Clinical Significance of Bone Marrow Involvement as Confirmed by Bone Marrow Aspiration vs. Bone Marrow Biopsy in Diffuse Large B-cell Lymphoma

Chattree Hantaweepant MD*, Yingyong Chinthammitr MD*,
Archrob Khuhapinant MD, PhD*, Sanya Sukpanichnant MD**

** Division of Hematology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
*** Department of Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background: *In diffuse large B-cell lymphoma (DLBCL), bone marrow (BM) involvement confirmed by BM biopsy confers a poor prognosis. However, in clinical practice, there may be disagreement in results between BM biopsy and BM aspiration in determination of BM involvement. It is unknown which of BM biopsy or BM aspiration better correlates with clinical outcome.*

Objective: *To evaluate clinical outcome of BM involvement as confirmed by BM aspiration vs. confirmation by BM biopsy in patients with DLBCL.*

Material and Method: *Clinical data, treatment, and outcome of 126 DLBCL patients with available BM aspirate slides who attended the Hematology Clinic at Siriraj Hospital between January 1, 2007 and December 31, 2009 were reviewed. BM aspirate slides were revised and interpreted by hematologists.*

Results: *BM involvement was found in 12.7% (16/126) by BM biopsy and 24.6% (31/126) by BM aspiration. Regarding BM biopsy results, rates of complete remission (CR) among patients with unequivocal involvement, equivocal involvement, and without involvement were 75.0%, 57.1%, and 77.7%, respectively (p = 0.464). Two-year overall survival (OS) rates among the three groups were not significantly different (p = 0.663). Regarding BM aspiration results, CR rates among patients with unequivocal involvement, equivocal involvement, and without involvement were 80.6%, 75.8%, and 72.7% (p = 0.755). Two-year OS rates among the three groups were not significantly different (p = 0.118). In multivariate analysis, BM involvement as determined by either BM biopsy or BM aspiration was not associated with CR rate or 2-year OS rates. However, the International Prognostic Index (IPI) and use of rituximab were found to be significantly associated with CR rate and OS.*

Conclusion: *In patients with DLBCL, BM involvement confirmed by either BM biopsy or BM aspiration appears not to influence the rate of complete remission or 2-year overall survival.*

Keywords: *Bone marrow aspiration, Bone marrow biopsy, Diffuse large B-cell lymphoma*

J Med Assoc Thai 2016; 99 (3): 262-9
Full text. e-Journal: *http://www.jmatonline.com*

Diffuse large B-cell lymphoma (DLBCL) is a heterogeneous disorder with varied clinical outcomes. The International Prognostic Index (IPI), which incorporates five clinical parameters including age, stage, performance status, serum lactate dehydrogenase (LDH) level, and number of extranodal sites, remains the primary tool used to predict outcome[1-3]. Presence of bone marrow (BM) involvement was a significant predictor of outcome in univariate analysis when it was evaluated during the development of IPI. A majority of studies that evaluated prognostic impact of BM involvement were performed before routine use of immunohistochemistry and the introduction of IPI.

In DLBCL, BM core biopsy is a useful diagnostic procedure for diagnosis, pretreatment staging, evaluation of response to chemotherapy, and restaging in disease relapse[4]. BM aspiration is a simple, minimally invasive technique that is considered complementary to BM biopsy. There are some inherent limitations associated with BM aspiration. Reticulin deposition that frequently accompanies lymphoma infiltration may prevent successful aspiration of BM. In addition, peripheral blood contamination may decrease sensitivity of detection of lymphoma cells. Accordingly, use of both BM biopsy and BM aspiration has been advocated in some reports[5,6]. In our practice, we perform both BM biopsy and BM aspiration in all

Correspondence to:
Chinthammitr Y, Division of Hematology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand
Phone: +66-2-4194448
E-mail: dryingyong@gmail.com

cases of DLBCL and there may be disagreement in results between BM biopsy and BM aspiration in determination of BM involvement.

It is unknown which of either BM biopsy or BM aspiration better correlates with clinical outcome of BM involvement. Clinical significance of BM involvement as determined by BM aspiration has not been examined in recent clinical trials. The aim of this study was to evaluate the clinical significance of BM involvement as confirmed by BM aspiration vs. confirmation by BM biopsy in patients with DLBCL.

Material and Method

Population

This retrospective cohort analysis reviewed medical records of 126 patients with DLBCL who attended the Hematology Clinic at Siriraj Hospital between January 1, 2007 and December 31, 2009. Patients were included in our study if they were 15 years of age or older with a biopsy-proven diagnosis of DLBCL according to current WHO criteria, were treated with R-CHOP, CHOP, or CHOP-like regimen with curative intent, had undergone a pretreatment unilateral posterior superior iliac crest BM aspiration and biopsy, and had complete clinical data. Patients with incomplete data or unavailable BM aspirate slides were excluded. After our study protocol was reviewed and approved by the Siriraj Institutional Review Board (SIRB), patient clinical information was collected. Collected data included patient history and physical examination, serum biochemistry including LDH, computed tomography (CT) scan results, and staging according to the Ann Arbor staging system. Performance status was measured according to Eastern Cooperative Oncology Group (ECOG) scale and IPI criteria scoring. Results of frontline treatment and survival status at two years were reviewed.

Interpretation of bone marrow aspiration and bone marrow biopsy

During staging of disease before treatment, BM aspirate was obtained from the posterior iliac crest, followed by BM biopsy from the same site in each patient. An aspirate needle was used for BM aspiration and a separate BM core biopsy needle was used to obtain a BM core biopsy (two-needle technique)[7]. Criteria for positive involvement of BM by BM aspiration were defined as presence of >30% lymphocytes and/or presence of atypical lymphocytes or blastoid cells, even if the proportion was lower than 30%[8]. Lymphoid infiltration was evaluated by examining 500 nucleated cells on slides. Criteria for equivocal involvement of BM by BM aspiration were defined as presence of <1% atypical lymphocytes or blastoid cells. One hundred twenty six DLBCL patients with available BM aspirate slides were reviewed. All slides were revised and interpreted by hematologists blinded to data and/or protocol that could bias their judgement and conclusion was drawn by agreement together.

Criteria for positive involvement of BM by BM biopsy were defined as presence of lymphomatous infiltrate by standard morphological assessment. In obscure cases of BM involvement by lymphoma, additional immunophenotypic analyses were performed. Criteria for equivocal involvement of BM by BM biopsy were defined as identification of only one large B-cell. If even minimal marrow involvement was suspected, additional immunophenotypic analyses were performed.

Primary outcome

Rate of two-year overall survival (OS) was defined as the percentage of patients in the study who were alive at two years after diagnosis. OS was defined from initiation of treatment to the date of last contact or death. Data whether patient was alive or dead at two years after treatment were available for all 126 patients. Date of death was known for all deaths.

Secondary outcome

Rate of complete remission (CR) was defined as percentage of patients who had disappearance of disease, both clinically and radiologically, after completion of treatment including no bone marrow involvement by repeated bone marrow biopsy in cases with bone marrow involvement before treatment.

Accuracy of BM aspiration and the relative contributions of BM aspiration and BM biopsy in detecting BM involvement in DLBCL.

Statistical analysis

The sample size was determined on the basis of the primary end point of overall survival. Two-year overall survival rates from other study[13] were 45% and 82% in patients with and without BM involvement by bone marrow biopsy, respectively. Using OS rates from that study, we calculated that a sample of 30 patients per cohort would give the study 80% power with the use of a two-sided test at an alpha level of 0.05. Moreover, to study the agreement between bone marrow aspiration and bone marrow biopsy on

documentation of bone marrow involvement, we increased the number of patients with no BM involvement to be threefold. Therefore, a sample size of cohort of "no BM involvement" was 90. For continuous variable, mean ± SD or median (range) was used according to the distribution of data. For categorical data, percentage was used. Clinical characteristics between cohorts were compared using ANOVA for continuous variables and Chi-square for categorical variables. OS was assessed using Kaplan-Meier survival analysis with log-rank test being used for comparisons between groups. Multivariate analysis was performed using Cox proportional hazards model to assess the independent effect of prognostic variables on overall survival whereas logistic regression was used to assess on complete remission rate. Relevant factors were considered simultaneously by use of the forward selection model. In multivariate analysis, equivocal BM involvement was considered as no BM involvement. Data were analyzed using SPSS version 13.0 for Windows (SPSS, Inc., Chicago, IL, USA).

Results

Patient characteristics

One hundred twenty six patients with DLBCL that met all of the stated inclusion criteria were identified. Baseline patient and disease characteristics according to BM aspiration and BM biopsy are presented in Table 1 and 2, respectively. For bone marrow aspirate (BMA) result, patients were divided into three groups, including negative bone marrow involvement (BMA-neg), equivocal bone marrow involvement (BMA-equi), and positive bone marrow involvement (BMA-pos). Mean age by group was 56.0±13.9 years, 57.2±14.4 years, and 57.0±11.9 years, respectively (p = 0.921). Proportion of male gender by group was 33.3%, 46.8%, and 54.8%, respectively (p = 0.212). Between the three BMA groups, there were no significant differences in IPI factors (e.g., age >60 years, stage III/IV, ECOG performance status, and >1 extranodal sites of involvement), IPI score and receiving rituximab combined with chemotherapy. However, it appeared that a significantly higher proportion of BMA-neg patients had raised LDH, when compared to the other two groups (p = 0.037). For bone marrow biopsy (BMB) result, patients were divided into three groups, including negative bone marrow involvement (BMB-neg), equivocal bone marrow involvement (BMB-equi), and positive bone marrow involvement (BMB-pos). Mean age by group was 56.3±13.9 years, 63.4±9.2 years, and 57.6±13.5 years, respectively (p = 0.406). Proportion of male gender by group was 42.7%, 71.4%, and 50.0%, respectively (p = 0.331). Between the three BMB groups, there were no significant differences in IPI factors, such as age >60 years, LDH elevation, ECOG performance status, and >1 extranodal sites of involvement. However, patients in the BMB-equi and BMB-pos groups had advanced Ann Arbor stage (stages 3, 4) in a significantly higher proportion than the BMB-neg group (p<0.001). Moreover, patients in the BMB-neg group had low IPI score in a significantly higher proportion than the other

Table 1. Baseline patient and disease characteristics according to bone marrow aspiration

Characteristic	BM aspiration (n = 126)			
	Negative (n = 33)	Equivocally positive (n = 62)	Positive (n = 31)	*p*-value
Age (years), mean ± SD	56.0±13.9	57.2±14.4	57.0±11.9	0.921
Male sex, n (%)	11 (33.3)	29 (46.8)	17 (54.8)	0.212
IPI factor, n (%)				
Age >60 years	14 (42.4)	30 (48.4)	13 (41.9)	0.793
Stage III/IV	19 (57.6)	35 (56.5)	17 (54.8)	0.976
LDH >ULN	21 (63.6)	33 (53.2)	10 (32.3)	0.037
ECOG >1	9 (27.3)	20 (32.3)	7 (22.6)	0.611
Extranodal sites >1	11 (33.3)	9 (14.5)	7 (22.6)	0.102
IPI risk groups, n (%)				
Low	11 (33.3)	21 (33.9)	12 (38.7)	0.877
Low intermediate	9 (27.3)	21 (33.9)	10 (32.3)	0.803
High intermediate	8 (24.2)	11 (17.7)	7 (22.6)	0.722
High	5 (15.2)	9 (14.5)	2 (6.5)	0.710
Rituximab use	17 (51.5)	39 (62.9)	19 (61.3)	0.545

IPI = International Prognostic Index; LDH = serum lactate dehydrogenase; ULN = upper limit of normal; ECOG = Eastern Cooperative Oncology Group

Table 2. Baseline patient and disease characteristics according to bone marrow biopsy

Characteristic	BM biopsy (n = 126)			
	Negative (n = 103)	Equivocally positive (n = 7)	Positive (n = 16)	*p*-value
Age (years), mean ± SD	56.3±13.9	63.4±9.2	57.6±13.5	0.406
Male sex, n (%)	44 (42.7)	5 (71.4)	8 (50.0)	0.331
IPI factor, n (%)				
Age >60 years	46 (44.7)	4 (57.1)	7 (43.8)	0.878
Stage III/IV	48 (46.6)	7 (100)	16 (100)	<0.001
LDH >ULN	56 (54.4)	1 (14.3)	5 (31.3)	0.235
ECOG >1	30 (29.1)	1 (14.3)	5 (31.3)	0.802
Extranodal sites >1	18 (17.5)	3 (42.9)	6 (37.5)	0.081
IPI risk groups, n (%)				
Low	41 (39.8)	1 (14.3)	2 (12.5)	0.050
Low intermediate	31 (30.1)	3 (42.9)	6 (37.5)	0.696
High intermediate	18 (17.5)	2 (28.6)	6 (37.5)	0.147
High	13 (12.6)	1 (14.3)	2 (12.5)	1.000
Rituximab use	61 (59.2)	5 (71.4)	9 (56.3)	0.876

IPI = International Prognostic Index; LDH = serum lactate dehydrogenase; ULN = upper limit of normal; ECOG = Eastern Cooperative Oncology Group

Table 3. Incidence of bone marrow (BM) involvement

	Negative	Equivocal	Positive
BM aspiration	33 (26.3%)	62 (49.2%)	31 (24.6%)
BM biopsy	103 (81.7%)	7 (5.5%)	16 (12.7%)

two groups (p = 0.05). There were no significant differences in proportion of patients treated with rituximab (p = 0.876) among the three BMB groups (Table 1, 2).

Incidence of bone marrow involvement

According to BMA results, 33 (26.3%) patients were in the BMA-neg group, 62 (49.2%) in the BMA-equi group, and 31 (24.6%) in the BMA-pos group. According to BMB results, 103 (81.7%) patients were in the BMB-neg group, seven (5.5%) in the BMB-equi group, and 16 (12.7%) in the BMB-pos group (Table 3).

Predictive factors for two-year overall survival

Regarding BMA results, two-year OS rate in patients with BMA-neg, BMA-equi, and BMA-pos was 61.9%, 80.5%, and 83.7%, respectively (Fig. 1; log-rank p = 0.118); even when comparing the three groups in patients treated with rituximab (log-rank p = 0.645) and without rituximab (log-rank p = 0.162). Regarding BMB results, two-year OS in patients with BMB-neg, BMB-equi, and BMB-pos was 76.2%, 71.4%, and 80.8%, respectively (Fig. 2). OS rates among the three groups were not significantly

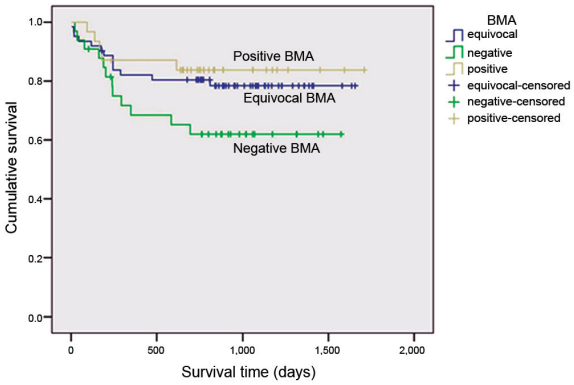

Fig. 1 Kaplan-Meier survival analysis comparing negative, equivocal, and positive bone marrow aspiration groups (p = 0.118).

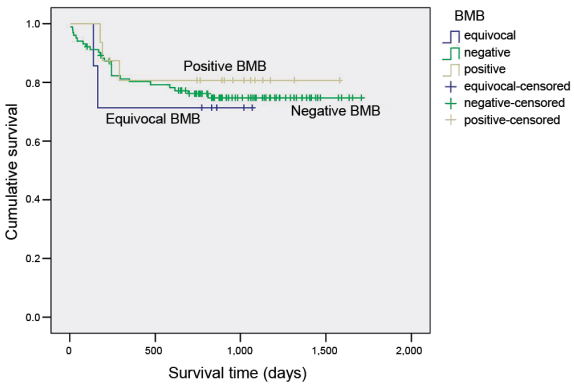

Fig. 2 Kaplan-Meier survival analysis comparing negative, equivocal, and positive bone marrow biopsy groups (p = 0.837).

different (log-rank $p = 0.837$), even when comparing the three groups in patients treated with rituximab (log-rank $p = 0.839$) and without rituximab (log-rank $p = 0.503$). However, two-year OS was significantly higher in patients treated with rituximab combined with chemotherapy, as compared to patients not treated with rituximab combined with chemotherapy ($p = 0.008$). Overall survival of higher IPI scores tended to be lower when compared with lower IPI scores ($p = 0.077$). In multivariate analysis, BM involvement either by BM biopsy or BM aspiration was not associated with OS whereas factors found to be significantly associated with OS were rituximab (HR 0.44; 95% CI, 0.22-0.89; $p = 0.022$), high-intermediate IPI risk group (HR 3.15; 95% CI 1.16-8.52; $p = 0.024$; compared to low IPI risk group), and high IPI risk group (HR 3.50; 95% CI 1.25-9.80; $p = 0.017$; compared to low IPI risk group) (Fig. 3, 4).

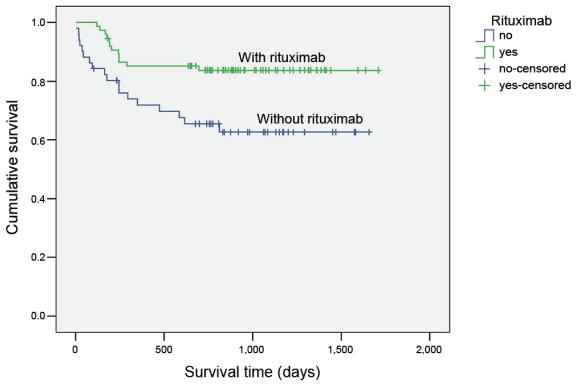

Fig. 3 Kaplan-Meier survival analysis comparing patients treated with and without rituximab ($p = 0.008$).

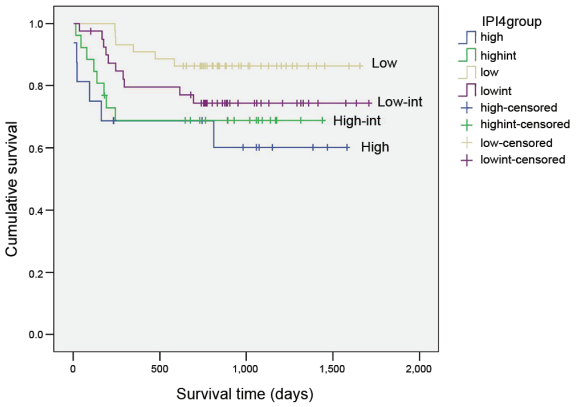

Fig. 4 Kaplan-Meier survival analysis comparing patients according to International Prognostic Index (IPI) risk groups ($p = 0.077$).

Predictive factors of complete remission

Regarding BMA results, CR rates in patients with BMA-neg, BMA-equi, and BMA-pos were 72.7%, 75.8%, and 80.6% ($p = 0.755$), respectively; even when comparing the three groups in patients treated with rituximab (log-rank $p = 0.977$) and without rituximab (log-rank $p = 0.691$) (Table 4). Regarding BMB results, CR rates in patients with BMB-neg, BMB-equi, and BMB-pos were 77.7%, 57.1%, and 75.0%, respectively ($p = 0.464$); even when comparing the three groups in patients treated with rituximab (log-rank $p = 0.249$) and without rituximab (log-rank $p = 0.847$) (Table 4). In multivariate analysis, BM involvement either by BM biopsy or BM aspiration was not associated with CR rate. However, the high-intermediate IPI risk group, high IPI risk group (compared to low IPI risk group), and use of rituximab were found to be significantly associated with CR rate ($p = 0.001$, 0.007, and 0.029, respectively).

Comparison of bone marrow aspirates and bone marrow biopsies in diagnosis of bone marrow involvement in DLBCL

In three (2.3%) specimens, both parameters (BMB and BMA) were positive, in 26 (20.6%) specimens, both parameters were negative, and in one (0.8%) specimen, both parameters were equivocal. As such, agreement between BMB and BMA was 23.8%. Discrepancies between the two parameters were found in 100 specimens (76.2%). The kappa statistic was -0.048 (95% confidence interval, -0.117 to 0.021) indicating poor agreement. To calculate sensitivity and specificity of BMA, we excluded the BMB-equi group (7 of 126, 5.5%) because we wanted the unequivocal results of BMB to be the gold standard. We then increased the specificity of BMA by moving the BMA-equi (52 of 126, 41.3%) into the BMA-neg group.

Table 4. Complete response rate according to bone marrow status

	Complete response rate			
	Negative	Equivocal	Positive	*p*-value
BM aspiration	24/33 (72.7%)	47/62 (75.8%)	25/31 (80.6%)	0.755
BM biopsy	80/103 (77.7%)	4/7 (57.1%)	12/16 (75.0%)	0.464

Table 5. Comparison of bone marrow aspirates and bone marrow biopsies in diagnosis of bone marrow involvement in DLBCL

BMA	BMB			Total
	Negative	Equivocal	Positive	
Negative	26 (78.8%)	3 (9.1%)	4 (12.1%)	33 (100%)
Equivocal	52 (83.9%)	1 (1.6%)	9 (14.5%)	62 (100%)
Positive	25 (80.6%)	3 (9.7%)	3 (9.7%)	31 (100%)

DLBCL = diffuse large B-cell lymphoma; BMB = bone marrow biopsy; BMA = bone marrow aspiration

Overall sensitivity and specificity of BMA were 18.7% and 75.7%, respectively. For BMA, overall positive predictive value (PPV) was 0.10 and negative predictive value (NPV) was 0.86 (Table 5).

Discussion

Our study found that BM involvement, as confirmed by BM biopsy, among patients with DLBCL was 12.7%, which is lower than other reports. Others have reported BM involvement rates (BM biopsy) in their DLBCL populations that vary between 15.7% and 44.0%[8-10]. This variation may reflect differences in study populations and/or the methods used to detect BM involvement. Sehn et al reported an incidence of BM involvement of 15.7%[8]. In that study, patients were excluded if they had CNS involvement at diagnosis or they were HIV positive. All patients received at least one cycle of R-CHOP. Flow cytometry, immunohistochemistry, and/or molecular studies were performed if BM involvement was equivocal. From the study by Kittivorapart and Chinthammitr, incidence of BM involvement was 17.4%[9]. That study included all DLBCL patients with complete clinical data, regardless of treatment. A study by Talaulikar et al, reported incidence of BM involvement to be 44%[10]. They included all patients with curative and palliative intent and performed flow cytometry, immuno-histochemistry, and molecular testing on all BM biopsies. In the present study, the authors included all patients who received standard anthracycline-containing chemotherapy, with and without rituximab, and who had been evaluated for response to frontline treatment. There was, however, no flow cytometry or molecular testing on BM aspirate or biopsies. Thus, the present study may not have included patients with very poor performance status or patients of very old age who could not tolerate standard anthracycline-containing chemotherapy. Patients who were lost to follow-up or died before evaluation of response were not included in the study; as such, some selection bias may have occurred. A previous study[10] showed that, among lymphoma patients, BM study with flow cytometry and molecular testing had higher sensitivity in determination of BM involvement than routine BM study. This may explain the lower rate of BM involvement in our study. Regarding BM aspiration, a previous study reported incidence of BM involvement in DLBCL to be 16.6%, which was lower than the finding from our study (at least 24.6%). However, the definition of BM involvement in previous study[10] was not described.

Level of agreement between BM biopsies and BM aspirates in the present study was 23.7% whereas kappa statistic was -0.048. This result differed from previous studies due to differences in populations and research methods. A study by Sah et al included 33 B-cell non-Hodgkin's lymphom (NHL) cases (10 of 33 were DLBCL) and added flow cytometry to increase sensitivity for detecting BM involvement[11]. Accordingly, the agreement level was 56%. The low sensitivity and low PPV in our study were similar to those from the study by Musolino et al[12]. In aggressive NHL (DLBCL and mantle cell lymphoma), sensitivity of BM aspiration was 40% and PPV was 0.29. The low sensitivity was due to the small degree of lymphoid infiltration in the BM biopsy and some cases required immunohistochemical stain to detect BM involvement. The low PPV was due to the low prevalence of BM involvement in aggressive NHL. Disagreement between BM biopsy result and BM aspiration result in determination of BM involvement in DLBCL (higher percentage of BM involvement by BM aspiration, as compared to BM biopsy) may be due to the fact that interpretation of morphology in BM aspiration is reader-dependent and heavily influenced by experience.

Regarding BM biopsy results from our study, there was no difference in rates of complete response and overall survival for the groups of patients with BM involvement, equivocal involvement, and no BM involvement. Overall survival results from our study partly differed from those from the study by Talaulikar et al[10], which included 36 patients with DLBCL, 34 of which were treated with standard anthracycline-containing chemotherapy regimens and two patients with palliative intent. In previous study[10], when examination of the BM aspirate and BM biopsy specimens using H&E staining was used to define BM involvement at staging, no obvious difference in survival was noted between patients with and without BM involvement (p = 0.13). However, when

additional diagnostic modalities (flow cytometry, immunohistochemistry, and immunoglobulin heavy chain gene rearrangement analysis) were used to define bone marrow involvement, there was significant difference in survival between patients with and without BM involvement ($p = 0.02$). This difference may be explained by differences in patient population and methods for detecting BM involvement. Another explanation why BM involvement had no effect on overall survival in our study may be because of the fact that we included only patients who received standard chemotherapy with curative intent, therefore, patients with BM involvement and poor performance status who did not receive standard chemotherapy were not included, thus possibly leading to selection bias.

Regarding BM aspiration results, this is the first study to evaluate the association between clinical outcome and BM aspiration in DLBCL. This study demonstrated that rate of complete response and rate of overall survival among patients with BM involvement, equivocal involvement, and without involvement were not significantly different ($p = 0.755$ and $p = 0.118$, respectively).

IPI was able to discriminate subgroups of patients with different rates of complete response and two-year OS in our study, confirming the utility of IPI in evaluation of prognosis in DLBCL. Rate of complete response was significantly higher in the group that received rituximab than in the group that received chemotherapy alone.

Some limitations of our study had to be mentioned. First, selection bias to include only patients with good performance status enough to get standard chemotherapy with curative intent was possible. Second, equivocal bone marrow involvement detected by BM aspiration was rater-dependent and the criterion of presence of <1% atypical lymphocytes or blastoid cells may be too sensitive with a low specificity. Third, the number of patients with bone marrow involvement detected by BM biopsy was small (16 cases) which was about half a calculated sample size (30 cases).

Conclusion

In patients with DLBCL, BM involvement confirmed by either BM biopsy or BM aspiration appears not to influence the rate of complete remission or rate of overall survival.

Disagreement between BM biopsy result and BM aspiration result in determination of BM involvement in DLBCL may be due to the fact that interpretation of morphology in BM aspiration is reader-dependent and influenced by experience.

What is already known on this topic?

Bone marrow involvement confirmed by bone marrow biopsy influenced the prognosis of patients with aggressive lymphoma.

What this study adds?

Bone marrow aspiration and biopsy at Siriraj Hospital did not influence the rate of complete remission or rate of overall survival in patients with diffuse large B-cell lymphoma.

Acknowledgements

The authors gratefully acknowledge the Division of Hematology, Department of Medicine and Department of Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University for their contributions to patient care and the support of our study.

Funding disclosure

This study was supported by a generous grant from the Thai Society of Hematology.

Potential conflicts of interest

None.

References

1. A predictive model for aggressive non-Hodgkin's lymphoma. The International Non-Hodgkin's Lymphoma Prognostic Factors Project. N Engl J Med 1993; 329: 987-94.
2. Sehn LH, Berry B, Chhanabhai M, Fitzgerald C, Gill K, Hoskins P, et al. The revised International Prognostic Index (R-IPI) is a better predictor of outcome than the standard IPI for patients with diffuse large B-cell lymphoma treated with R-CHOP. Blood 2007; 109: 1857-61.
3. Ziepert M, Hasenclever D, Kuhnt E, Glass B, Schmitz N, Pfreundschuh M, et al. Standard International prognostic index remains a valid predictor of outcome for patients with aggressive CD20+ B-cell lymphoma in the rituximab era. J Clin Oncol 2010; 28: 2373-80.
4. Atac B, Lawrence C, Goldberg SN. Metastatic tumor: the complementary role of the marrow aspirate and biopsy. Am J Med Sci 1991; 302: 211-3.
5. Barekman CL, Fair KP, Cotelingam JD. Comparative utility of diagnostic bone-marrow

components: a 10-year study. Am J Hematol 1997; 56: 37-41.
6. Lee SH, Erber WN, Porwit A, Tomonaga M, Peterson LC. ICSH guidelines for the standardization of bone marrow specimens and reports. Int J Lab Hematol 2008; 30: 349-64.
7. Islam A. Bone marrow aspiration before bone marrow core biopsy using the same bone marrow biopsy needle: a good or bad practice? J Clin Pathol 2007; 60: 212-5.
8. Sehn LH, Scott DW, Chhanabhai M, Berry B, Ruskova A, Berkahn L, et al. Impact of concordant and discordant bone marrow involvement on outcome in diffuse large B-cell lymphoma treated with R-CHOP. J Clin Oncol 2011; 29: 1452-7.
9. Kittivorapart J, Chinthammitr Y. Incidence and risk factors of bone marrow involvement by non-Hodgkin lymphoma. J Med Assoc Thai 2011; 94 (Suppl 1): S239-45.
10. Talaulikar D, Dahlstrom JE, Shadbolt B, McNiven M, Broomfield A, Pidcock M. Occult bone marrow involvement in patients with diffuse large B-cell lymphoma: results of a pilot study. Pathology 2007; 39: 580-5.
11. Sah SP, Matutes E, Wotherspoon AC, Morilla R, Catovsky D. A comparison of flow cytometry, bone marrow biopsy, and bone marrow aspirates in the detection of lymphoid infiltration in B cell disorders. J Clin Pathol 2003; 56: 129-32.
12. Musolino A, Guazzi A, Nizzoli R, Panebianco M, Mancini C, Ardizzoni A. Accuracy and relative value of bone marrow aspiration in the detection of lymphoid infiltration in non-Hodgkin lymphoma. Tumori 2010; 96: 24-7.
13. Chung R, Lai R, Wei P, Lee J, Hanson J, Belch AR, et al. Concordant but not discordant bone marrow involvement in diffuse large B-cell lymphoma predicts a poor clinical outcome independent of the International Prognostic Index. Blood 2007; 110: 1278-82.

การศึกษาความสัมพันธ์ระหว่างผลการรักษากับผลของสเมียร์ไขกระดูกและผลของชิ้นเนื้อไขกระดูกในผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองชนิด diffuse large B-cell lymphoma (DLBCL)

ฉัตรี หาญทวีพันธุ์, ยิ่งยง ชินธรรมมิตร์, อาจรบ คูหาภินันทน์, สัญญา สุขพณิชนันท์

ภูมิหลัง: *มีการศึกษาผลของชิ้นเนื้อไขกระดูกต่อผลการรักษาในผู้ป่วย DLBCL พบว่าการมีรอยโรคในไขกระดูกสัมพันธ์กับการพยากรณ์โรคที่ไม่ดี แต่ยังไม่เคยมีการศึกษาเกี่ยวกับผลของสเมียร์ไขกระดูกต่อผลการรักษาของผู้ป่วย*

วัตถุประสงค์: *เพื่อประเมินผลของการมีรอยโรคในไขกระดูกต่อผลการรักษาในผู้ป่วย DLBCL*

วัสดุและวิธีการ: *ทำการศึกษาย้อนหลังกลุ่มผู้ป่วย DLBCL 126 ราย ที่รับการรักษาที่โรงพยาบาลศิริราช ระหว่าง พ.ศ. 2549 ถึง พ.ศ. 2552 และมีการนำสเมียร์ไขกระดูกของผู้ป่วยทุกรายมาเก็บข้อมูลใหม่*

ผลการศึกษา: *จากการประเมินชิ้นเนื้อไขกระดูกพบมีรอยโรค 16 ราย คิดเป็นร้อยละ 12.7 และพบรอยโรคจากการตรวจสเมียร์ไขกระดูก 31 ราย คิดเป็นร้อยละ 24.6 อัตราการตอบสนองอย่างสมบูรณ์หลังการรักษาในกลุ่มที่มีรอยโรคในชิ้นเนื้อไขกระดูก กลุ่มที่ผลยังไม่แน่ชัดและกลุ่มที่ไม่มีรอยโรคคิดเป็นร้อยละ 75.0, 57.1 และ 77.7 ตามลำดับ (p = 0.464) อัตราการรอดชีวิตที่ 2 ปี ของทั้ง 3 กลุ่มไม่แตกต่างกัน (p = 0.663) อัตราการตอบสนองอย่างสมบูรณ์หลังการรักษาในกลุ่มที่มีรอยโรคในสเมียร์ไขกระดูก กลุ่มที่ผลยังไม่แน่ชัดและกลุ่มที่ไม่มีรอยโรคคิดเป็นร้อยละ 80.6, 75.8 และ 72.7 ตามลำดับ (p = 0.755) อัตราการรอดชีวิตที่ 2 ปี ของทั้ง 3 กลุ่มไม่แตกต่างกัน (p = 0.118) จากการวิเคราะห์พหุตัวแปรพบว่าการมีรอยโรคในชิ้นเนื้อไขกระดูกและในสเมียร์ไขกระดูก ไม่มีผลต่ออัตราการตอบสนองอย่างสมบูรณ์หลังการรักษาและอัตราการรอดชีวิตที่ 2 ปี ในขณะที่ international prognostic index (IPI) และการใช้ยาไรทูซิแม็บมีผลต่ออัตราการตอบสนองอย่างสมบูรณ์หลังการรักษาและอัตราการรอดชีวิต*

สรุป: *การมีรอยโรคในไขกระดูกของผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองชนิด DLBCL จากการตรวจพบในชิ้นเนื้อไขกระดูกหรือสเมียร์ไขกระดูก ไม่มีผลต่ออัตราการตอบสนองอย่างสมบูรณ์หลังการรักษาและอัตราการรอดชีวิตที่ 2 ปี*
