Successful salvage high-dose chemotherapy and autologous stem-cell transplantation in HIV-related germ-cell tumor

Testicular germ-cell tumors (GCT) occur more frequently in human immunodeficiency virus (HIV)-infected patients than in the general population [1]. Initial studies indicated that the outcome of patients with HIV-related GCT was poor compared with those without HIV infection [2, 3]. Nevertheless, since the introduction of highly active antiretroviral therapy the outcome has improved due to a decrease in HIV-related deaths [4].

Most patients with GCT who achieve a complete response to initial chemotherapy are cured, with relapses occurring in <10% of cases. Although the initial salvage treatment approach remains controversial, after two or more treatment regimens, salvage high-dose chemotherapy (HDCT) followed by autologous peripheral blood stem-cell transplantation (PBSCT) is generally the only curative option [5, 6]. As recently shown, sequential HDCT is better tolerated than single HDCT [7].

Only very limited data are available on HIV-related GCT patients who relapse after initial chemotherapy. HDCT plus PBSCT has been reported to be effective in relapsed HIV-related lymphoma [8, 9]. We report on the first case of salvage HDCT in a patient with relapsed HIV-related GCT.

In December 2006, a 33-year-old man underwent orchiectomy followed by adjuvant radiotherapy (25.2 Gy) for stage I seminoma. Beta human chorionic gonadotropin (β-HCG), α-fetoprotein (AFP), and lactate dehydrogenase (LDH) initially were within the normal range. He was known to be seropositive for HIV since June 2001 (Centers for Disease Control and Prevention category A3) when he was started on antiretroviral therapy (ART) with nevirapine and lamivudine–zidovudine.

In September 2007, the patient was found to have enlarged right inguinal and right paravesical lymph nodes along with a solitary lung metastasis. Right inguinal lymph node resection revealed GCT of mixed histology and the patient received three courses of cisplatin, etoposide, and bleomycin which resulted in a complete remission. However, in April 2008, a second right inguinal relapse was diagnosed with β-HCG and LDH being elevated to 4 U/l (normal range < 3 U/l) and 468 U/l (normal range < 250 U/l), respectively. On examination, there was no evidence of extragonadal disease.

In May 2008, the patient underwent a second salvage regimen of HDCT plus PBSCT. Four courses of HDCT were administered using cisplatin, etoposide, bleomycin, vincristine, and dacarbazine. The patient tolerated the HDCT well but developed severe neutropenic fever after the fourth cycle requiring treatment with broad-spectrum antibiotics. After one month, he was found to be in complete remission and was discharged.

In conclusion, salvage HDCT plus PBSCT may be an option for patients with HIV-related GCT who relapse after initial chemotherapy.
range < 240 U/l), respectively. Four courses of cisplatin, etoposide, ifosfamide (VIP) were administered as second salvage therapy. A marker-negative partial response was achieved and the patient started on oral etoposide (100 mg/m² given on days 1–21). After two courses, however, the right inguinal/paravesical mass increased in size again to 3.6 × 2.9 cm with no further metastases being detected on cancer staging. At that time (September 2008), β-HCG, AFP, and LDH were within the normal range. There was no evidence for an immune reconstitution inflammatory syndrome because the patient was already on ART for >7 years. Moreover, except during May 2006 (HIV RNA 85 copies/ml) and May 2007 (viral load 192 copies/ml) HIV RNA has continuously remained below the detection limit. There was also no evidence for an infectious process which might have caused lymph node enlargement.

The patient received another course of VIP plus granulocyte colony-stimulating factor (10 µg/kg) for peripheral blood stem-cell mobilization. Subsequently, a total of \(14 \times 10^6\) CD34+ cells/kg body weight was collected. On 2 October 2008, the patient was started on three sequential courses of high-dose carboplatin 1.200 mg/m² and etoposide 1.200 mg/m² (CE) [4]. A total of 3.6 × 10^6 CD34+ cells/kg body weight were transplanted after each course of HDCT. Neutrophil engraftment occurred on days +10, +12, and +14, respectively. Platelet count >20 × 10^9/l was observed on days +11, +13, and +18, respectively. Toxicity was moderate: episodes of neutropenic fever were observed after the first and third course of HDCT, World Health Organisation grade 2 diarrhea developed after the second and third course of HDCT, and grade 2 oral mucositis occurred after the third course of CE. ART, switched to nevirapine and emtricitabine–tenofovir in October 2007 in order to avoid myelotoxic effects possibly related to lamivudine–zidovudine, was continued throughout the entire treatment program. HIV viral load proved negative when determined before start of first and third HDCT and 2 months after the third PBSCT. CD4 lymphocyte count was 183/µl at start of mobilization chemotherapy, 272/µl before third HDCT, and 169/µl 2 months and 173/µl 5 months after the third PBSCT.

Eight weeks after the completion of HDCT there was no evidence of residual GCT on positron emission tomography/computed tomography (PET/CT) scan. Thus, secondary surgery was not indicated. However, in June 2009—6 months after the third transplant—the patient complained of tenderness in the right loin. PET/CT scan revealed two enlarged lymph nodes of 2 × 2 and 2 × 3 cm located in the right iliac fossa as well as a space occupying lesion of 6-cm infiltrating right pelvic floor muscles. No further metastases were found. LDH was elevated to 622 U/l (normal range < 250 U/l), while AFP and β-HCG were within the normal range. The patient suffers no HIV-associated diseases and was started on gemcitabine/paclitaxel-containing salvage chemotherapy on 23 June 2009. His latest CD4 lymphocyte counts were 61/µl (July 2009) with a viral load below the detection limit.

We conclude that sequential HDCT plus PBSCT for relapsed GCT is feasible in the setting of HIV. Patients with HIV-related GCT should no longer be excluded from HDCT programs.

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