

Clinical utility of computed tomography-guided core needle biopsy in the diagnostic re-evaluation of patients with lymphoproliferative disorders and suspected disease progression

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Background: Histological transformation is a common clinical event in patients with lymphoproliferative diseases, often requiring a modification in therapy. Minimally invasive biopsy techniques have been used for initial diagnosis of these disorders but their role has not been systematically evaluated in disease progression. The purpose of this study was to evaluate the yield of computed tomography (CT)-guided core needle biopsy in patients with lymphoproliferative disorders and suspected disease progression.

Patients and methods: We performed a retrospective analysis of the records of patients with known lymphoproliferative disorders who underwent CT-guided core needle biopsy during the course of their disease, between 1990 and 2002.

Results: A total of 130 patients with lymphoproliferative disorders (91 patients with non-Hodgkin's lymphoma, 21 with Hodgkin's disease, 10 with chronic lymphocytic leukemia, six with combined malignancies and two with Castleman's disease) underwent CT-guided core needle biopsy 4.7 ± 5.1 (standard deviation) (range 0–40) years after initial diagnosis. The procedure was diagnostic in 98 cases (75.4%). In 22 patients (17%) a subsequent open biopsy was performed, and in 10 (7.6%) the final diagnosis remained unconfirmed. Histological transformation was found in 20 cases (15.4%), of which 19 were suspected clinically. A new diagnosis (malignant and non-malignant) was apparent in 18 cases (13.9%) and relapsed or ongoing evidence of the original disease was found in 82 (63%).

Conclusions: CT-guided core needle biopsy is a reliable procedure in patients with suspected histological transformation of lymphoproliferative disorders, and should be used as the initial tool for pathological re-evaluation.

Key words: core needle biopsy, diagnosis, image-guided, lymphoproliferative disorders, transformation

Introduction

Patients with lymphoproliferative disorders undergo periodic clinical, radiological and pathological reassessment during their clinical course. Re-evaluation is required in order to assess response to therapy, remission or progression. Histological progression may demand a modification of the treatment plan using a more aggressive treatment protocol. Thus, repeated biopsies from the site of primary disease or from previously uninvolved organs are often needed. Previously, an open biopsy was necessary to obtain sufficient tissue for the diagnosis of lymphoproliferative disease. In the last decade there has been a growing body of evidence that image-guided core needle biopsies are sufficient for pathological diagnosis of lymphoma [1–7], since both biopsy and immunohistochemical techniques have dramatically improved. The advantage of core needle biopsy is obvious since it is a minimally invasive procedure with a very low complication rate [1–7]. The use of

computed tomography (CT) as the imaging tool has the advantage of permitting accurate planning, and it enables a biopsy to be performed from deep or small masses [4]. Most studies on CT-guided core needle biopsy to date assessed this technique in the initial diagnosis of lymphoma [2–5]. In this report we review 130 records of patients with known lymphoproliferative disorders who underwent repeated biopsy during the course of their disease due to suspected recurrence or histological transformation of their disease. The aim of this study was to evaluate the diagnostic accuracy of the technique, and to assess whether CT-guided core needle biopsy should be considered as the initial tool in these patients.

Patients and methods

Patients

We performed a retrospective analysis of records of patients with lymphoproliferative diseases who had undergone CT-guided core needle biopsy during the course of their disease. Evaluation of each record included details of initial diagnosis (date, organ biopsied and initial pathological diagnosis) and details of further pathological evaluation (date, reason for pathological re-evaluation, organ biopsied, CT-guided core needle biopsy result, the need for repeated

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Table 1. Characteristics of 130 patients who underwent computed tomography-guided core needle biopsy

Primary diagnosis	
Non-Hodgkin's lymphoma	91 (70%)
Hodgkin's lymphoma	21 (16%)
Chronic lymphocytic leukemia	10 (7.7%)
Combined malignancies	6 (4.7%)
Castleman's disease	2 (1.6%)
Sex	
Male	66 (50.7%)
Female	64 (49.35%)
Age (years) at reevaluation (mean and range)	53.6 (14–88)
Time (years) from initial diagnosis to reevaluation (median and range)	3.2 (0–40)

biopsy if the procedure was inconclusive and final pathological result). All biopsies for reevaluation were performed between 1990 and 2002.

Biopsy technique

The biopsy technique has been previously described in detail [3].

Histological preparations

Histological results were based on the interpretation of biopsy material prepared by the standard techniques used in the pathology department of our hospital. Immunoperoxidase staining was performed in all cases on 5- μ m sections of formalin-fixed paraffin-embedded tissue of the biopsies. The histological appearance on the hematoxylin and eosin-stained slides dictated the choice of immunohistochemical stains. When lymphoma was suspected, an extended panel of immunohistochemical stains was used, which included leukocyte-common antigen (LCA), CD20 (L26), CD3, CD45RO, CD8, CD4, LN1 (CDw75), LN2 (CD74), CD30 (Ki-1, Ber-H2), CD15 (LeuM1) and Tdt. All antibodies were obtained from Dako (Glostrup, Denmark), except for cytokeratin K-18 (Sigma, St Louis, MO, USA) and LN1, LN2 and UCHL-1 (Zymed, San Francisco, CA, USA) [2].

Statistical analysis

We calculated the number and per cent of patient characteristics. Since there were no a priori hypotheses tested, we do not report *P* values. We calculated time from initial diagnosis to re-evaluation using the core biopsy procedure and time from reevaluation to death using the Lifetest procedure in SAS (Cary, NC, USA). In the latter analysis censoring occurred at date of last follow-up.

Results

A total of 130 patients underwent pathological reevaluation using CT-guided core needle biopsy between 1990 and 2002. Patient characteristics are shown in Table 1. The mean time from diagnosis to repeat biopsy was 4.7 ± 5.1 years (range 0–40 years, median 3.2 years).

The most common reason for pathological reevaluation was suspected recurrence after complete remission in 73 patients (56%). Other indications are noted in Table 2, and include clinical suspicion of transformation (based on symptoms or increased

Table 2. Pathological reevaluation of 130 patients who underwent computed tomography (CT)-guided core needle biopsy

Indication for biopsy	
Suspected recurrence	73 (56%)
Suspected histological transformation	49 (38%)
Other	8 (6%)
Site of biopsy	
Abdomen and pelvis	36 (28%)
Retroperitoneum	16 (12%)
Thorax	35 (27%)
Peripheral lymph nodes (cervical, axillary and groin)	31 (24%)
Bone	12 (9%)
Final diagnosis obtained by	
CT-guided core needle biopsy	98 (75%)
CT-guided core needle biopsy and subsequent open biopsy	22 (17%)
Diagnosis obtained from different biopsy site	6 (4.7%)
Recurrence suspected, not confirmed	1 (0.7%)
Resolved process	1 (0.7%)
Lost to follow-up	2 (1.5%)

levels of lactate dehydrogenase etc.). The site of biopsy is noted in Table 2.

A pathological diagnosis was confirmed by CT-guided core needle biopsy in 98 patients (75.4%), of whom three required two or three such procedures. Some patients required a subsequent open biopsy in order to reach a diagnosis; and in 10 patients (7.6%) a diagnosis could not be confirmed or further biopsy was deemed unnecessary on clinical grounds (Table 2).

The final histological diagnoses after CT-guided core needle biopsy included relapse of original disease in 55 patients (42.3%), ongoing disease without change in histology in 27 (20.7%), histological transformation to a higher grade of disease in 20 (15.4%), new malignant disease in 12 (9.3%), new non-malignant disorder in six (4.6%) and insufficient tissue for diagnosis in 10 (7.7%) (Figure 1). New malignant diseases were mostly carcinomas. New non-malignant diseases were sarcoidosis, mediastinal fibrosis, bronchiolitis obliterans organizing pneumonia, progressive transformation of germinal center, cirrhosis and reactive lymph node. The biopsy in these cases was performed because of clinical suspicion of relapse in five cases and clinical progression in one case.

Of 49 patients who were reevaluated due to clinical suspicion of transformation to a higher grade of lymphoma, 19 (39%) indeed had evidence of histological transformation, 22 (45%) had no change in their diagnosis, five (10%) had a new diagnosis (including three cases of carcinoma, one case of lymphoma, one case of sarcoid) and three (6%) had insufficient tissue (pie chart, Figure 1).

There were no reported complications after the procedure.

At the time of this review, 71 of 130 patients (54.6%) have died, with median time to death from second biopsy of 32 months

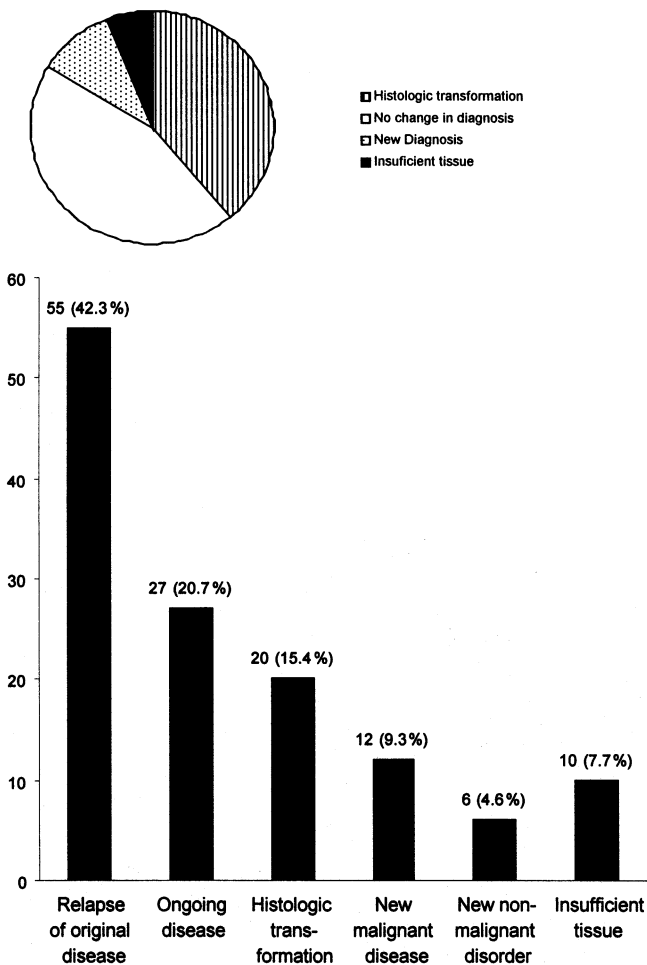


Figure 1. Final results of pathological reevaluation in 130 patients undergoing computed tomography-guided core needle biopsy and 49 patients (pie chart—see text for numbers and percentages) with suspected disease transformation.

(range 1–146). The time from second biopsy to death is shown in Figure 2. Of 20 patients who had a histological transformation of their lymphoma, six (30%) were alive 1–5 years after diagnosis. The remaining 14 patients have died, with a median survival of 6 months.

Discussion

Patients with lymphoproliferative disease may require repeated pathological reevaluation. Indications for reevaluation include suspected recurrence of the primary disease or suspected histological progression to a higher grade disease. Disease progression is not uncommon and is estimated to occur in 25–40% of patients with follicular lymphoma [8, 9]. It is thought to be underestimated since many patients do not undergo repeated biopsy upon clinical progression [10], due to the need for surgical intervention. The overall prognosis of patients with histological progression is relatively poor with a median survival of 7–22 months, although this depends on the stage and previous chemotherapy. The prognosis is better in early-stage disease and in patients who were not pre-

viously exposed to anthracycline-containing regimens [9]. Therefore, it is crucial to determine the correct histological diagnosis early in the work-up.

Fine-needle aspiration was the first minimally invasive tool used for biopsy [11]. This technique had the advantage of differentiating benign from malignant masses, although it usually could not provide the precise diagnosis or the exact subtype of lymphoma. Core needle biopsy is now commonly used for histological diagnosis in patients with suspected lymphoma, and several reports have confirmed the reliability and safety of this procedure [1–7]. CT guidance is the most commonly used modality in our institution as it has the advantage of permitting biopsies of deep and small masses. The core biopsy can be taken from peripheral nodes [5], but its major advantage is in cases of deep tissue or organ involvement, where general anesthesia can be avoided. Both safety and yield have been reported to be high in biopsies taken from the mediastinum [4, 5], the abdomen and the retroperitoneum [1, 5] and other organs [1, 2]. Previous series included mainly patients at presentation of their disease, or a combination of patients at diagnosis and follow-up. The largest previous study of CT-guided core needle biopsy performed for reevaluation of lymphoma included 92 patients with suspected recurrence or progression who underwent 109 procedures [1]. These procedures yielded precise diagnosis of lymphoma in 89% of cases.

In the present series, we describe the clinical characteristics and the yield of CT-guided core needle biopsy in a larger group of patients with a history of lymphoproliferative disease. The diagnostic yield of the procedure in this study was 75.4%, slightly less than that reported by De Kerviler and colleagues [1]. There are no data from which to evaluate the reasons for this difference.

The major indication for reevaluation was suspected recurrence, and the second most common reason for biopsy was suspected histological transformation (Table 2). Indeed, most cases had no change in the histological type of lymphoma, having either relapse (42.3%) or ongoing disease (21%). There was a tendency to ‘over-suspect’ disease transformation (only 30.7% of patients in this group had histological progression), with the sensitivity of clinical suspicion being 94.1% and the positive predictive value 30%. Only one patient had evidence of histological transformation when it was not clinically suspected. A new diagnosis entity was found in a total of 16 patients (12.4%), either malignant or non-malignant, again emphasizing the need for accurate diagnosis for further therapeutic decisions.

The need for pathological evaluation may in itself be a poor prognostic sign, with a median survival of 32 months for all patients who underwent the procedure. An especially short survival was noted in patients with histological transformation.

We conclude that image-guided core biopsy should be considered as the initial tool for the pathological reevaluation of lymphoproliferative disorders during follow-up due to its high yield (75.4%) and lack of complications. This minimally invasive technique can serve as an important guide for clinical decision-making whenever there is a suspicion of clinical progression, since histological transformation may require a modification of the treatment regimen, and since new, previously unsuspected, diagnoses are not uncommon.

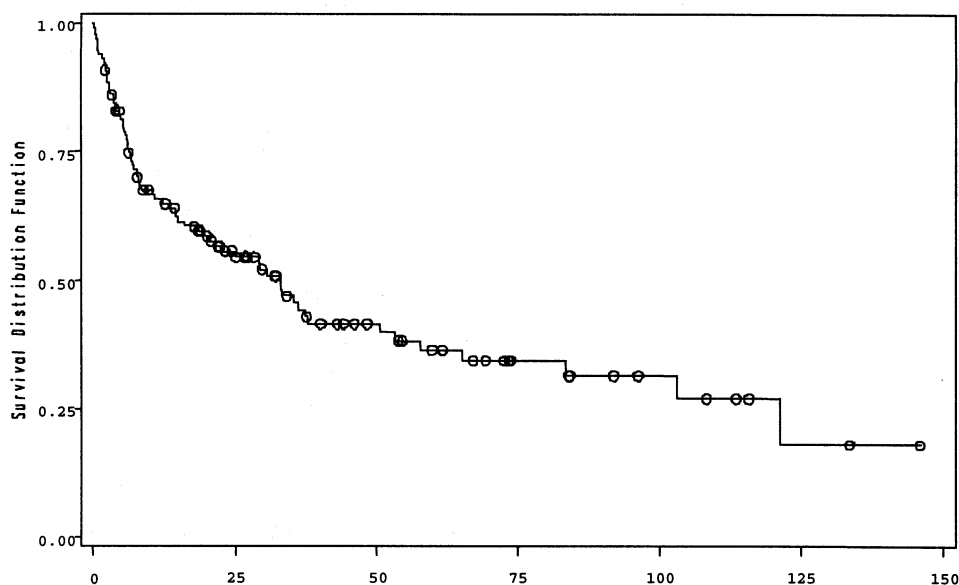


Figure 2. Time from second biopsy to death in 130 patients undergoing pathological re-evaluation using computed tomography-guided core needle biopsy. Circles represent censoring at last follow-up.

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