nation of blood products. In this case, the transmission of a strain of *P. rettgeri* originated from the same donor, resulted in the death of two patients. Although Gram negative bacilli have been described as contaminants of blood products, we have not found any references concerning *P. rettgeri*.[2,3] In the present case, the donor could not be studied, but the contamination was probably the result of an asymptomatic bacteriemia in an apparently healthy donor. The fact that cultures from the frozen plasma were negative could be explained by a germicide effect of a storage temperature below –30ºC, by an effect of antibodies and complement present in plasma, or because the microbes are predominantly carried by leukocytes.

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Key words

Bacterial sepsis, Providencia rettgeri, transfusions

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Autologous stem cell transplantation in chronic carriers of hepatitis B virus and hepatitis C virus affected by onco-hematologic diseases

Sir,

Hepatitis B virus (HBV) reactivation, which follows withdrawal of immunosuppressive therapy or standard and high-dose chemotherapy is a well-known complication in chronic HBV carriers;[1,2] the same complication was recently reported also for chronic hepatitis C virus (HCV) carriers.[3,4]

The incidence of these viral infections is high in onco-hematologic patients[5,6] and, for the reason mentioned above, the management of such patients is often difficult. This observation prompted us to evaluate retrospectively hepatic toxicity in 11 onco-hematologic patients (5 carriers of HBsAg and 6 of HCV-RNA) submitted to autotransplantation at our institute between March 1992 and June 1998.

Table 1. Patients' characteristics.

Characteristics	*No. of patients*
Male	7
Female	4
Age median (range)	41 (26-56)
Diagnosis	
Diffuse large B-cell lymphoma	4
Marginal zone lymphoma	2
Follicular centre lymphoma	2
Mantle cell lymphoma	1
Breast cancer	1
Chronic myelogenous leukemia	1
Virology	
HCV-RNA	6
HBsAg	5
First-line treatment	
Non-Hodgkin's lymphoma	
' 6 cycles of CHOP	2
' 6 cycles of F-MACHOP	7
Breast cancer	
' 6 cycles of FEC	1
Chronic myelogenous leukemia	
' IFN	1

Abbreviations: CHOP = vincristine; cyclophosphamide; doxorubicin; prednisone; F-MACHOP = vincristine; cyclophosphamide; 5-fluorouracil; cytosine-arabinoside; doxorubicin; methotrexate; prednisone; FEC = cyclophoshamide; epirubicin; 5-fluorouracil.

Nine of these patients (4 HBsAg) were affected by non-Hodgkin's lymphoma (NHL), 1 (HCV) by chronic myelogenous leukemia and 1 (HBsAg) by breast cancer (BC) (Table 1).

During first-line treatment (Table 2) only one patient, an HBsAg carrier affected by NHL and treated according to the F-MACHOP regimen, developed a reactivation of chronic hepatitis one month after the last cycle of chemotherapy. He was admitted for supportive therapy and recovered fully in two months. Three months later he was submitted to autotransplantation. During the transplant and for the following six months, he was treated with prophylactic doses of lamivudine (100 mg/die).[7] The entire transplant procedure was tolerated well and he is currently alive in complete remission (CR) and with normal liver function tests. The other patients tolerated both first-line therapy and transplantation well. Engraftment was observed in all and hematologic and extra-hematologic toxicities were mild (Table 2).

In the immediate post-transplantation period (one month from transplant) only the BC patient (an HBsAg carrier) developed hepatitis (transaminase levels ×20-40 upper level of normal) not associated with the detection of HBV-DNA. No other complications or toxic deaths were observed.

Table 2. Transplant-related data.

Conditioning regimens		
Non-Hodgkin's lymphoma	BAVC°	
Breast cancer	Thiotepa/cyclophosphamide#	
Chronic myelogenous leukemia	Busulphan/melphalan@	
	Median	*Range*
BM MNC $\times 10^8$/kg b.w. reinfused	0.47	0.28-1.0
PB MNC $\times 10^8$/kg b.w. reinfused	2.5	1.0-5.7
Days to PMN > 0.5×10^9/L	12	8-19
Days to PMN > 1×10^9/L	13	9-24
Days to Plt > 20×10^9/L	14	9-32
Days to Plt > 50×10^9/L	21	10-49
No. of blood units transfused	2	0-8
No. Plts aphereses transfused	3	0- 19
No. of G-CSF doses post ASCT*	11	6-18
No. of febrile patients	6	
No. Gram ± septicemia	2/0	
No. FUO	4	
No. febrile days/patients	5	3- 13
Days of antibiotics	9	8-21
Days of hospitalization	18	15-30

*Abbreviations. °Carmustine 200 mg/m² on day –4; cytosine-arabinoside 150 mg/m² twice daily, etoposide 150 mg/m² twice daily and cyclophosphamide 45 mg/kg once daily all from day –5 to day –2; #thiotepa 250 mg/m² from day –9 to day –6; cyclophosphamide 50 mg/kg from day –5 to day –2; @busulphan 4 mg/kg, p.o. from day –6 to day –3; melphalan 60 mg/m², i.v. day –2. BM = bone marrow; PB = peripheral blood; MNC = mononuclear cell; PMN = neutrophils; PLT = platelets; FUO = fever of unknown origin. *300 µg/administration.*

As of February 1999, with an overall survival of 56 months (range 20-122), 10/11 patients are alive in CR, while one, affected by NHL, is alive with disease 52 months from transplant.

The small toxicity observed in our series does not allow us to consider the whole procedure devoid of any risk, but suggests that also chronic HCV-HBV carriers with high-risk disease should be considered for intensification programs including autotransplant.

Several options have been proposed to prevent virus reactivation in such patients:[8,9] i) to monitor them very closely; ii) to withdraw cytotoxic drugs at the end of each course of treatment gradually; iii) to reinstitute immunosuppressive therapy at the first sign of liver dysfunction. Recently, much progress seems to have been derived from the use of second generation nucleoside analogs, such as lamivudine and famciclovir, which have been shown to be effective in inhibiting HBV replication.[10] Lamivudine suppresses HBV replication directly by incorporation of its monophosphate form into DNA by the HBV polymerase, which results in chain termination. Since it is devoid of side effects (particularly on hematopoiesis), it should be kept in mind as a therapeutic option in patient care. However the effectiveness of these agents in preventing HBV reactivation in HBsAg positive patients receiving chemotherapy or submitted to transplantation remains to be assessed in larger clinical trials.

No pharmacological options are currently available for HCV.

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Key words

Chronic HBV-HCV carriers, autologous stem cell transplantation

Acknowledgments

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

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