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MR Features of Myelofibrosis : Correlation with Bone Marrow Biopsy Findings[1]

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Purpose : To characterize the magnetic resonance (MR) imaging features of myelofibrosis and compare them with bone marrow biopsy findings.

Material and Methods : The authors retrospectively reviewed sagittal T1- and T2 weighted and short tau inversion recovery (STIR) images of the thoracolumbar spine of six patients (five males and one female, mean age 46) with biopsy-proven myelofibrosis. Marrow signal intensity of the thoracolumbar spine was classified with respect to those of muscle and fat, based on the consensus of two radiologists after visual inspection. These MR features were compared with the degree of fibrosis and marrow cellularity, as determined by bone marrow biopsy.

Results : In all patients, marrow signal intensity of the thoracolumbar spine was reduced on T1 and T2 weighted images (invariably low on T1 weighted images, low (2/6) to intermediate (4/6) on T2 weighted images). On STIR images, marrow signal intensity was variable (high (3/6) or low (3/6)), and this correlated with degree of fibrosis, not with marrow cellularity. The signal intensity of marrow with mild to moderate fibrosis was high on STIR images, while that of marrow with marked fibrosis was low.

Conclusion : MR imaging features of myelofibrosis were characterized as low on T1 weighted images and low to intermediate on T2 weighted images. In addition, the signal intensity of STIR imaging correlated with degree of fibrosis.

Index Words : Bone marrow, MR

Magnetic resonance (MR) imaging is currently widely used as the noninvasive imaging modality of choice in evaluating the pattern of bone marrow (1). Although variable, the normal marrow pattern related to age in individual bones has been relatively well established by many authors, especially focusing on fat marrow conversion (2-6). This allows us to more clearly understand various processes affecting bone marrow, which include delayed or absent fat marrow conversion, reconversion to cellular marrow, depletion or replacement of cellular marrow, or neoplasm (1, 7). Most current knowledge of normal bone marrow pattern or marrow disorders is based mainly on the conventional spin echo technique with T1-weighted imaging because of its ability to distinguish fat from other tissues. In recent years, there have been many efforts to improve quantitative or qualitative assessment of bone marrow disorders, such as short tau inversion recovery (STIR), chemical-shift, or other imaging (1, 8, 9).

Myelofibrosis is a descriptive term given to various disorders that produce a stromal reaction of fibrosis of the marrow. In this condition, the normal medullary fat and marrow elements are replaced by reticulin and collagen (10). For the evaluation of this disease, a bone marrow biopsy has, until now, been essential; without it the diagnosis cannot be made with certainty. This is, however, an invasive and painful procedure, and attempts to aspirate bone marrow may often lead to a dry tap.

In this study, we performed a retrospective review

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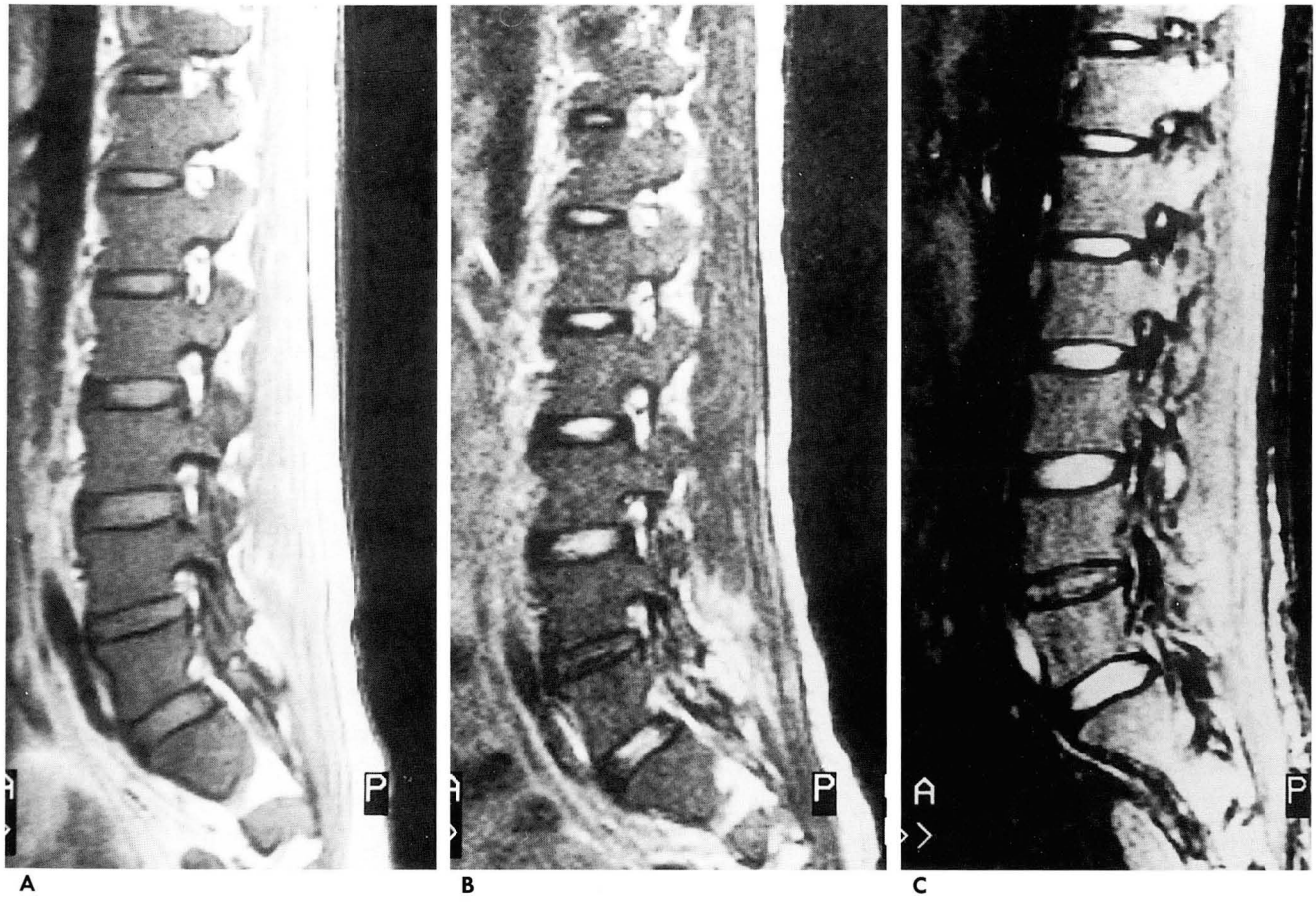
of T1- and T2-weighted and STIR images in patients with myelofibrosis, in which MR imaging features were determined and compared to the degree of fibrosis and marrow cellularity on bone marrow biopsy findings.

Materials and Methods

A retrospective review of MR examinations of seven patients (five males, two females) was performed. The patients were between the ages of 26 and 52 years (mean, 46). All were shown by bone marrow biopsy routinely performed at the posterior iliac crest, usually within 3 weeks (mean 13 days) of MR examination, to have myelofibrosis. Each bone marrow biopsy finding was reviewed by a blinded clinical pathologist. Tissue sections were stained with hematoxyline and eosin (H & E) to determine marrow cellularity, and silver methenamine to ascertain the degree of fibrosis. Of six patients, three were found to have myelofibrosis with agnogenic myeloid metaplasia, another two had myelofibrosis secondary to leukemia, and the remain-



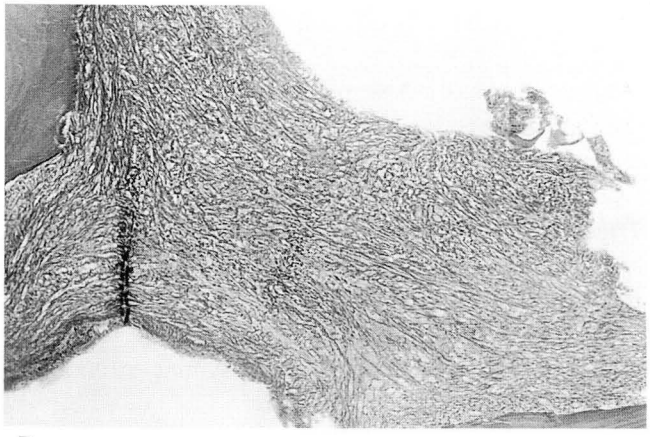


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Fig. 1. A 32-year-old man (patient 3) with myelofibrosis secondary to acute lymphoblastic leukemia. Marrow signal intensity of the thoracolumbar spine is low on T1-weighted parasagittal image (**A**), low on T2-weighted image (**B**), and low on STIR image (**C**). Microphotograph of the bone marrow biopsy shows hypercellularity (100%) with diffuse and marked fibrosis. (Silver methenamine stain, × 100) (**D**)

ing one had myelofibrosis with secondary leukemic transformation. The degree of fibrosis was variable and classified as mild, moderate or marked by visual inspection. The cellularity of bone marrow was also variable, ranging from less than 10% to 100%.

In six patients, MR imaging of the thoracolumbar spine was performed with a 0.5 Tesla superconducting MR unit (Gyroscan T5, Phillips, Netherlands). Sagittal T1- and T2-weighted spin echo and STIR images were obtained using the following protocols; initially, sagittal T1 weighed images (TR/TE=560/30 msec) of the thoracolumbar spine was obtained with a slice thickness of 5mm and 0.5mm intersection gap. These were followed by sagittal T2-weighted images (TR/TE =1800/90 msec) with the same thickness and gap. In addition, STIR images (TR/TE=1400/30 msec) with an inversion time of 120 msec were obtained. The slice thickness of these images was 7mm, with 1.4mm intersection gap. Data were collected with a 205 × 256 matrix and a 320mm field of view on all pulse sequences.

Using conventional T1- and T2-weighted images, the signal intensity of bone marrow of the thoracolumbar spine was classified as low, intermediate or high, based on the consensus of two radiologists after visual inspection. "Low signal" was less than or equal to the signal intensity of paravertebral muscle, "intermediate signal" was between the signal intensities of paravertebral muscle and subcutaneous fat, and "high signal" was equal to or greater than the signal intensity of subcutaneous fat. On STIR images, in which the signal from the fat component is suppressed, marrow signal intensity was rated as high or low in relation to the paravertebral muscle.

Results

Bone marrow and MR findings in seven patients are summarized in the Table 1. In all patients, marrow signal intensity of the thoracolumbar spine was reduced on T1- and T2-weighted images. On T1-weighted images, marrow signal intensity was invariably low (Fig. 1A, 2A), on T2-weighted images, it was low to intermediate on T2-weighted images. Two of six patients (33%) had low signal intensity (Fig. 1B), whereas four (67%) had intermediate signal intensity (Fig. 2B). On STIR images, marrow signal intensity of the thoracolumbar spine was variable: three patients (50%) showed low signal intensity (Fig. 1C), while the signal intensity of three (50%) was high (Fig. 2C).

In all patients, increased reticulin and collagen were histopathologically confirmed on bone marrow biopsy. The degree of fibrosis was mild in two patients (29%) (Fig. 2D), moderate in one (14%) and marked in three (57%) (Fig. 1D). It correlated relatively well with the marrow signal intensity on STIR imaging, which was invariably high in patients with mild to moderate myelofibrosis. On the contrary, that of patients with marked fibrosis was low on STIR images.

Marrow cellularity varied from lower than 10% to 100% including less than 10% in one patients (17%), 30% in one (17%), 50% in one (17%), and 100% in three patients (50%).

Discussion

Myelofibrosis is characterized by excessive fibroblast proliferation and collagen and reticulin deposition, with replacement of normal medullary fat and other marrow components, and is accompanied by myeloid metaplasia of various organs, such as the spleen, liver and lymph nodes. In this condition, similar clinical syndromes may be seen in three distinct settings; progressive hepatosplenomegaly and bone marrow fibrosis arise insidiously without an identifiable preceding cause (termed agnogenic (idiopathic) myeloid metaplasia). A similar picture of myelofibrosis with myeloid metaplasia may sometimes evolve in the course of polycythemia vera and, less frequently, chronic granulocytic leukemia. The third is myeloid metaplasia with

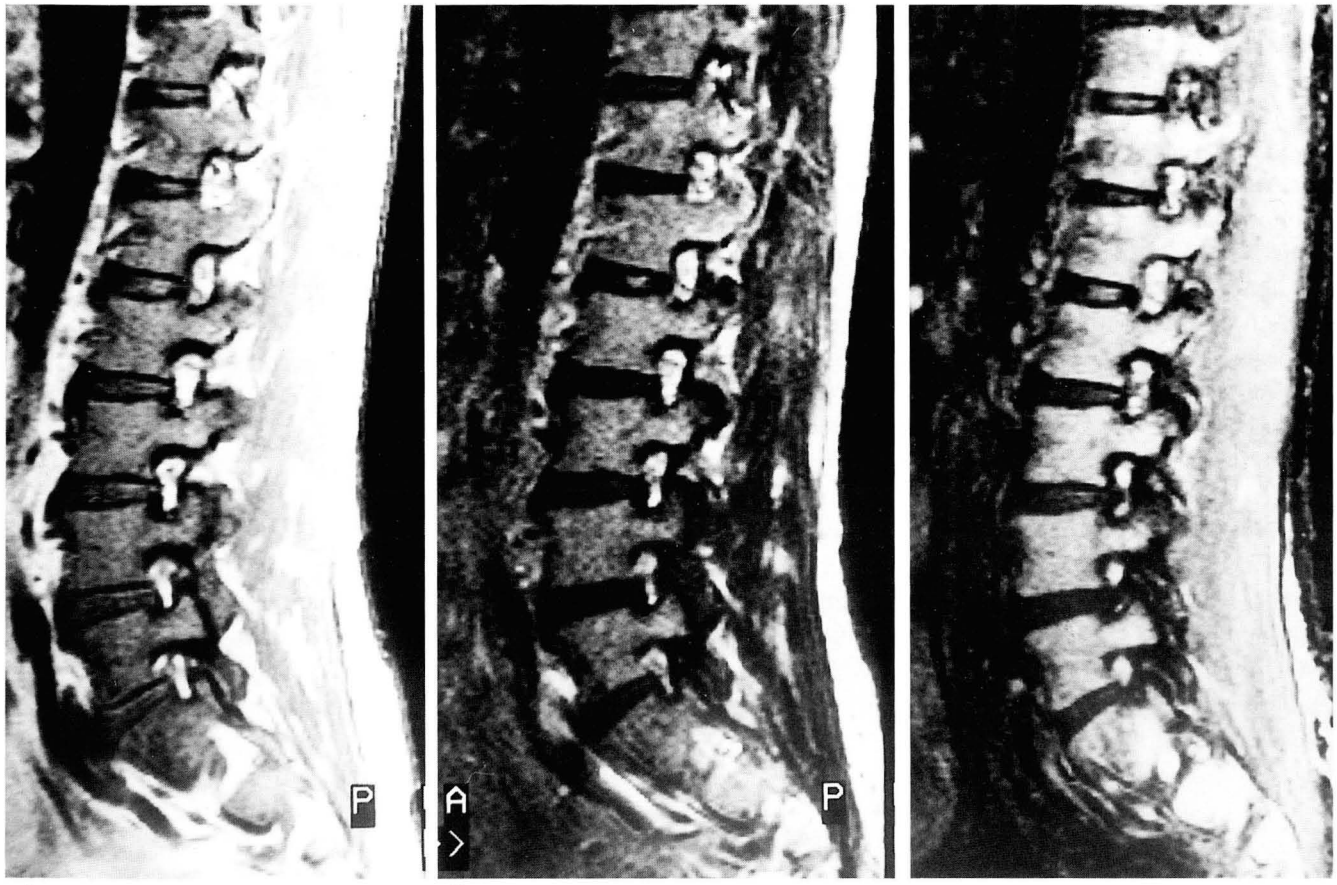
Table 1. Bone Marrow Biopsy and MR Findings

Patient/ Sex/Age	Clinicopathologic diagnosis	Marrow cellularity(%)	Degree of fibrosis	MR signal intensity		
				T1WI	T2WI	STIR
1/M/42	MSL	30	marked	low	low	low
2/F/38	MMM	〈10	marked	low	intermediate	low
3/M/32	MSL	100	marked	low	low	low
4/M/62	MMM	100	moderate	low	intermediate	high
5/M/49	MMM	50	mild	low	intermediate	high
6/M/52	MLT	100	mild	low	intermediate	high

MSL: myelofibrosis secondary to leukemia, MMM: myelofibrosis with myeloid metaplasia, MLT: myelofibrosis with leukemic transformation, T1WI: T1-weighted image, T2WI: T2-weighted image, STIR: short tau inversion recovery image

varying degrees of reactive marrow fibrosis that may occur secondary to a wide spectrum of chronic disorders including metastatic carcinoma, leukemia and lymphoma, tuberculosis, Gaucher's disease, Paget's disease, and exposure to toxins such as benzene, fluorine, phosphorus, or X-ray (11).

Although the cause of marrow fibrosis, which is accompanied by myeloid metaplasia, is not clear, one hypothesis is that neoplastic megakaryoblasts and megakaryocytes release growth factors, such as platelet-derived growth factor, which stimulate fibroblasts or other connective tissue cells to synthesize collagen or reticulin (12). In this condition, marrow cellularity is variable, ranging from 100%, with a slight increase in reticulin, to complete depletion of the hematopoietic elements, with marked fibrosis (13, 14). Moreover, in cases in which secondary hematologic malignancy is combined (leukemic transformation), marrow cellularity may apparently increase. In our series, the existence of myelofibrosis was in all patients



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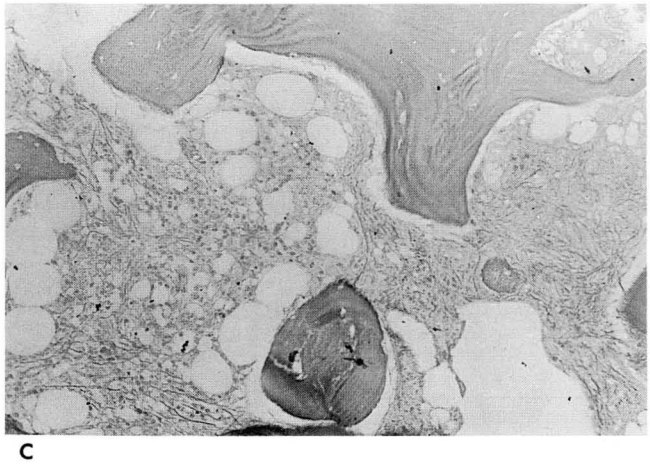

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Fig. 2. A 49-year-old man (patient 5) with myelofibrosis with myeloid metaplasia. Marrow signal intensity of the thoracolumbar spine is low on T1-weighted parasagittal image (**A**), intermediate on T2-weighted image (**B**), and high on STIR image (**C**). Microphotograph of the bone marrow biopsy reveals normocellularity (50%) with focal, mild fibrosis. (Silver methenamine stain, ×100) (**D**)

proven by bone marrow biopsy; it confirmed an increase of reticulin and collagen, which replaced normal medullary fat. Marrow cellularity and the degree of fibrosis in each case was variable, depending not on clinical setting but on its own stage.

MR findings of myelofibrosis were first reported in two patients by Lanir et al (15). They observed a very low, mainly homogeneous signal in the bone marrow of the lumbosacral spine and pelvis. In a study of ten patients with myelofibrosis, Kaplan et al observed that marrow signal intensity on T1 weighed images of the lumbosacral spine was moderately to markedly decreased (16). In our series, similarly, the marrow signal intensity of all patients was invariably lower than that of paravertebral muscle on T1-weighted images. In addition, marrow signal intensity was apparently diminished, low or intermediate on T2-weighted images.

Conventional spin echo MR images cannot, however, determine the degree of marrow cellularity, since the signal characteristics of fibrosis and of cellular structure, are similar. On STIR imaging, in which the fat marrow signal is suppressed as signal void, T1 and T2 contrast of tissues other than fat are additive; thus, contrast sensitivity is greatly enhanced (9). We initially assumed, therefore, that STIR imaging might be helpful in predicting marrow cellularity in myelofibrosis, since the bone marrow filled with profuse hematopoietic cellular component (hypercellular marrow) might show increased signal intensity on STIR imaging, when compared to the fibrotic component. In the present study, however, marrow cellularity did not correlate well with marrow signal intensity on STIR imaging. In general, marrow cellularity is expressed as the ratio of the volume of hematopoietic cells to the total volume of marrow space (cells plus fat and other stromal elements) (17). In myelofibrosis, since stromal elements such as reticulin, collagen and fibroblast are markedly increased in the marrow cavity, the proportion of hematopoietic cells occupying the marrow cavity is too small to effect signal intensity. Instead, the marrow signal intensity on STIR imaging correlates with the degree of fibrosis. Among the six patients, marrow signal intensity was invariably high on STIR images of the three with mild to moderate myelofibrosis, whereas that of the three with marked fibrosis was low. On the basis of this observation, we suggest that in myelofibrosis, marrow signal intensity on STIR imaging might depend more on the degree of fibrosis than on marrow cellularity.

This study mat have certain limitations. First, the findings of bone marrow biopsy, performed at the posterior iliac crest, may not exactly indicate the general state of the marrows of the thoracolumbar spine, so this may cause interpretational bias in the correlation of marrow signal intensity and degree of fibrosis. In addition, our study population is too small to draw a statistical conclusion, so in order to obtain from the analysis of our results a quantitative assessment of bone marrow disorder, further investigation is needed.

In summary, marrow signal intensity of the thoracolumbar spine in patients with myelofibrosis was characterized as low on T1-weighted imaging, and low to intermediate on T2-weighted imaging. In a proper clinical settings, these characteristic MR findings are helpful in the diagnosis of myelofibrosis. In addition, marrow signal intensity on STIR imaging may correlate with degree of fibrosis.

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골수섬유증의 자기공명영상 소견 : 골수생검 소견과의 비교[1]

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목 적 : 골수섬유증의 자기공명영상 소견의 특징을 기술하고 골수생검소견과 비교하고자 하였다.

대상 및 방법 : 병리조직학적으로 확진된 골수섬유증 환자 6명 (남자 5명, 여자 1명, 평균 연령 46세)을 대상으로 흉요추 T1, T2 강조 및 STIR 시상영상을 2명의 방사선과 의사가 후향적으로 관찰하였다. T1과 T2 강조영상은 근육과 지방을 기준으로, STIR 영상은 근육을 기준으로 신호강도를 분류하고, 이들 자기 공명영상소견과 골수조직소견에서의 섬유화 정도 및 세포 충실도를 비교하였다.

결 과 : 모든 환자에서 흉요추의 골수 신호강도가 T1과 T2 강조영상에서 감소되어, T1 강조영상에서는 모든 환자에서 저신호강도를 보였고, T2 강조영상에서는 저신호강도(2/6) 또는 중간 신호강도(4/6)를 보였다. STIR 영상에서는 다양한 양상을 나타내어, 3명에서는 고신호강도를, 3명에서는 저신호강도를 보였다. 이러한 STIR 영상에서의 신호강도는 골수조직 소견에서의 세포 충실도와 관련이 없었으나, 섬유화 정도와는 연관성을 보여 섬유화 정도가 낮은 환자에서는 STIR 영상에서 고신호강도로, 섬유화 정도가 높은 환자에서는 STIR 영상에서 저신호강도로 관찰되었다.

결 론 : 골수섬유증은 T1 및 T2 강조 자기공명영상에서 신호강도가 감소하는 특징적인 소견을 보였고, STIR 영상에서 신호강도는 골수생검 소견의 섬유화 정도와 관련이 있었다.