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Ultrasound-guided core-needle biopsy is effective in the initial diagnosis of lymphoma patients

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Abstract

Background and Objective. **With the development and refinement of new guidance methods for percutaneous biopsies, many investigators have reported studies supporting a role for radiologically guided core-needle biopsy in the diagnosis of malignant lymphoma under certain clinical circumstances. The aims of this report are to evaluate the efficacy of findings at ultrasound (US)-guided core-needle biopsy of abdominal lymphoma on patient care and define the key determinants of clinical success.**

Design and Methods. **US-guided core needle biopsies were performed in 55 patients with abdominal lymphoma: 44 non-Hodgkin's lymphoma (NHL) and 11 Hodgkin's disease (HD); 41 had had no prior lymphoma and 14 had previously diagnosed lymphoma. All the biopsies were performed under US control using a 21-gauge modified Menghini needle. Overall, 53/55 (96%) patients were treated on the basis of biopsy findings only, including 14/14 (100%) patients with a history of lymphoma and 39/41 (93%) patients with no such history.**

Results. **In 46/53 (87%) patients it was possible to assess the specific histotype. No differences between the diagnostic rates of HD and high grade-NHL were recorded. There were no complications related to the biopsies.**

Interpretation and Conclusions. **Our data indicate that abdominal US-guided core-needle biopsy should be considered as an effective and safe procedure in the diagnosis of patients with lymphoma offering the possibility of determining the tumor subtype and the subsequent specific treatment.**

Key words: ultrasonography-guided core-needle biopsy, Hodgkin's disease, non-Hodgkin's lymphoma, diagnosis, specific treatment

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The prognosis of lymphomas, Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL), has dramatically improved over the past three decades due, in part, to greater accuracy of diagnosis, staging and monitoring of the course of the disease. Imaging of the lymphatic system is a crucial step in determining the proper therapeutic approach; the evaluation of deeply located, non-palpable retroperitoneal and pelvic lymph nodes was formerly a diagnostic obstacle, and prior to the advent of ultrasonography[1] and computed tomography (CT)[2] accurate staging was based on bipedal lymphangiography.[3]

In the last decade attempts have been made to obtain pathologic staging of lymphoma using less invasive techniques: in order to evaluate abdominal involvement, laparoscopy with multiple hepatic and splenic biopsies often substitutes laparotomy with splenectomy.[4] More recently, ultrasonography and CT have been used to guide fine needle aspiration for cytologic biopsies in this setting, with accuracies that range from 68% to 94% and sensitivities that range from 66% to over 90%.[5-19] The cytologic material alone is insufficient for the diagnosis since tissue sections are essential for specific histotype evaluation. So tissue biopsy is important in the diagnosis and management of patients with lymphoma; in addition, repeat biopsies are important to confirm recurrence or progression, or a change in the histopathology.

This report concerns our experience with the application of ultrasound (US)-guided core-needle biopsies in the management of lymphoma patients at diagnosis and at relapse.

Materials and Methods

Patients

From 1989 to 1996, US-guided core-needle biopsies were performed in 55 patients, 41 with previously undiagnosed malignancy and 14 with a known lymphoma (9 NHL, 5 HD). Patients not deemed suitable for biopsy because of coagulopathy, inability to cooperate, or anatomic and vascular contraindications

noted on the US or CT scan were excluded; informed consent was obtained from all patients. The subjects ranged in age from 16 to 76 years (median age 44 years): 32 were males and 23 females. All patients were out-patients.

All biopsies were performed in the abdomen, and in particular in the following sites: para-aortic/retroperitoneal lymph nodes, 26; liver, 22; kidney, 3; spleen, 2; abdominal mass, 2. Disease status and histology at the time of biopsy are listed in Table 1.

Biopsy technique

All the biopsies were performed under US control; a real-time machine (Hitachi Ansaldo AU 560) with a 3.5 MHz convex transducer was used. The biopsies were done chosing the most convenient route, avoiding the pleura and the great vessels. The skin was sterilized and local anesthesia was administered. The transducer was sterilized or wrapped in a sterile covering. Surecut 21-gauge needles (TSK Laboratory, Tokyo, Japan) were used for the US guided biopsies.

In patients with focal lesions, the biopsy was done within the lesion; in the others it was taken from the parenchyma. One to three needle passages were performed and if the material obtained was not considered sufficient for histologic evaluation, the procedure was repeated. The biopsies were taken in all cases on an out-patient basis (6 hours in bed, fasting, with ice applied and compressed on the skin). Six hours after the tissue core biopsy, a control US examination was performed to ascertain whether complications had occurred.

Conditions necessary to do the biopsy were: prothrombin activity more than 50%, platelet count higher than 70,000/μL and 12 hours of fasting before the biopsy.

Histologic preparations

Formalin-fixed, paraffin-embedded tissue samples were available in 53 cases. From these, 4-mm thick sections were cut and stained according to the following methods: hematoxylin and eosin (H&E), Giemsa, periodic acid-Schiff, and Gomori silver impregnation for reticulin fibers. Additional sections were obtained for immunophenotypic analysis, which was performed according to the alkaline phosphatase anti-alkaline phosphatase complexes (APAAP) technique[20] and by applying a panel of antibodies including the key-markers listed in the REAL classification.[21] The latter was used for diagnosing all the examples of malignant lymphoma.[21]

Results

Diagnostic tissue was obtained in 53 of the 55 biopsies (96%); in the 2 other cases (one in retroperitoneum, and one in the hepatic hilus lymph nodes) the failure to obtain diagnostic material was attributed to necrosis and/or fibrosis.

The tissue samples allowed a refined diagnosis in 46/53 cases (87%), while in the remaining 7 they were sufficient to recognize the existence of lymphomatous involvement (6 NHL, 1 HD), but not the histologic subtype (Tables 2 and 3). Nevertheless, the diagnostic data on the latter 7 patients were sufficient to define a specific therapeutic approach.

Table 1. Histopathologic findings and disease status at the time of biopsy.

Histology	*Diagnosis*	*Relapse*	*Progression*	*Total*
HD	6	5	/	11
NHL	35	5	4	44
Total	41	10	4	55

Table 2. Immunohistochemical diagnosis by needle biopsy in 46 patients.

Histologic subtype	*No. of patients*
HD:	
Nodular sclerosis	10
NHL:	
Lymphoplasmacytic	3
Follicle center, follicular	8
Diffuse large B-cell	14
Diffuse mediastinal large B-cell	1
Precursor T-lymphoblastic	1
Peripheral T-cell, unspecified	1
Anaplastic large cell	1
Unclassified:	
HD	1
High-grade	6

In 39 patients, core-needle biopsy was the first invasive diagnostic procedure for staging and/or restaging. In particular, in 9 patients already diagnosed as having lymphoma, liver (n= 8) or kidney (n= 1) biopsies were done to evaluate possible hepatic or renal lymphoma infiltration because the initial staging had shown the presence of suspicious hepatic or renal lesions. In all the 8 hepatic cases the biopsy was negative for lymphoma: 5 were negative, 2 showed chronic hepatitis, and 1 liver echinococcosis. These data were essential for the choice of therapy: all patients obtained a CR with only local radiotherapy. The renal biopsy was positive for localized renal carcinoma; this patient had surgical treatment for the renal tumor and was then treated for NHL. Table 3 summarizes the diagnoses in the lymphoma-staging negative biopsies.

In the remaining 30 patients the core-needle biopsy was the only invasive diagnostic procedure: there were 24 cases of NHL and 6 cases of HD.

Concerning the 14 patients who had had a previ-

ous diagnosis of lymphoma, 10 underwent biopsy at the time of relapse and 4 during disease progression. It was possible to obtain a specific histologic subclassification for all of them. In particular, in 4 NHL patients (one in relapse and three during progression) the histology had changed to another NHL type (from follicular cell lymphoma to diffuse large B-cell lymphoma). The sensitivity of biopsy diagnosis of lymphoma in various clinical settings in 46 patients is presented in Table 4.

The final histopathologic subtypes of 39 patients are listed in Table 2. All 53 patients with diagnostic (lymphoma-positive, lymphoma-negative or non-lymphomatous positive) biopsy received specific therapy on the basis of the lymphoma diagnosis or because the biopsy result was essential for systemic chemotherapy or local radiotherapy treatment. In contrast, in the two patients in whom biopsy was unsuccessful (both at diagnosis), surgical intervention was required to establish the final diagnosis.

No complications related to the biopsies occurred.

Table 3. Non-lymphomatous neoplasm biopsy findings (liver and kidney) in 9 non-Hodgkin's lymphoma patients at the initial staging time.

Normal liver	5
Chronic hepatitis	2
Liver echinococcosis	1
Renal carcinoma	1

Table 4. Lymphoma diagnosis rate by histology and disease status in 46 patients.

Histology	*Diagnosis*	*Relapse*	*Progression*	*Total*
HD	6/6 (100%)	5/5 (100%)	—	11/11 (100%)
NHL	24/26 (92%)	5/5 (100%)	4/4 (100%)	33/35 (94%)
Total	30/32 (93%)	10/10 (100%)	4/4 (100%)	44/46 (95%)

Discussion

The particularly high overall accuracy of radiologically guided percutaneous biopsy in the diagnostic phase of abdominal lymphoma patients[5-19] has opened interesting new possibilities in the *diagnosis-specific treatment* concept. The role of US-guided core-needle biopsy in the definitive tissue diagnosis of metastatic lymph nodes is well established, but its use in the primary evaluation of lymphomas has so far been somewhat limited.

In our study, the overall diagnostic success rate was 96%; all these cases of abdominal lymphoma were specifically treated according to the core-needle biopsy findings alone and did not require surgical biopsy; specific classification in terms of histologic subtype between NHL or HD was possible by means of immunohistochemical techniques in 87% of the patients. We confined the study to the abdomen but with successful results not only from lymph nodes but also from the liver, kidney, and spleen. In particular, liver and kidney biopsies were useful at the time of staging to evaluate neoplastic or infectious lesions.

In this study the US-guided core-needle biopsy was equally efficacious in establishing a new lymphoma diagnosis (30/32, 93%) or confirming relapse or lymphoma progression (14/14, 100%). Whether or not a distinction needs to be made between these two sets of patients has been a point of controversy in the literature. Some investigators[14,22] have accepted image-guided biopsy of abdominal lymphoma in patients with a history of lymphoma but argue that an excisional biopsy is needed in patients at initial presentation. On the other hand, the results of others[15,18,19] have challenged these concepts by showing that surgery was avoided in more than 50%,[15] 82%,[18] and 85%[19] of the patients at initial presentation. The results of our study, with a success rate of 93% for the first diagnosis subset of patients, confirm that excisional biopsy can very frequently be avoided. Whereas the data of the other studies were obtained with *CT-guided* core-needle biopsy, our data represent, to the best of our knowledge, the largest study reported in the literature concerning the efficacy of *US-guided* core-needle biopsy as a first-line procedure at initial clinical presentation.

The debate concerning the needle size is still open: many investigators believe that even if a diagnosis of lymphoma can be achieved with fine-needle biopsy, large histologic sections (and therefore larger needles) are often necessary to identify the lymphoma subtype in order to permit specific treatment.[5,7,9,23] Recently, however, Silverman *et al*.,[15] compared fine vs large needle biopsies and found no difference between them as far as concerned accuracy in tumor grade determination. Our results confirm this finding, since in 87% of our patients we achieved a diagnosis of specific subtype using a 21-gauge needle. Furthermore, this percentage is similar to that achieved by other authors who used larger needles.[18,19]

There are definite indications for US-guided core-needle biopsy in patients with NHL and HD: i) accurate and efficient establishment of the diagnosis of masses not initially known to be lymphomas prior to an excisional biopsy with a specific treatment possibility depending on the subtype classification; ii) acquisition of tissue for ancillary studies such as cytogenetics and molecular genetics when required; iii) evaluation of treatment in lymphoma patients with relapse or progression; iv) overall initial staging in NHL and HD to verify any ambiguous image from the liver, spleen, or kidney; v) evaluation of the neoplastic or infectious nature of particular lesions especially in the liver.

We believe it should be possible to use this very simple, economic technique, which can be also be performed on out-patients, on a large scale, avoiding laparotomy and/or laparoscopy. Above all, this technique obviates risk and discomfort for the patient. For guiding the biopsy, US is both less costly and easier to use than CT.[24-26]

Contributions and Acknowledgments

PLZ and AC were the principal investigators involved in the conception of the study, its design, and the writing of the paper. MM, AL and DF helped the principal investigators (PLZ and AC) with data analysis interpretation. FG, MB, PA collected the study data. SAP, SA and GFO reviewed all the histopathologic material. ER and ST critically revised the paper and gave the final approval for its publication.

Disclosures

Conflict of interest: none.

Redundant publications: no substantial overlapping with previous papers.

Manuscript processing

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