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Ultrasound and Ultrasonically Guided Biopsy in Hepatic Lymphoma

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Abstract—*From August* 1982 *to December* 1985, 125 *patients with lymphoma in different periods of the disease, underwent abdominal ultrasound (US) examination. The value of US in detecting lymphomatous involvement of the liver was determined in* 75 *histologically proved patients, to improve the US accuracy rate we combined it with ultrasonically guided fine needle aspiration biopsy (UGFNAB), whenever a focal lesion was disclosed in the liver. US had a sensitivity of* 61.5%, *a specificity of* 93.5% *with an overall accuracy of* 88%. *No specific pattern of involvement was revealed by US. The UGFNAB allowing a cytological diagnosis avoided false positive results and improved overall accuracy from* 88 *to* 93%. *We therefore believe that US should be regarded as the first imaging method to detect hepatic involvement by lymphoma and when a focal lesion is disclosed the UGFNAB should be the first invasive procedure to obtain a definite cytological diagnosis.*

INTRODUCTION

ULTRASONOGRAPHY (US) has been quite successful in the detection of hepatic malignancy, such as hepatocellular carcinoma and metastasis [1, 2]. In lymphoma, the ability and effectiveness of US for detection abdominal nodal extent of the disease have been reported [3] and the results are similar to that from computed tomography (CT) [4], but no data are available in the literature on the value of US in demonstrating involvement of a strategic site as the liver. Zornoza and Ginaldi [5] reported the value of CT and radionuclide scans in evaluating lymphoma of the liver, and more recently, for this purpose Weinreb *et al.* [6] reported the results of Magnetic Resonance Imaging (MRI) in a series of 13 patients with hepatic lymphoma. The purpose of our investigations was to determine the role of US in the evaluation of hepatic lymphoma and, to improve the diagnostic accuracy of this imaging technique, we combined it with guided fine needle aspiration biopsy (FNAB), as previously reported [7].

MATERIALS AND METHODS

From August 1982 to December 1985, 125 unselected patients with histologically proved lymphoma, aged 19–80 years, were examined at the Ist Medical Division, Hospital of Piacenza. There were 66 males, and 59 women, 24 had Hodgkin disease (HD) and 101 non-Hodgkin lymphoma (NHL).

The patients were in different periods of the disease, 27 had been treated and were relapsing or incompletely staged in other hospitals, 98 had never been treated.

The type of lymphoma was determined according to the Kiel classification [8] for NHL, and the Rye classification for HD [9]; the patients were staged according to the Ann-Arbor [10] staging scheme. All patients underwent abdominal US examination, and the US liver study was part of abdominal examination for each patient.

Scans were performed with a real time linear array scanner (Hitachi EUB 22-EUB 26), in transverse, longitudinal and oblique planes at 1 cm intervals or less. The US diagnosis of liver involvement by lymphoma was based on the presence of single or multiple focal lesions, hepatomegaly alone was not considered a positive finding because it does not correlate well with pathologic evidence of tumor involvement [5, 6, 11]. Whenever a focal mass, with suspicious of involvement, was disclosed in the liver (12 cases), ultrasonically guided fine needle aspiration biopsy (UGFNAB) was carried into the lesion according to the principles previously reported [7]. The definite diagnosis of liver involvement by lymphoma was based on findings obtained in pathological staging, with percutaneous, laparoscopy or laparotomy biopsies.

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The liver was histologically studied in 75 patients, 16 HD, 59 NHL, and proof of hepatic involvement was obtained within 2 weeks period either before or after the US examination, the patients received no treatment in the intervening time. The results of US and UGFNAB were checked with histological findings and accordingly classified as true positive, true negative, false positive or false negative.

RESULTS

As shown in Table 1 the value of US in detecting the lymphomatous involvement of the liver was considered in 75 patients that underwent hepatic biopsies. The liver was involved by lymphoma in 13 patients (11 NHL and 2 HD) and was free of lymphoma in 62. Among 13 patients with liver lymphoma, 8 (with NHL) showed focal lesions in the liver and were correctly diagnosed by US (sensitivity 61.5%), 5 (2 with HD and 3 with NHL), without focal lesions and subsequently false negative results, showed microscopic involvement. Among the 62 cases with no lymphomatoses involvement of the liver, 58 were correctly interpreted as true negative by US (specificity 93.5%) and 4 cases had hypoechoic focal lesion in the liver, but these lesions were related to diseases different from hepatic lymphoma, as showed later biopsy specimens (US false positive for liver involvement by lymphoma); the overall accuracy rate was of 88%. Detailed data of the 12 cases with focal lesions of the liver (8 true positive and 4 false positive for hepatic lymphoma at US examination) are presented in Table 2. All these patients had NHL; in the cases with histologically proved hepatic lymphoma, the hypoechoic pattern was the most frequent US appearance, the lesions were multiple in 5 and single in 3, were well defined, oval or round with small internal echoes, ranged in size from 1.5 to 8 cm; hepatomegaly was present in 4 cases.

By UGFNAB, performed in the 12 patients,

Table 1. Results of US liver scans in 75 histologically proven patients

Histologically proved patients: 75 cases	Results of US study Positive	Negative
No. of patients with lymphomatous involvement of the liver: 13 cases	8*	5
No. of patients without lymphomatous involvement of the liver: 62 cases	4	58*

*Indicate correct diagnosis.
US sensitivity: 8/13 (61, 5%); specificity: 58/62 (93, 5%); overall accuracy: 66/75 (88%).

Table 2. Clinical data, ultrasonographic (US) findings and results of US guided biopsy in patients with lymphoma and hepatic focal lesions

Patient No.	Sex/Age (years)	Type of lymphoma	Sonographic patterns number and dimension of lesions (cm)	Suspicion of hepatic lymphoma at US examination	Definite cytological diagnosis of guided biopsy specimens
1	M/48	Centroblastic	Hypoechoic with debris multiple 2–4	+	Lymphoma
2	M/59	Lymphoblastic	Hypoechoic, single 7 × 3	+	Lymphoma
3	M/66	Centroblastic	Anechoic, single 4 × 3	+	Lymphoma
4	M/72	Lymphoplasmacytoid	Hypoechoic, multiple 1, 5–3	+	Lymphoma
5	F/49	Immunoblastic	Hypoechoic, multiple 3–2	+	Lymphoma
6	F/70	Lymphoplasmacytoid	Echogenic with hypoechoic areas, single 3	+	Lymphoma
7	F/64	Immunoblastic	Hypoechoic with debris, multiple 1–8	+	Lymphoma
8	F/40	Lymphoblastic	Hypoechoic, multiple 2–5	+	Lymphoma
9	F/30	Immunoblastic	Hypoechoic, single 2	+*	Liver tissue with fatty infiltration
10	M/69	Centroblastic	Hypoechoic, single 2,5 × 3,5	+*	Liver tissue with fatty infiltration
11	M/75	Centroblastic	Hypoechoic, single 3 × 2	+*	Simple cyst
12	F/64	Lymphoplasmacytoid	Hypoechoic single 3 × 5	+*	Hepatocarcinoma

*Four cases false positive (for lymphoma) at US examination, correctly diagnosed by UGFNAB.

lymphoma was cytologically detected in 8 (6 of them had high grade malignancy disease); 3 of the remaining 4 findings showed to be, respectively liver tissue with fatty infiltration in 2 cases, cyst in 1 case and in the fourth patient a previously unappreciated hepatocarcinoma was diagnosed.

By this technique the overall accuracy increased from 88% to 93%, there were no false positive and false negative results, no complications related to the procedure. All these findings but one (the cyst) were histologically confirmed by laparoscopy with biopsy or laparotomy.

DISCUSSION

Hepatic involvement by lymphoma occurs at the initial presentation, in more than 20% of patients with NHL [12] and in 10% of patients with HD [13]; autopsy series demonstrated hepatic involvement in more than 50% of patients who die from lymphoma [14, 15]. The presence of hepatic disease is of great significance, affects staging and therapeutic decision; by contrast the clinical recognition of hepatic involvement at initial staging or in follow-up is rather difficult [5, 6]. A variety of non-invasive diagnostic technique have been employed to determine the presence of lymphoma in the liver. In a series of patients with hepatic lymphoma reported by Zornoza and Ginaldi [5], CT was found to have a sensitivity of 57%, a specificity of 88% and an overall accuracy of 85%; radionuclide scans had a sensitivity of 71%, a specificity of 81% with an overall accuracy of 80%.

Thomas *et al.* [16] using an experimental organ-specific Ethiodiol-Oil-Emulsion-13 (EOE 13), CT contrast agent, reported an improvement in the detection rate for hepatosplenic lymphoma compared with routine CT scans; but a comparison of the liver studies was not statistically significant because of the small number of cases. Ginaldi *et al.* [17] reported a review of hepatic lymphoma detected by US, the patterns of involvement were described and were considered non-specific. In their study only the patients who showed US suspicion of hepatic involvement by lymphoma were confirmed histologically by biopsy or autopsy, no histological data of the liver were reported about the remaining patients, so the accuracy of the method was not evaluated. In a recent report MRI was not better than CT in evaluating the lymphomatous involvement of the liver in 13 patients with hepatic lymphoma [6]. The present study is, to our knowledge, the first report on the accuracy of US in detecting lymphomatous involvement of the liver, and the results with a sensitivity of 61.5%, a specificity of 93% and an overall accuracy of 88% are favorable, compared with those obtained by radionuclide scans, CT, [5] and MRI [6]. Pathologically, the most common type of intrahepatic involvement of HD is a diffuse infiltration [18] that, with difficulty, can be suspected by US and by other imaging techniques, while in NHL the tumor nodules looking like metastatic carcinoma are found as frequently as diffuse hepatic involvement [19] and tumor masses are more frequent in NHL of high grade malignancy [20]. All of our US true positive patients had NHL, 6 of them (75%) had high grade malignancy disease (Table 2). These observations could explain the high percentage (61.6%) of cases with focal lesions of the liver, in our series of patients with hepatic lymphoma. Our US positive patients, as well as those reported with CT [5] showed focal masses within the liver parenchyma, and the detection of hepatic focal lesions in a patient with lymphoma has a high degree of correlation with the involvement of the disease [16]; however the US and CT patterns are not specific as previously reported [5, 17] and as demonstrated by our four false positive cases, one of them, having an hepatocarcinoma.

We point out that a pathologic confirmation of the lesions can be obtained by UGFNAB, a safe and cheap technique. Cytological diagnosis of hepatic involvement by lymphoma was usually easy, since our patients had a known lymphoma previously diagnosed by biopsy of a superficial lymph-node, and in a recent report [21], fine needle aspiration cytology, in patients with known lymphoma, was considered very useful in staging, in recurrence and in differential diagnosis between lymphoma and other diseases.

In our series the overall accuracy improved when US results were compared with US + UGFNAB, however the diagnostic improvement obtained by UGFNAB, was limited only to the cases US false positive, for the cases US false negative this technique gave no improvement since it was performed only on patients with focal lesions of the liver.

It was of special interest that UGFNAB had no false positive results; and without pathological confirmation four patients with false positive results at US examination of the liver should be erroneously staged and subsequently treated.

US as well as CT provide data on other abdominal organs spleen, kidney, and lymphnodes; although CT is considered the method of choice for the examination of the retroperiteneum [22], Drouet *et al.* [23] and Matter [22] suggest that US can be chosen as the first procedure in the evaluation of retroperitoneal lymphnodes, reserving CT as a complement when US is technically insufficient.

From our results, we believe that US because of lack of biological risk, non-invasiveness, rapidity of execution and cheapness, should be regarded as the first imaging method to detect hepatic involve-

ment by lymphoma. When a focal lesion is disclosed, UGFNAB should be considered the first invasive procedure for cytohistological diagnosis. However we must remember that a normal US scan of the liver does not exclude the presence of microscopic disease; that US examination of retroperitoneum may be technically insufficient because of fat or gas, and the management of patients with lymphoma must be planned with these points kept in mind.

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