ance was excellent and hematologic and non-hematologic toxicities were milder than with the ICE regimen. Moreover, days of neutropenic fever, hospitalization and consumption of antibiotics were reduced. Unfortunately, no cytogenetic response was obtained. To date the patient has been transplanted with full engraftment and no major complications.

Several factors have been associated with the ability and capacity to mobilize hemopoietic progenitor cells in CML such as intensity and type of chemotherapy, time from diagnosis, phase of the disease and previous treatment with IFN-α.[3-8] Our patient had several of these bad prognostic factors in both mobilization attempts. Although more intensive chemotherapy regimens have been associated with better mobilization, in our patient, the milder mini-ICE regimen was associated with successful mobilization and with milder hematologic and non-hematologic toxicities. A similar observation has been recently reported.[9,10] Furthermore, the mini-ICE regimen showed no difference in terms of cytogenetic response or progenitor yield when compared with the ICE regimen.[9,10] Although additional patients are necessary to confirm our data, they suggest that a second attempt to mobilize progenitor hemopoietic cells using the well-tolerated mini-ICE regimen should be tried in patients who have failed to get benefit from other intensive chemotherapy regimens.

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Key words

Chronic myelogenous leukemia, mini-ICE regimen, ICE regimen, mobilization, peripheral blood progenitor cells.

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Lamivudine for the prevention of hepatitis B virus reactivation during autologous stem cell transplantation. A case report

Reactivation of hepatitis B virus (HBV) is a frequent complication during chemotherapy; it may give rise to hepatitis, hepatic failure and death and may prevent further chemotherapy from being administered. We present a case in which the use of lamivudine allowed autologous stem cell transplantation to be performed after a hepatitis flare-up, suggesting a possible role for this drug in preventing HBV reactivation during chemotherapy.

Sir,

Hepatitis B virus (HBV) reactivation following chemotherapy withdrawal may result in hepatitis, hepatic failure and death.[1,2] In fact, immunosuppressive therapy leads to enhanced viral replication and to an increased number of infected hepatocytes. Withdrawal of the drugs results in partial restoration of immunocompetence with subsequent rapid destruction of hepatocytes.[1] It was recently reported that nucleoside analogs such as lamivudine (a reverse transcriptase inhibitor approved for the therapy of HIV infection) is effective in suppressing HBV replication by incorporation of its monophosphate form into DNA, which results in chain termination.[3]

We report the case of a 40-year old male, known to be HBsAg positive for 17 years, without any signs of active hepatitis, who was diagnosed as having mantle cell lymphoma (MCL) stage IIIA, in March 1997. He was treated with six cycles of chemotherapy according to the F-MACHOP protocol[4] between March and July 1997, without any complications.

Thirty days after the end of chemotherapy he presented the full clinical picture of an acute hepatitis, with SGOT at 2,820 U/L, SGPT at 1,525 U/L and total bilirubin at 14 mg/dL.

HBV-DNA (detected by nested polymerase chain reaction as described by Kaneko *et al.*[5]) was positive (having been negative before starting chemothera-

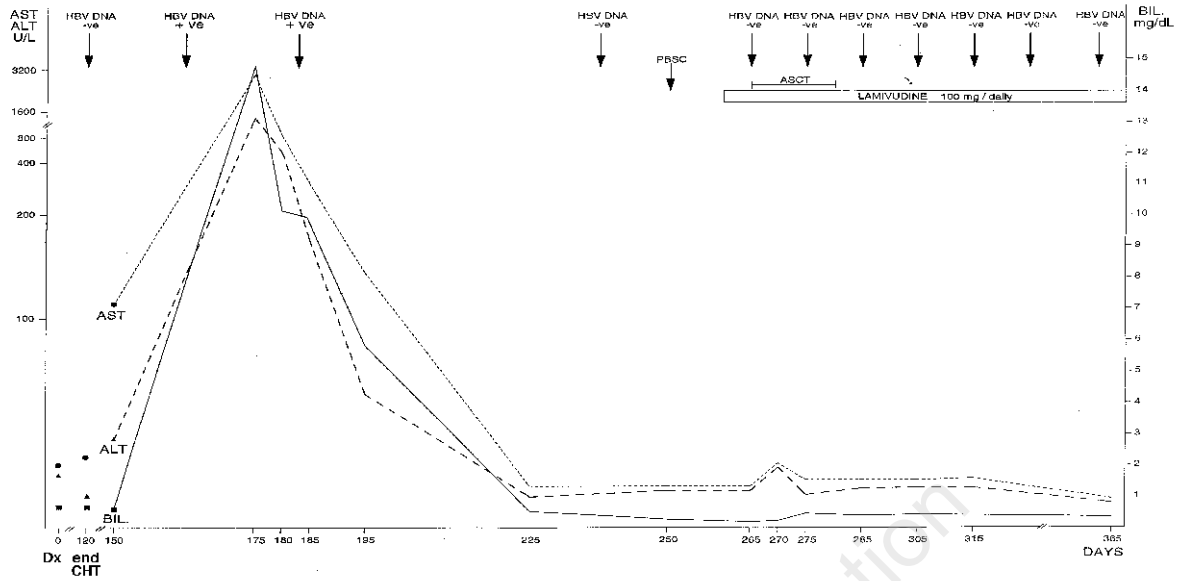

Figure 1. Clinical course and main laboratory data of the patient. ***Dx = diagnosis. end CHT = end of chemotherapy (6 cycles of F-MACHOP). PBSC = peripheral blood stem cell harvest after G-CSF priming. ASCT = autologous stem cell transplantation after conditioning with BAVC.***

py). The patient recovered spontaneously in 70 days. HBV-DNA was negative by day 90.

In accordance with our protocol for MCL,[6] he underwent G-CSF-primed peripheral blood stem cell harvest and was then started on lamivudine 100 mg/daily, with the purpose of preventing HBV reactivation during the procedure of autotransplant. After being on lamivudine for twenty days, he was conditioned with BAVC and reinfused with 5.2×10^6 CD34 cells/kg b.w.

He reached an ANC of 500/µL at day +10 and 1,000/µL at day +11; a Plt count of 20,000/µL at day +12 and of 50,000/µL at day +13; he needed 3 Plt aphereses and 8 administrations of G-CSF and was treated with antibiotic therapy for a Gram-positive sepsis. He was then discharged from the hospital on day +14 and was maintained on lamivudine for 6 months afterwards.

During this period he was regularly monitored with twice-monthly blood counts, transaminase levels and HBV-DNA: all these parameters remained normal/negative throughout the period.

Currently, 28 months from diagnosis and 20 months from transplant, the patient is in complete remission, with normal liver function tests and HBV-DNA negative.

HBV reactivation may represent a potentially harmful problem during administration of chemotherapy, particularly high-dose chemotherapy, and in some patients prevents transplantation. Therefore treatment for prevention of HBV reactivation is needed to protect HBV carriers against chemotherapy-induced hepatic failure.

Since lamivudine is devoid of side effects, particularly those on hemopoiesis, it seeems to be an effective therapeutic option in HBsAg positive patients needing chemotherapy and transplantation.

This drug was recently shown to be superior to famciclovir in terms of HBV-DNA reduction and response in the treatment of chronic hepatitis B,[7] and also to be effective in the prevention of graft infection following liver transplantation.[8] The optimal duration of therapy after transplantation has not been established yet, on the one hand it should be kept long enough to prevent HBV relapses, on the other hand it should be suspended quite rapidly to avoid the development of resistance due to mutations. We suggest that administration of lamividine for four to six months after the last chemotherapy administered accomplishes these needs.

To our knowledge, no other cases of prophylactic lamivudine therapy in patients with HBV infection undergoing autologous stem cell transplantation have been reported so far. Thus the case herein described indicates a possible role for lamivudine in preventing HBV reactivation during antineoplastic chemotherapy.

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Key words

Lamivudine, hepatitis B virus, autologous stem cell transplantation.

Funding

This work was supported by AIL 30 ore per la vita and Treviso AIL, Italy.

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Effectiveness of extracorporeal photochemotherapy in treating long-term refractory chronic graft-versus-host disease

We report two cases of severe refractory progressive chronic graft-versus-host disease (cGvHD) which improved dramatically after extracorporeal photochemotherapy. This procedure, based on functional changes of lymphocytes induced by 8-methoxypsoralen and UVA administered to leukapheresis collections, could be a useful treatment for cGvHD, even after many years of unsuccessful immunosuppressive approaches.

Sir,

About 25% of pediatric recipients of allogeneic marrow transplantation develop chronic graft-versus-host disease (cGvHD), which may be limited or extensive with multiorgan involvement, especially of the skin, mouth, gut, liver and eyes.[1] Since 1990 some authors have reported that refractory cGvHD, besides benefitting from standard immunosuppression, can also benefit from extracorporeal photochemotherapy (ECP), which consists of sensitization of peripheral leukocytes by 8-methoxy-psoralen (8-MOP) and extracorporeal exposure of leukeapheresis collections to UVA.[1-4]

We describe two pediatric patients successfully treated with ECP for severe persistent cGvHD after many years of ineffective immunosuppression.

Case #1. A 14-year old girl transplanted for acute lymphoblastic leukemia from her HLA-identical brother in 1988, developed progressive refractory cGvHD, which subsequently involved the skin (lichen-planus-like papulae, scleroderma, diffuse alopecia), mucosa (oral sicca-syndrome), gut (dysphagia, diarrhea, weight loss), musculoskeletal system (contractures, arthritis), lungs (obstructive respiratory impairment), and immuno-hematopoietic system (pancytopenia, positivity for autoantibodies, recurrent respiratory infections), with a Lansky performance score lower than 70%. For eight years steroids, cyclosporin-A, azathioprine, thalidomide (Grunenthal GmbH, Stolberg Rhld, Germany), methotrexate, lymphoid irradiation and PUVA courses were used in various combinations. Since the cGvHD did not resolve and severe side-effects (hypertension, insulin-dependent diabetes, cataracts, peripheral polyneuropathy) developed, in May 1996 ECP treatment was started. At that time, the patient's C-reactive protein (CRP) concentration was 48 mg/L, anti-nuclear (ANA) and anti-DNA antibodies were strongly positive, and complement fraction 3 and 4 (C3 and C4) levels were 65 and 14 mg/dL, respectively. Improvements were seen after three ECP procedures, which were continued without side-effects for a total of 21 procedures,[3] by which time the skin lesions had markedly improved, joint contractures had almost completely resolved, arthritis had disappeared, respiratory function tests had almost normalized, upper respiratory infections occurred very rarely and daily insulin requirement was lower. The Lansky performance score increased to 90%. CRP, C3, and C4 levels returned to normal values, anti-DNA antibodies became negative, whilst ANA remained positive. Immunosuppression was progressively tapered down and discontinued in June 1998 without reacutization of the GvHD.

Case #2. A 5-year old boy, transplanted in 1992 for Fanconi's anemia from his HLA-identical brother, developed progressive extensive cGvHD, barely controlled by standard immunosuppression, which flared again in the oral mucosa six years after the transplantation, despite steroid treatment being resumed in combination with thalidomide and azathioprine. In July 1998 ECP was started and improvements were noticed after three ECP procedures, which were continued without side-effects for a total of 12 procedures. The Lansky performance score increased to 90% and oral lesions almost completely disappeared. Steroid treatment was progressively tapered down and then discontinued. The planned schedule was interrupted because of poor venous access and, a few months after, cGvHD flared up again and conventional treatment was resumed.

Leukaphereses were performed by means of a continuous flow cell separator using peripheral venous access; at least two blood volumes were processed;