



BONE MARROW INVOLVEMENT IN LYMPHOBLASTIC LYMPHOMA AND SMALL NON-CLEAVED CELL LYMPHOMA: THE ROLE OF TREPHINE BIOPSY

MARICEL SUBIRÀ, ALICIA DOMINGO,* AMPARO SANTAMARÍA, RAMON BORDES,^o VICTOR ROMAGOSA,^o JESUS SOLER[#]

Unitat d'Hematologia Biològica, Departament d'Hematologia i ^oServei d'Anatomia Patològica, Hospital de la Santa Creu i Sant Pau, Barcelona; *Servei d'Hematologia i ^oServei d'Anatomia Patològica, Ciutat Sanitària de Bellvitge, L'Hospitalet de Llobregat, Barcelona; Spain

ABSTRACT

Trephine biopsy (TB) combined with bone marrow aspiration (BMA) is the most common method for evaluating bone marrow (BM) involvement in non-Hodgkin's lymphomas. Nevertheless, the role of TB in high-grade lymphomas remains controversial. We reviewed the results of 42 consecutive BMAs and TBs performed simultaneously in 29 patients with lymphoblastic lymphoma (LL) and small, non-cleaved cell lymphoma (SNCL). In LL, BM involvement was documented in 35.4% of the cases by BMA and 22.5% of the cases by TB. In

SNCL it was documented in 45.4% of the cases by BMA and 36.3% by TB. There were no statistically significant differences ($p > 0.05$) in the rates of BM involvement found by TB or BMA in the two types of lymphoma, although BMA appeared to be more sensitive than TB. These observations suggest that routine TB may not be necessary in assessing BM involvement in patients with LL and SNCL.

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Detection of bone marrow (BM) involvement in malignant lymphomas is important since it influences staging, treatment and prognosis.¹ Both trephine biopsy (TB) sections and BM aspiration (BMA) smears have been routinely used to detect lymphoma involvement. However, TBs are a distressing procedure for most patients, they increase the work load for the laboratory and they delay diagnosis. In contrast, BMAs are less time consuming, less distressing and provide results within 24h. with excellent morphological details, which allow the identification of small numbers of interstitial atypical cells as well. TB is the best procedure for evaluating focal marrow involvement by lymphoma, but the identification or interpretation of individual or small groups of immature cells is difficult.² However, in high-grade lymphomas (HGL), marrow infiltration is frequently interstitial or diffuse, and thus the value of TB over BMA remains unproven. In the present study we have reviewed the findings obtained from 42 consecutive BM smears and TB sections in 29 patients with Lymphoblastic lymphoma (LL) and small, non-cleaved cell lymphoma (SNCL).

Patients and Methods

Thirty-one simultaneous BMAs and TBs were performed on 20 patients with LL and 11 of these tests were done on nine patients with SNCL. Studies

were done at the time of diagnosis (n=36) or during the course of the disease (n=6). The morphological typification of the tumor cell population was performed in the diagnostic biopsy (lymph node or thymic mass). TB sections and BM smears were reviewed by two independent observers in order to evaluate the adequacy of sections and smears and evaluate the histologic and cytologic findings in a blind manner and in random order. For analysis of the efficacy of TB and BMA, the results were classified as positive or negative. Where there was a discrepancy between the observers, the TB sections and BM smears were reviewed simultaneously and a final decision was made.

BM trephine biopsies were performed by bone penetration with an Islam needle in a posterior iliac crest. The biopsy specimens (at least 1.5 cm in length) were paraffin embedded after fixation and decalcification. The sections were cut at four μ m and were stained with Giemsa and hematoxylin-eosin. A total of three slides for each staining procedure were done. The pattern of BM involvement was classified as focal (paratrabeular or random), interstitial or diffuse.

BM aspirates were obtained after the biopsy through the same skin incision and in the adjacent bone. Smears were stained with May-Grünwald Giemsa and 200 cells were counted. BM involvement by lymphoma was defined by more than 5%

of the lymphoblasts.

Statistical analyses were done for each type of lymphoma using a parametric test for matched data (McNemar test).

Results

The results of trephine histology and cytomorphology are summarized in Table 1. In LL, the overall incidence of BM infiltration was 35.4%. In 11 out of 31 (35.4%) studies there were more than 5% atypical lymphoblasts in marrow smears, and in seven other cases a minimal (< 5%) infiltration was observed, but these were considered negative by definition. In TB sections, a diffuse infiltration pattern was observed in 7 out of 31 (22.5%) studies. All of them had infiltration in BM smears. Trephine histology failed to detect BM infiltration in four cases with positive BM smears. In SNCL, BM infiltration was observed by BM smears in 5 out of 11 cases (45.4%). With TB, however, BM infiltration was observed in 4 out of 11 cases (36.3%), and usually presented a diffuse pattern. Statistical analyses showed no differences ($p>0.05$) between the proportions of BM involvement by TB or BMA in the two types of lymphoma studied.

Discussion

At present, adequate examination and interpretation of BM is mandatory for the staging and treatment of non-Hodgkin's lymphomas. Both TB sections and BM smears are considered standard procedures for this purpose and both are routinely performed in all types of lymphomas in most institutions.

There were no statistically significant differences in the rates of BM involvement found by TB and BMA in any of the two histological subtypes studied. However, BM smears appeared to be superior to TB. In four cases of LL and in one case of SNCL, the BM smears showed infiltration while the concomitant TB sections were negative. In addition, there were no positive TB that had negative BM smears. Unlike other types of lymphomas that may

show focal infiltration by TB, LL and SNCL usually infiltrate the BM with a diffuse or interstitial pattern.^{2,3} Thus, it is not surprising that BM smears are as sensitive as or more sensitive than TB in these subtypes of lymphomas.

Other authors have obtained similar results. Schowonzen *et al.*⁴ reviewed the results of TB and BMA in 14 HGL. In two out of six SNCL and in two out of eight LL, BM involvement was demonstrated both by TB and BMA with no differences between the two procedures. The authors concluded that for patients with LL and SNCL, marrow smears are as sensitive as TB. Foucar *et al.*⁵ studied 10 SNCL and 10 LL. Two SNCL had BM involvement both by TB sections and BM smears. In six LL, BM smears showed infiltration but TB sections were positive in only five. Similar findings were obtained by Murphy *et al.*,⁶ who did not find any cases of LL or SNCL that showed a positive TB without a positive BM smear. At present, the progress made in immunocytochemistry and immunohistochemistry could improve the results of cytomorphology and histology in the detection of lymphoblastic cells by BMA and TB. To our knowledge no study has compared the findings obtained from morphological and immunocytochemical evaluation of BMA with histological and immunohistochemical evaluation of TB.

In conclusion, in LL and SNCL, the pattern of BM infiltration is usually diffuse or interstitial, and cytologic examination of BM smears appears to be at least as sensitive as TB histology in detecting BM invasion. We suggest that TB may not be necessary for the initial study and follow-up evaluations of BM involvement in patients with LL and SNCL. However, a prospective study that compares cytomorphology – immunocytochemistry with histology – immunohistochemistry could be necessary to confirm our observations and evaluate the impact of the new immunological markers in the staging of high-grade lymphomas.

Table 1. Results of cytomorphology and trephine histology.

Diagnosis	# of studies (# of pts)	Cytomorphology		Histology				#Neg. studies
		#pos	#neg	#pos.	studies	F	I	
LL	31 (20)	11	20*	0	0	7	7	24
SNCL	11 (9)	5	6	0	1	3	4	7
Total	42 (29)	16	26	0	1	10	11	31

*In 7 cases, a minimal (< 5%) infiltration by suspicious lymphoblasts was observed although this was not considered as a positive result.

Abbreviations used: D: diffuse involvement, F: focal involvement, I: interstitial involvement, LL: lymphoblastic lymphoma, Neg: negative, Pos: positive, SNCL: small non-cleaved cell lymphoma.

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