



Detection of non-Hodgkin's lymphoma liver disease in cirrhotic patients

Sir,

Computer tomography (CT) scan and ultrasound scan (US) are the preferred methods for staging sub-diaphragmatic non-Hodgkin's lymphoma (NHL),¹ but their sensitivity in detecting focal lesions in the liver may be reduced if fibrosis is present. We investigated 6 NHL patients who also had a viral liver disease (chronic active hepatitis or cirrhosis) by US and CT liver scans and liver biopsy. US was performed using a Spazio-Hitachi instrument with a 3.5 MHz probe. With the exception of two patients, who underwent laparotomy as a diagnostic procedure, liver biopsy was performed under US guidance using a Menghini fine needle with automatic aspiration (1.2 mm in diameter x 150 mm in length), or a Chiba fine needle (0.7 mm x 150 mm). The needle crossed the focal lesion for at least 3 cm, thus also exploring the surrounding hepatic tissue. In patient #6, with no evidence of focal lesions, the biopsy was carried out in the left hepatic lobe. In all patients prothrombin time prolongation was ≤ 5 seconds with respect to control plasma and platelet count was $\geq 50,000/\mu\text{L}$.

The immunohistochemistry panel included LCA, CD20, CD45RO and CD3; in three patients, the presence of clonal B-lymphocytes was assessed by light chain restriction.

Table 1 summarizes our data. US showed focal lesions in three patients, while CT scan detected focal lesions in one patient and none in the remaining (Figure 1). US-guided biopsies were well tolerated and uncomplicated. The samples, obtained by a single pass of the needle, measured about 1 mm in diameter and had a length of 25-40 mm; they were all informative, changing the stage in 5/6 patients. Histology documented severe chronic active hepatitis in two patients and overt cirrhosis in four; 5/6 patients (all HCV+) showed NHL involvement, as suggested by an excess of B cells and proved by light chain restriction in three of them. The single HBsAg+ patient had increased transaminases without evidence of focal lesions; liver histology excluded involvement by lymphoma.

As in patients with hepatocellular carcinoma,² even in this small series of NHL patients, US proved more accurate than CT scan in identifying small (≤ 1 cm) focal lesions in cirrhotic livers. However, diffuse lymphoma involvement can only be detected by biopsy. An US-guided fine needle biopsy can substitute more invasive methods such as larger cutting needle biop-

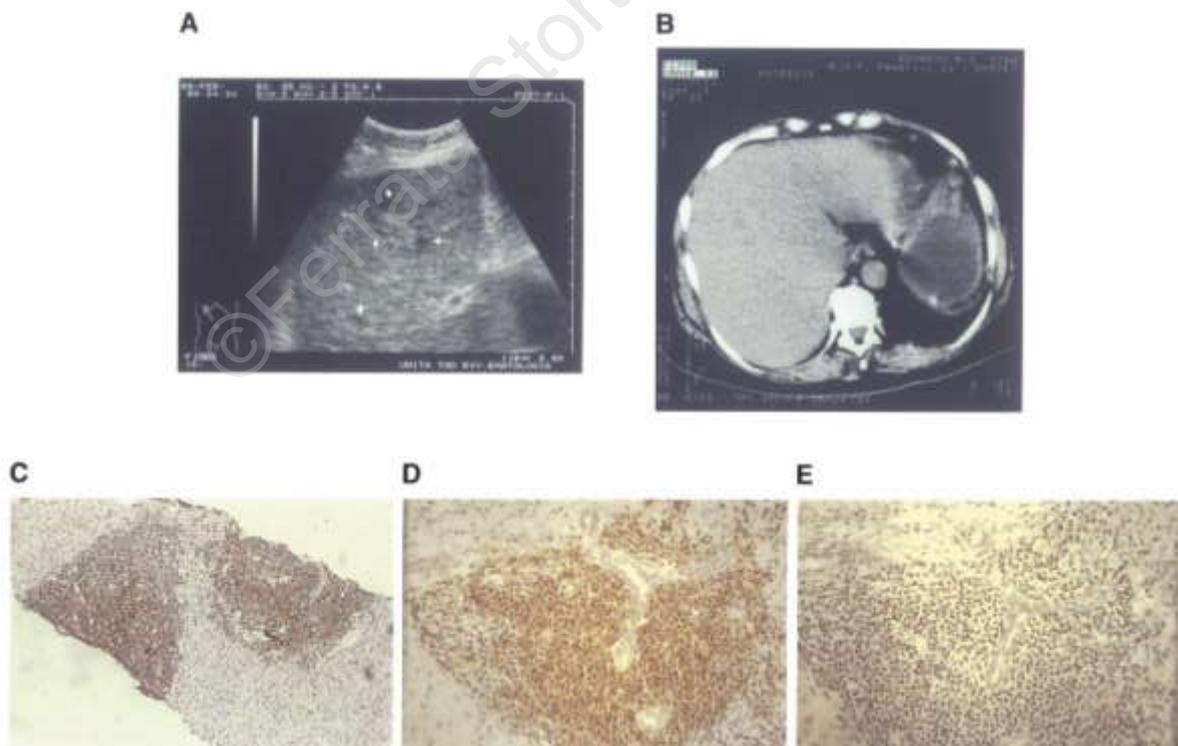


Figure 1.
A. Ultrasound scan of patient #4, showing small nodular hypoechoic lesions (arrows) in the context of a fibrotic liver.
B. Liver CAT scan of the same patient, showing no detectable focal lesions. The spleen was previously ablated.
Liver biopsy of the same patient, which stained positive for CD20 (C) and κ (D), and was negative for λ (E).

Table 1. Patient characteristics, liver imaging, histological findings and outcome.

Pt.	Sex/ age	Type of liver disease	NHL grade*	Disease status, clinical stage	US	CT	Biopsy procedure used	Liver involvement by NHL		CHT	CR	OS mo.
								B cell excess	LC restriction			
1	M/73	HCV+ cirrhosis	I	staging, II B	small (≤ 1 cm) nodular hypochoic lesions	no focal lesion	US-FNAB	yes	not done	CEOP	yes	15+
2	F/54	HCV+ cirrhosis	H	diagnosis, IIE A	no focal lesion	same as US	laparotomy	yes	k	VICED ^o	yes	18+
3	F/53	HCV+ cirrhosis	I	diagnosis, IIS B	no focal lesion	same as US	laparotomy	yes	k	CEOP	yes	22+
4	F/55	HCV+ CAH	L	follow-up, III B	small (≤ 1 cm) nodular hypochoic lesions	no focal lesion	US-FNAB	yes	k	CEOP	no	1 [#]
5	F/57	HCV+ cirrhosis	I	relapse, II B	large (≥ 3 cm) nodular hypochoic lesions	same as US	US-FNAC	yes	not done	VICED ^o CEOP	no	1 [#]
6	M/32	HBsAg+ CAH	H	restaging, IV B	no focal lesion	same as US	US-FNAB	no	no	MACOP-B DHAP a BMT	no	6 [#]

*according to the Working Formulation: L = low; I = intermediate; H = high; US = ultrasound scan; CT = computer tomography; LC = light chain; CHT = chemotherapy regimens; CR = complete remission; OS = overall survival, months; US-FNAB = ultrasound-guided Menghini cutting fine needle biopsy; US-FNAC = ultrasound-guided Chiba fine needle biopsy; CAH = chronic active hepatitis; # = deceased of lymphoma progression; ^oa CHOP-like regimen with the addition of etoposide (10).

sy (diameter 1.8-2.0 mm) or laparoscopic/laparotomic biopsy.

A majority of our patients had HCV-related liver disease. Recent reports have stressed the association between HCV infection and B-cell NHL.³⁻⁸ In our small series of HCV+ patients the liver seems an exceedingly frequent extranodal target for NHL cells, considering that less than 10% of unselected NHL patients show liver involvement. We may speculate that a pre-existing non-clonal lymphoid infiltration may favor a subsequent localization of clonal cells.

We treated our patients with standard chemotherapy regimens: 5 patients received CHOP-like regimens and one MACOP-B and DHAP followed by autologous transplantation. Three patients are experiencing a prolonged disease free survival (Table 1). Thus, it seems that the coexistent HCV infection does not affect overall survival of NHL patients, as already noticed in patients with low-grade lymphoma.⁹ Our observations deserve further investigation in larger cohorts of patients in order to define the prognostic profile and the optimal management of patients with NHL and virus-induced liver disease.

Marco Picardi, Amalia De Renzo, Giorgio Falzarano,
Raffaella Vecchione,* Maria D'Armiento,* Bruno Rotoli

Divisions of Hematology and *Pathology,
Federico II University Medical School, Naples, Italy

Key words

Non Hodgkin's lymphoma, HCV-related cirrhosis, ultrasound-guided liver biopsy

Correspondence

Prof. Bruno Rotoli, Divisione di Ematologia Clinica, Nuovo Policlinico, via S. Pansini 5, 80131 Naples, Italy. Phone: international +39-081-7462068 – Fax: international +39-081-7462165.

References

- Mende U, Zierhut D, Ewerbeck V, Haas R, Volcker HE, Zoller J. Ultrasound criteria for staging and follow-up of malignant lymphoma. *Radiologe* 1997; 37:19-26.
- Honda H, Onitsuka H, Adachi E, et al. Hepatocellular carcinoma: prospective assessments of the T-factor with CT, US and MR imaging. *Abdom Imaging* 1993; 18:247-52.
- De Vita S, Sacco C, Sansonno D, et al. Characterization of overt B-cell lymphomas in patients with hepatitis C virus infection. *Blood* 1997; 90:776-82.
- Silvestri F, Pipan C, Barillari G, et al. Prevalence of hepatitis C virus infection in patients with lymphoproliferative disorders. *Blood* 1996; 87:4296-301.
- Mazzaro C, Zagonel V, Monfardini S, et al. Hepatitis C virus and non-Hodgkin's lymphomas. *Br J Haematol* 1996; 94:544-50.
- Zuckerman E, Zuckerman T, Levine AM, et al. Hepatitis C infection in patients with B-cell non-Hodgkin lymphoma. *Ann Intern Med* 1997; 127:423-8.
- Izumi T, Sasaki R, Miura Y, Okamoto H. Primary hepatosplenic lymphoma: association with hepatitis C virus infection. *Blood* 1996; 87:5380-1.
- De Rosa G, Gobbo ML, De Renzo A, et al. High prevalence of hepatitis C virus in patients with B-cell lymphoproliferative disorders in Italy. *Am J Hematol* 1997; 55:77-82.
- Silvestri F, Barillari G, Fanini R, et al. Impact of hepatitis virus infection on clinical features, quality of life and survival of patients with lymphoplasmacytoid lymphoma/immunocytoma. *Ann Oncol* 1998; 9:499-504.
- De Renzo A, Notaro R, Pezzullo L, et al. Etoposide and idarubicin in a modified CHOP-like regimen (VICED) for aggressive non-Hodgkin's lymphomas. *Leuk Lymphoma* 1998; 30:153-62.