Safety of Autologous Stem Cell Transplantation in Patients with Known HTLV-1/2 Infection: A Case Series of 4 Patients

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Human T-cell Lymphotropic Virus type 1 and 2 (HTLV-1/2) are delta retroviruses endemic to the Caribbean and Japan.[1] HTLV-1 is known to cause two distinct and devastating diseases, adult T-cell leukemia-lymphoma (ATLL) and tropical spastic paraparesis/HTLV-1 associated myelopathy (HAM).[2] The rate of progression to ATLL occurs in less than 5% of HTLV-1 infected individuals. In addition, the latency from infection to disease manifestation is on the order of decades.[3]

The approach to autologous stem cell transplantation (AutoSCT) in immunosuppressed individuals has evolved significantly over the past several years. Historically, patients with HIV infection rarely underwent autologous transplantation due to concern for opportunistic infections. More recently, this population is routinely transplanted and included in clinical trials because outcomes in well-selected patients with HIV approximate those from a population without HIV.[4]

Patients who test positive for HTLV-1/2 during evaluation for AutoSCT are at risk for complications due to virus re-activation and clinical disease during the transplant process and immunological recovery. Studies on the association between immunosuppression and development of HAM or ATLL in humans infected with HTLV-1/2 are sparse and have resulted in mixed findings.[5-10] This is the first case series to document outcomes of this population in AutoSCT. It describes four patients who tested positive for HTLV-1/2 and who underwent AutoSCT without opportunistic infections, development of HAM or ATLL.

Patients were identified retrospectively through a query of the clinical data warehouse at Boston Medical Center. Approval for this study was obtained by the Institutional Review Board of Boston Medical Center in accordance with federal regulations and the Declaration of Helsinki. Cases were included if patients tested positive for serum HTLV-1/2 IgG with confirmatory testing by line immunoassay, and then underwent AutoSCT. Patients were assessed at the frequency indicated by their respective disease conditions for which they underwent AutoSCT and were observed for clinical signs and symptoms of ATLL or HAM.

Four patients were identified in the chart review. Demographic and disease characteristics are described in Table 1. Two patients tested positive for HTLV-1 antibody and two tested positive for HTLV-2 antibody. The median follow-up for these patients from date of transplantation was 22.4 months (range, 7.3-38.6). Median time to neutrophil and platelet engraftment was 9.5 days (range, 8-10) and 10 days (range, 9-14) respectively. None of these four patients developed complications related to HTLV-1/2 infection during the follow-up period. One patient died on day + 221 due to a recurrence of cholangiocarcinoma leading to liver failure, and the other three remained alive at the time of last follow-up.

The present case series provides support for the relative safety of AutoSCT in patients who are asymptomatic carriers of HTLV-1/2. It also suggests that engraftment times for HTLV-infected individuals are comparable to engraftment times for those individuals not infected with HTLV-1/2.

In the bone marrow transplant literature, there is one report of HTLV-1 associated malignancy after autologous stem cell transplantation.[11] In this report, onset of ATLL occurred fifteen months following AutoSCT for anaplastic large cell lymphoma (ALCL). Polymerase chain reaction (PCR)-based analyses suggested that a small population of the T-cell clone may have existed in the lymphoid tissue at the time of ALCL diagnosis and proliferated over time, however given that it was not the dominant clone, the patient was managed as ALCL.

The remainder of studies that describe the development of ATLL or HAM in an immunosuppressed patient population exist as case reports and case series in renal transplant recipients. One recent and notable case series showed the development of HAM in four out of ten renal transplant recipients where the host had been HTLV-1 negative and the donor was HTLV-1 positive.[12] There were zero out of thirty renal transplant recipients who had previously tested positive for HTLV-1 who developed disease from HTLV-1 positive donors. This may be because the HTLV-1 positive recipients had pre-existing immunity prior to undergoing renal transplantation and immunosuppression, whereas the HTLV-1 negative recipients became infected while immunocompromised. It is therefore possible that the patients in the present case series had already developed immunity which served to protect them during and after AutoSCT.

In conclusion, this report documents favorable outcomes of HTLV-1/2-infected patients who undergo AutoSCT. One limitation to this study was that viral loads were not

assessed before or after transplantation. Known risk factors for progression from HTLV-1/2 infection to clinical disease include high proviral load, advanced age, and family history of ATLL.[13] It would therefore be reasonable to consider these risk factors while counseling patients on the relative benefits of stem cell transplantation in patients positive for HTLV-1/2. Larger studies are needed to define specific risk factors for the development of ATLL and other complications of HTLV-1/2 infection in the setting of AutoSCT.

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