Key words
Daunorubicin, liposome, acute leukemia.

Correspondence
Domenico Russo, M.D., Division of Hematology, University Hospital, p.le S. Maria della Misericordia, 33100 Udine, Italy. Phone: international +39-0432-559662 – Fax: international +39-0432-559661 - E-mail: domenico.russo@drmm.uniud.it

References

1. Forssen EA, Ross ME. Daunoxome treatment of solid tumors: preclinical and clinical investigations. J Liposome Res 1994; 4:481-512.
2. Money-Kyrle JE, Bates E, Ready J, Gazzard BG, Phillips RH, Boag FC. Liposomal daunorubicin in advanced Kaposi's sarcoma: a phase II study. Clin Oncol 1993; 5:367-371.
3. Michieli M, Damiani D, Ermacora A, Masolini P, Michelutti A, Baccarani M. Liposome encapsulated daunorubicin doubles anthracycline toxicity in cell lines showing a non-PGP related multidrug resistance. Haematologica 1999; 84:1151-2.
4. Verdonck LF, Lokhorst HM, Roovers DJ, van Heugten HG. Multidrug-resistant acute leukemia cells are responsive to prolonged exposure to daunorubicin: implications for liposome-encapsulated daunorubicin. Leuk Res 1998; 22:249-56.
5. Michieli M, Damiani D, Ermacora A, et al. Liposome-encapsulated daunorubicin for PGP-related multidrug resistance. Br J Haematol 1999;106:92-9.
6. Gill PS, Espina BM, Muggia E, et al. Phase I/II clinical and pharmacokinetic evaluation of liposomal daunorubicin. J Clin Oncol 1995; 13:996-1003.

Usefulness of the prognostic score for advanced Hodgkin's disease in patients with human immunodeficiency virus-associated Hodgkin's lymphoma

Prognosis of Hodgkin's disease (HD) in HIV-infected patients has not been extensively studied. The *International Prognostic Factors Project on Advanced Hodgkin's Disease* (IPFPAHD) score has been applied in a series of 12 patients with HIV-related HD in advanced stages treated with combination chemotherapy. The IPFPAHD scores were 5 (4 cases), 4 (1), 3 (6) and 2 (1). Median overall survival for patients with score ≥4 was 3.5 months vs 38 months for patients with scores 2-3 (p=0.01). All patients with score 5 died. These results indicate that IPFPAHD score is also useful for predicting the outcome of advanced HD in HIV-infected patients.

Sir,

The prognosis of Hodgkin's disease (HD) in advanced stages is still poor.[1,2] In 1998 the *International Prognostic Factors Project on Advanced Hodgkin's Disease* (IPFPAHD) developed a score to assess the prognosis of patients with advanced HD .[3] The variables included in this score were: serum albumin < 40 g/L, Hb < 105 g/L, male sex, age ≥45 yr, stage IV, WBC count $\geq 15\times10^9$/L and lymphocyte count $< 0.6\times10^9$/L or < 8% of differential count. Patients with human immunodeficiency virus (HIV) infection are usually excluded from prognostic scores in both HD and non-Hodgkin's lymphomas (NHL) because of their poor prognosis. Since prognosis in HIV-associated lymphomas has improved in recent years, we have evaluated the usefulness of the IPFPAHD score in HIV-associated HD.

Table 1. Main prognostic variables of patients with advanced HD and HIV infection.

Pt	Age (yr)	Gender	Stage	Hb (g/L)	WBC ($x10^9$/L)	Lymph. ($x10^9$/L)	Serum albumin	Score IPFPAHD	OS (mo)
1	22	M	IVB	66	1.01	0.16	24	5	0.5
2	28	M	IVB	68	2.0	0.1	26	5	9
3	32	M	IIIB	119	21.0	2.8	35	3	15
4	32	M	IIB	91	5.2	1.3	25	3	37
5	59	M	IB	108	4.1	1.9	40	2	8+
6	32	M	IVB	93	0.6	0.25	27	5	3
7	24	M	IVA	126	7.2	1.2	34	3	36+
8	28	M	IVB	113	4.5	0.2	31	4	29+
9	28	M	IVB	110	5.8	1.3	25	3	36
10	36	F	IVB	85	3.6	0.8	26	3	39+
11	36	M	IVB	110	4.5	1.3	31	3	15+
12	35	M	IVB	100	2.7	0.3	25	5	3

M: male; F: female; OS: overall survival; IPFPAHD: International Prognostic Factors Project on Advanced Hodgkin's Disease.

From 1990 to 1999, 15 cases of HIV-associated HD were diagnosed in a single center in a cohort of 1,700 patients with HIV infection (prevalence 0.88%). The main risk behaviors for HIV infections were intravenous drug abuse (6 cases), heterosexual promiscuity (5) and homosexuality (4). Four cases had a previous diagnosis of AIDS. Histologic subtypes were lymphocyte depletion (6 cases), mixed cellularity (6) and nodular sclerosis (3). Extranodal disease was present in 10 cases (5 in bone marrow, 2 in liver and 3 in liver and bone marrow). Mean (±SD) CD4 lymphocyte count was 101×10^9/L (±86) (range 10-291).

No treatment was given to 1 patient, 13 received combination chemotherapy (COPP 3, COPP/ABV 8, ABVD 2) and the remaining one was treated with mantle radiotherapy. Complete response was observed in 7 of the 14 evaluable cases (50%), and relapse occurred in two of them. At the time of writing 9 patients have died (7 from progression of HD and 2 from opportunistic infections). Median overall survival (OS) for the whole series was 37 months. Twelve patients had advanced HD (stages III or IV in 10,stage IB with bulky mediastinal mass in one and stage IIB in another) (Table 1). The IPFPAHD scores were 5 (4 cases), 4 (1), 3 (6) and 2 (1). Median overall survival (OS) for patients with score ≥4 was 3.5 months vs 38 months for patients with scores 2-3 (p=0.01). All patients with score 5 died.

Unlike immunocompetent individuals, HIV-infected patients have high histologic grade HD and advanced stages,[4-7] as can be observed in our series. Since we recently observed that the International Prognostic Index (IPI) is useful for prognosis assessment in AIDS-associated NHL,[8] we have evaluated the usefulness of the IPFPAHD score in the assessment of prognosis of

patients with AIDS-associated HD. Although our series is small, our results indicate that parameters obtained in the IPFPAHD study (from which HIV-infected patients were excluded) are also useful for predicting the outcome of advanced HD in HIV-infected individuals. However, due to the small number of cases in this series, the results of our study should be confirmed in larger series based on a multicenter databases of patients with AIDS-related HD.

Josep-Maria Ribera, Jose-Tomás Navarro, Albert Oriol, Manuel Vaquero, Javier Grau, Evarist Feliu*

*Hematology, and *Pathology Services, Hospital Universitari Germans Trias i Pujol. Badalona, Universitat Autònoma de Barcelona, Spain*

Funding

Supported in part by the grant FIJC-P-EF-98 from the International José Carreras Leukemia Foundation, Spain.

Correspondence:

Josep-Maria Ribera, M.D., Hematology Service. Hospital Universitari Germans Trias i Pujol. C/Canyet s/n, 08916 Badalona, Spain. Phone: international +34.93.4978868 – Fax: international +34.93.4978843 – E-mail: jmribera@ns.hugtip.scs.es

References

1. Anselmo AP, Cavalieri E, Enrici RM, et al. Combined modality therapy in advanced Hodgkin's disease: a report on 218 patients with a median follow-up of eight years. Haematologica 1998; 83:645-50.
2. Brusamolino E, Anselmo AP, Klersy C, et al. The risk of acute leukemia in patients treated for Hodgkin's disease is significantly higher after combined modality programs than after chemotherapy alone and is correlated with the extent of radiotherapy and type and duration of chemotherapy: a case-control study. Haematologica1998; 83:812-23.
3. Hasenclever D, Diehl V. A prognostic score for advanced Hodgkin's disease. International Prognostic Factors Project on Advanced Hodgkin's Disease. N Engl J Med 1998; 339:1506-14.
4. Rubio R. Hodgkin's disease associated with human immunofediciency virus infection. A clinical study of 46 cases. Cooperative Study Group of Malignancies Associated with HIV Infection of Madrid. Cancer 1994; 73:2400-7.
5. Tirelli U, Errante D, Dolcetti R, et al. Hodgkin's disease and human immunodeficiency virus infection: clinicopathologic and virologic features of 114 patients from the Italian Cooperative Group on AIDS and Tumors. J Clin Oncol 1995; 13:1758-67.
6. Errante D, Zagonel V, Vaccher E, et al. Hodgkin's disease in patients with HIV infection and in the general population: comparison of clinicopathological features and survival. Ann Oncol 1994; 5:S37-40.
7. Serraino D, Carbone A, Franceschi S, Tirelli U. Increased frequency of lymphocyte depletion and mixed cellularity subtypes of Hodgkin's disease in HIV-infected patients. Italian Cooperative Group on AIDS and Tumours. Eur J Cancer 1993; 14:1948-50.
8. Navarro JT, Ribera JM, Oriol A, et al. International prognostic index is the best prognostic factor for survival of patients with AIDS-related non-Hodgkin's lymphoma treated with CHOP. A multivariate study of 46 patients. Haematologica 1998; 83:508-13.

Mini-ICE regimen allows mobilization of peripheral blood progenitor cells in a patient with chronic myelogenous leukemia failing the ICE protocol

We report the case of a 41-year old patient diagnosed with CML in first chronic phase who achieved successful mobilization of peripheral blood progenitor cells primed with the mini-ICE regimen two years after failing with the ICE regimen. Of note, hematologic and non-hematologic toxicities were milder with the former schedule.

Sir,

Autologous hematopoietic progenitor cell transplantation is an attractive investigational approach for chronic myelogenous leukemia (CML).[1,2] In patients with this disorder, stem cells may be mobilized from marrow by using chemotherapy or growth factors, but the optimal method and timing remain to be adequately defined.[3-8]

A 41-year old male was diagnosed with Philadelphia chromosome-positive CML in chronic phase in December 1992 and began treatment with busulfan. HLA-typing demonstrated the lack of a related or suitable unrelated donor. In July 1994 the patient began therapy with interferon-α (IFN-α) which was stopped because of the absence of cytogenetic response. He was referred to our institution in March 1996 and then received chemotherapy with the ICE regimen,[3] consisting of idarubicin, cytosine arabinoside and etoposide plus glycosylated G-CSF. The patient developed grade 4 hematologic toxicity requiring 45 days to recover > 0.5×10^9/L granulocytes and being dependent on platelet transfusion at discharge, after 58 days of hospitalization. Extra-hematologic toxicity consisted of cutaneous rash, severe mucositis and prolonged neutropenic fever that was managed with intravenous antibiotics for 28 days and amphotericin B for 22 days. Despite eight apheresis procedures only 0.5×10^6 $CD34^+$ cells/kg were collected, with minimal or no cytogenetic remission. In January 1998 he was treated with IFN-α plus cytosine arabinoside and then because no cytogenetic response occurred he was switched to hydroxyurea. Nearly six years after diagnosis, in November 1998, he received chemotherapy with the mini-ICE regimen (same dosage as in the ICE regimen but for only 3 days), plus glycosylated G-CSF. This procedure was initially managed on an out-patient basis, but the patient had to be admitted for 10 days because of an axillary infection. The times to recover >0.5×10^6/L granulocytes and > 20×10^6/L platelets were 22 and 26 days, respectively. Four leukaphereses, starting on day +23 yielded a total of 4.39×10^6 $CD34^+$ cells/kg, without cytogenetic response in the apheresis products.

The patient here described had been treated for six years with several regimens including hydroxyurea, IFN-α and IFN-α plus cytosine arabinoside. A previous mobilization attempt with the ICE regimen had been unsuccessful. More than two years later, a second attempt at progenitor cell collection was decided, using the less intensive mini-ICE regimen.[9] Toler-