Quantitative MR Imaging of Bone Marrow in Leukemia

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Abstract **Objectives** to investigate the role of signal intensity ratio (SIR) of MR Imaging in the characteristic diagnosis and tumor burden evaluation in leukemias by measurement of spinal marrow SIR in LL and ML separately. **Methods** Spinal marrow in 20 LL patients and ML patients on initial consultant were examined with MR imaging. The diagnosis of leukemia in all the patients was proved by iliac marrow cytological examination. MR imaging of spinal marrow was performed with 0.5T super-conducting system. T1-weighted imaging with spin-echo techniques and T2-weighted imaging with turbo spin-echo techniques were obtained. The SIR of spinal marrow to spinal cord in leukemia were calculated on midline sagittal T1-weighted imaging. Meanwhile, peripheral blood routine examination and bone marrow cytological examination was performed. **Results** The SIR of spinal marrow in 20 LL patients and 10 ML patients were 0.72±0.11, 0.73±0.11 respectively. There was no statistical difference between LL and ML (P =0.836). The SIR of spinal marrow in LL negatively correlated with the percentage of immature lymphocyte in marrow (r =-0.836, P =0.000), while the SIR of spinal marrow in ML negatively correlated with the percentage of immature myelocyte in marrow (r =-0.673, P=0.033) **Conclusions** The SIR of spinal marrow is limited in the characteristic diagnosis of leukemia because of its inability in differentiating LL from ML. The SIR of spinal marrow can be used to evaluate tumor burden in leukemia.

Key Words Magnetic Resonance Imaging; Bone Marrow; Leukemia

MR imaging in bone marrow and its correlation with clinical laboratory variables in leukemia had been investigated globally. T1 relaxation time of spinal marrow in leukemia was coincidently suggested to be significant prolongation in contrast to normal marrow. As regards the correlation between MR imaging and the clinical laboratory features, the T1 relaxation time was found relevant to certain variables, such as the amount of white blood cell in peripheral blood, the percentage of blast cell in marrow, whereas, the available results varied dramatically in each individual correlation investigation [1-8]. However, lymphoid leukemia (LL) and myeloid leukemia (ML) with different histological character, even though belong in the same classification of leukemia, are completely different in the matter of histological cellularity, histological differentiation, chemical composition and the proliferative rate of tumor cell. A potential discrepancy between either leukemia is therefore, believed to lie in the feature of MR imaging. However, a few relevant studies had yet separated lymphoid leukemia from myeloid leukemia to carry out a systemic comparison[1, 3].

The current study was designed to divide leukemia into ML and LL, subsequently, the signal intensity ratio (SIR) of spinal marrow on MR imaging and its correlation with clinical laboratory variables were separately measured to determine the role of quantitative MR imaging in the characteristic diagnosis and tumor burden evaluation in leukemia.

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MATERIALS AND METHODS

Patients

From 1992 to 2002, 30 patients with leukemia on initial consultant in our hospital were included, with a age from 2 to 74 years (median 15 years). There were 25 males and 5 females in a sexuality ratio of 5:1, and 18 patients with acute lymphoid leukemia, 2 patients with chronic lymphoid leukemia, 1 patient with acute myeloid leukemia and 9 patients with chronic myeloid leukemia respectively. Spinal MR imaging and peripheral blood routine test and marrow biopsy were performed in all the patients. The diagnosis of all the patients with leukemia was proven by the means of marrow cytological examination.

MR Imaging

MR imaging of spinal marrow was performed on a 0.5-T superconducting imaging system (Gyroscan T5-II, Philips Medical System, Netherland, B.V.). T1-weighted images were performed with a spin echo technique and

T2-weighted images with a turbo spin echo technique. The imaging parameters were as follows, repetition time/echo time/number of signal acquisition on T1WI was 420-450msec/20-30msec/2-8, on T2WI 2220msec/ 150msec/2-6 respectively. All the patients were imaged in supine position. A matrix of 256×256, a field of view of 150-320 mm, a section thickness of 4 mm and a gap of 0.4 mm were used. Sagittal and transverse images, with a complementation of coronal images were obtained with a rectangular surface coil used. As the contrast between abnormal marrow and normal marrow was relatively optimal on T1-weighted imaging[9], the signal intensity ratio (SIR) between spinal marrow and spinal cord was thereby measured on T1-weighted images. The signal intensity of spinal marrow and spinal cord at same anatomical region and same imaging slice were measured separately with the technique of region of interests from the midsection of the sagittal T1-weighted images, in which marrow signal intensity in 3 vertebral bodies were selected for the measurement of SIR if the spinal marrow was diffusely infiltrated, alternatively, 3 lesions were selected or the measurement repeated three times (less than 3 lesions) if the spinal marrow was focally involved. The averaged signal intensity was calculated and the ratio of average signal intensity between spinal marrow and spinal cord was then determined as the SIR.

Clinical Laboratory Examination

All involved clinical laboratory examinations were accomplished by hematologist in 3 days when MR imaging was implemented. The peripheral blood was collected for routine blood test, i.e. the amount of hemoglobin, erythrocyte, white blood cell and platelet. Additionally, marrow biopsy was performed on the location of posterior or anterior superior iliac spine for marrow cytological examination. The marrow smears was stained according to the method of Wright. The cellulariy, cell classification counts, the percent of immature cell and mature cell in marrow were observed microscopically. The cellularity of marrow in this regard, was classified into 5 grades as follows, in grade 1, extremely hypoplasia marrow with a ratio of the percentage of mature erythrocyte to that of nucleated cell as 300:1; in grade 2, hypoplasia marrow with the above ratio of 50: 1; in grade 3, hyperplasia marrow with the ratio of 20:1; in grade 4, obviously hyperplasia marrow with the ratio of 10:1; in grade 5, extremely hyperplasia marrow with the ratio of 1:1. The percentage of immature cell indicated here was defined as the proportion of the cell in immature phase to the entire nucleated cell in marrow. The approach to the immature cell percentage was thus slightly different between LL and ML, as the lymphoblast and prolymphocyte represented the immature cells in LL, oppositely, myeloblast and promyelocyte were indicated as immature cells in ML. Simultaneously, the mature cell percentage was defined as the proportion of cell except for immature cells, i.e. cells in mature phase, to the whole nucleated cells.

Statistics Analysis

The SIR and clinical laboratory variables were stated with mean ± standard deviation ($\bar{x}\pm s$), in particular the cellularity of marrow was describe with median. The comparison of SIR between LL and ML was statistically analyzed with *t* test. The correlation between the SIR and varied clinical laboratory parameters was statistically analyzed with Pearson or Spearman correlated statistics. The statistical difference was considered significant with a $P<0.05$. SPSS for windows (10.0 Edition) was used for all statistical analysis.

RESULTS

SIR of Spinal Marrow

The mean SIR of spinal marrow measured on T1WI in LL and ML were 0.72±0.11, 0.73±0.11 (standard deviation) respectively. There was no significant difference in the SIR between LL and ML (*t* test, $t=0.209$, $P=0.836$). On T1WI, the spinal marrow in all the patients with leukemia manifested lower signal intensity. The observed abnormal marrow with lower signal intensity was found to be diffusely involved in 18 patients with LL and 9 patients with ML, as focally infiltrated in 2 patients with LL and 1 patient with ML respectively. (Fig.1a-d)

Marrow Cytological Examination

All the marrow smears were stained according to the method of Wright for cytological examination. The marrow in 20 patients with LL and 10 patients with ML all displayed hyperplasia to a variable degree on cytological examination. Immature leukemia cell was found in marrow, as the percentage of immature lymphocyte in LL was 26.8%±31.4% and the percentage of immature myelocyte in ML 14.7%±16.6%.

The SIR of spinal marrow in LL negatively correlated with the percentage of immature lymphocyte in marrow($r=-0.836$, $P=0.000$), while the SIR of spinal mar-

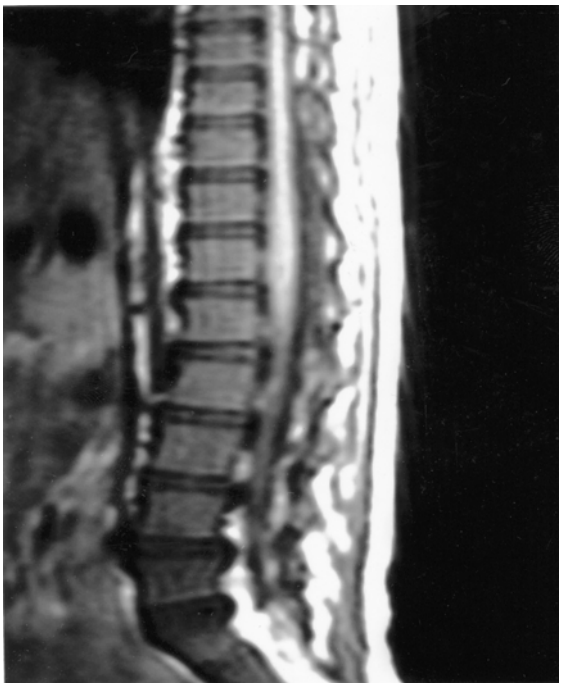

Fig. 1a

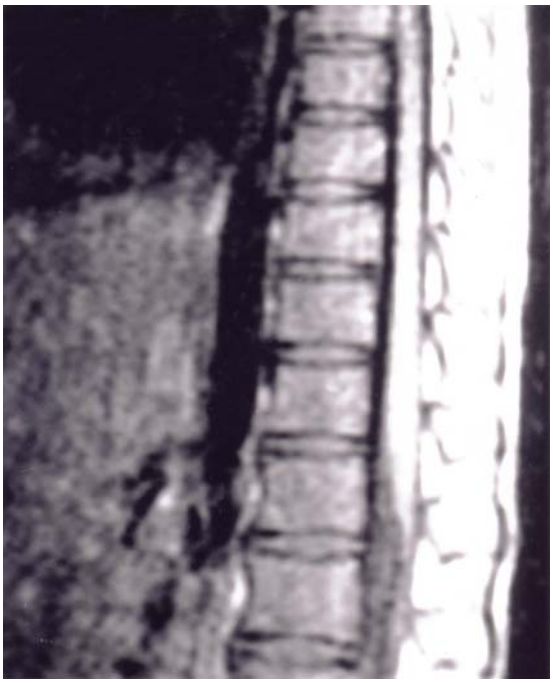

Fig. 1b

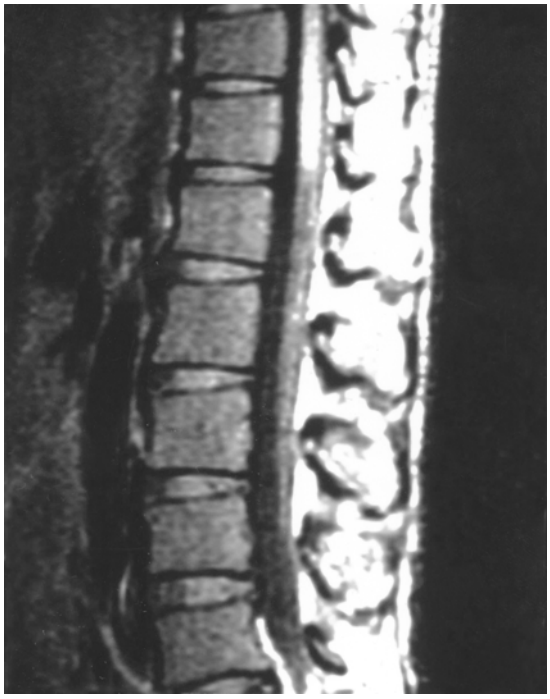

Fig. 1c

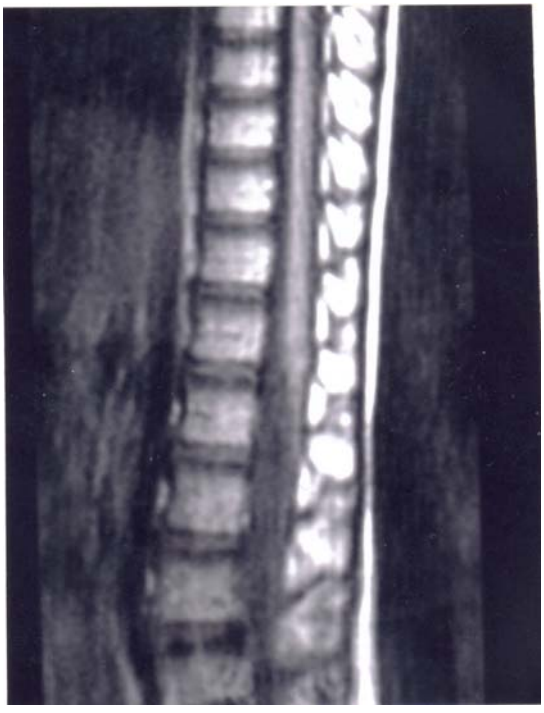

Fig. 1d

Fig.1 SIR of Spinal Marrow in Leukemia
A patient with AML, Spinal marrow showed diffuse hypo-intensity signal on T1WI, SIR=0.67 (a);
Another patient with CML, Spinal marrow also showed diffuse hypo-intensity signal on T1WI, SIR=0.71(b);
A patient with ALL, Spinal marrow showed diffuse hypo-intensity signal on T1WI, SIR=0.62(c);
Another patient with ALL, Spinal marrow showed diffuse hypo-intensity signal on T1WI, SIR=0.86(d).

Correlation between SIR with Clinical Laboratory Variables (Table 1)

Table 1 Correlation of SIR in 20 LL Patients and 10 ML Patients with Clinical Laboratory Variables

	LL			ML		
	Mean±SD	r	p	Mean±SD	r	p
WBC(10^9/L)	19.1±25.5	-0.049	0.88[b]	103.7±177.3	0.357	0.432[b]
BG(10^9/L)	4.59±3.99	-0.346	0.27[c]	57.0±77.4	0.036	0.939[b]
BL(10^9/L)	4.23±2.80	-0.225	0.482[c]	10.0±17.8	0.321	0.482[b]
Plt(10^9/L)	134.5±105.9	0.564	0.054[c]	180.7±109.7	0.213	0.646[c]
BB(10^9/L)	26.8±31.4	-0.142	0.659[b]	14.7±16.6	0.019	0.968[b]
Hb(g/L)	107.6±21.9	0.317	0.315[c]	98.2±10.0	0.233	0.616[c]
MB(%)	64.9±37.0	-0.836	0.000[c]	32.2±37.7	-0.673	0.033[b]
MG(%)	17.9±22.2	0.551	0.079[b]	63.9±18.9	0.556	0.195[c]
ML(%)	10.5±8.9	0.17	0.618[c]	7.79±4.97	-0.259	0.576[c]
C	4[a]	-0.084	0.796[b]	4[a]	0.289	0.530[b]

WBC: peripheral leukocyte, BG: peripheral differential leukocyte, BL: peripheral lymphocyte, Plt: blood platelet, BB: immature cell in peripheral blood, Hb: hemoglobin, MB: immature cell in marrow, MG: mature myelocyte in marrow, ML: mature lymphocyte, C: marrow cellularity. a: median. b: Spearman's correlation analysis c: Pearson's correlation analysis.

row in ML negatively correlated with the percentage of immature myelocyte in marrow (r=-0.673, P=0.033). There was no correlation found between individual clinical laboratory parameter with the SIR in LL and in ML as well (P>0.05).

DISCUSSION

Quantitative MR Imaging in differentiation between LL and ML

In the present study, the measured SIR was defined as the ratio between the signal intensity of spinal marrow and the spinal cord, which reduced the influence of the signal noise and the adopted surface coil as nearly as possible on the accuracy in the measurement of SIR. Spinal cord had been proven a satisfying internal system for reference[10], as the signal intensity of spinal cord was relatively kept unchanged on T1WI. Therefore, the SIR in our study was dependent on the signal intensity of the spinal marrow, indicated an indirect reflection of the T1 relaxation time of marrow. Although there are an underlying difference in the histological cellularity, histological differentiation, chemical composition and the proliferative rate of tumor cell between LL and ML, no statistical difference was found in the SIR of marrow between LL and ML. Consequently, the characteristic diagnosis could not be solely made according to the measured SIR, inconsistent with the finding of Vande Berg et al[1] as the T1 relaxation time in lymphoid leukemia was more prolonged than that in myeloid leukemia, whereas consistent with observation of Jensen et al[3]. Now that the marrow had not by far been adequately investigated in a condition of separation between LL and ML, the value of SIR in the characteristic diagnosis of leukemia is yet needed to be established by furthermore investigation with a large number of patients.

SIR in the evaluation of tumor burden of leukemia

In the clinical practice, tumor burden of leukemia was evaluated usually depended on the invasive methods of marrow biopsy and/or puncture. Those methods however possess the limits of themselves[6]. In our study, whether in LL or ML, the marrow SIR was not found to correlate whatever parameters of peripheral blood examination and the marrow cellularity, which probably resulted from the influence of various factors on the results of individual parameters of peripheral blood examination. The value of the peripheral blood examination, on one hand maybe vary if measured at different interval time, on the other hand may be delayed in response, i.e. reflecting the change of marrow cellularity promptly. With regard to the correlation between the marrow SIR and the parameters in cytological examination, the SIR of leukemia was found correlated negatively with the percentage of immature myelocyte in marrow, positively with the percentage of mature myelocyte respectively if overall analyzed with a combination of LL with ML. This result indicated with more mature myeloctye, less immature myelocyte in marrow, the higher SIR, the

shorter T1 relaxation time. More mature myelocyte undoubtedly indicates less immature myelocyte in the marrow of ML. However, in the marrow of LL, this observation was vulnerable for marrow of LL occasionally is almost full of immature lymphocyte, even if no myelocyte could be found microscopically on the marrow smears. In the current study, the immature lymphocyte in the marrow ranged from 90% to 100% in 7 patients with LL, even 100% in one patient. On this basis, it is of important to separate LL from ML whenever to analysis the marrow of leukemia. After separately analysis of LL and ML in our study, either marrow SIR was negatively correlated with the percentage of immature cell in the marrow, not positively with the percentage of mature myelocyte again. This result suggested that the lower SIR, more immature cell in marrow, the larger the tumor burden as well. The SIR of marrow is therefore indicated a hint to evaluate the tumor burden of marrow in LL and ML. In a similar research, Vande Berg et al[1] found that the T1 relaxation time of marrow in acute lymphoid leukemia was not in relation to the peripheral leukemia cell, marrow cellularity and marrow blast cell, as in acute myeloid leukemia correlated with the marrow cellularity and blast cell, not with the peripheral leukemia cell, which partially consistent with our results. Owing to inadequate relevant studies with LL and ML separated, the exactly correlation between the SIR and quantitative parameters of marrow cytological examination remains further clarification.

In the current study, quantitative MR imaging was performed on a 0.5 tesla machine without the capacity of chemical shift imaging and 1H-spectroscopy.Although the adopted spin echo sequence is inferior to the chemical shift imaging in the detection of abnormal marrow. Spin echo sequence is a widespread technique and highly reproducible as the measurement of SIR. At same time, the clinical value of chemical shift imaging in practice and the application of 1H-spectroscopy at this aspect are needed for further research[11].

In summary, quantitative measurement of SIR on MR imaging could not distinct LL from ML, thereby is limited in the differential diagnosis of LL and ML, but a significant correlation between the SIR and the percentage of immature cell suggested a potentiality of assessment tumor burden of marrow with SIR in leukemia.

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