretroviral therapy for a prolonged period after transplantation for psychosocial reasons, which explains the continued high VL.

We report here on the largest single institution series of patients with HIV-L on HAART treated with ASCT. All patients received the same high-dose chemotherapy conditioning and achieved long-term engraftment with stem cell rescue in a time course similar to HIV− patients. Pre-engraftment infectious complications
were similar to the HIV− setting with bacterial infections predominating. Conditioning regimen-related complications were also similar to the HIV− setting in that there was no increase in mucositis or hepatotoxicity associated with combining HAART and high-dose chemotherapy. After transplantation, several opportunistic infections that occurred responded well to treatment. In the majority of patients we have seen recovery of immune function as manifest by low VL and rising CD4 counts. This is similar to changes in immune parameters in HIV-L patients treated with CHOP and concomitant antiretroviral therapy. Future studies will address the pharmacokinetic effects of myeloablative therapy in combination with HAART and the reconstitution of immune function after ASCT. The effects of this approach on lymphoma-free survival remain to be seen. The surviving patients have been followed for a median of 19.0 months (range, 12-36 months). Two patients relapsed with disease in the bone marrow at 40 days and 95 days, respectively, and died. All other patients remain in remission.

The advent of effective antiviral therapy now allows us to administer dose-intensive and potentially curative chemotherapy to HIV-infected individuals with lymphoma. Infectious complications can be managed through a combination of prophylaxis and close monitoring after transplantation. Hence, HIV status should no longer by itself preclude ASCT for treatment of lymphoma.

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References

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