Effect of G-CSF Therapy on Central and Peripheral Bone Marrow: Evaluation by MRI and \(^1\)H MRS

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Purpose:

Granulocyte-colony stimulating factor (G-CSF) stimulate the proliferation, differentiation, and survival of hematopoietic progenitor cells [1]. It is used in patients with malignancies receiving myelosuppressive anti-cancer drugs to decrease the incidence of infections or for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukopheresis. In clinical routine the success of the bone marrow stimulation is controlled by complete blood cell counts with differential and platelet counts.

This investigation was undertaken to study the capability of MRI and \(^1\)H MRS to assess the effect of G-CSF therapy directly in the central and peripheral bone marrow. The MRI and MRS data were compared with those of healthy volunteers and those of patients with histologically confirmed malignant bone marrow infiltrations caused by plasmocytoma and metastases.

Patients, Materials and Methods:

MRI and MRS examinations included studies of central (lumbar spine) and peripheral (femoral head, neck, shaft) bone marrow. 13 cancer patients receiving high dose chemotherapy or before stem cell separation were examined before and after G-CSF therapy, another 6 were studied only after bone marrow stimulation (13 male, 6 female, mean age 52 years). Ten patients suffering from histologically verified diffuse plasmocytoma (5 male, 5 female, mean age 58 years) and 10 with bone marrow metastases (4 male, 6 female, mean age 54 years) and 20 healthy volunteers (13 male, 7 female, mean age 36 years) were also examined. The results of MRI and MRS were compared with those of the patients before and after G-CSF treatment.

The MR examinations were performed on a 1.5-T whole body system (Gyroscan ACS II, Philips Medical Systems). MRI and localized \(^1\)H MRS of the selected part of the lumbar spine or the femur were performed using the body coil as transmitter and a circular surface coil of 17 cm diameter as receiver. The imaging protocol consisted of a T1-weighted SE acquisition (TR/TE 500ms/15ms) and an opposed phase gradient echo sequence (TR/TE/a 400ms/6.9ms/70°) in sagittal orientation for lumbar examinations and coronal orientation for femoral examinations with 4mm slice thickness and 0.5mm slice gap. Contrast enhanced studies were not included because of two different examination areas in one examination session. So MRS studies would not be possible in both localizations without repetitive patient positioning. Localized MR spectra from a cubic volume of about 8cm³ (spine) and 5cm³ (femur shaft) respectively were acquired by 90°-180°-180° double spin echo excitation (PRESS) [2]. Transverse relaxation times (T2) were measured by variation of the interval between the first and the second echo in the volume selection scheme. Shortest possible echo delay (TE) was 40ms, and a series of seven SE spectra with TE increasing up to 150ms and with eight signal averages was acquired within 3 minutes. T2 and S0 were determined from a linear regression of ln (S/TE). Because a rather long TR of 3000ms was applied, the calculated S0/S0w is a good approximation for the ratio of the equilibrium magnetizations and thus for the relative fat/water contents of bone marrow. Localized shimming of the volume of interest yielded spectral linewidths of about 0.5 ppm. MRI examinations were evaluated by two experienced readers in consensus. Calculated T2 values and water/fat fractions were compared intrindividually before and after G-CSF treatment and analyzed in comparison with the results of peripheral blood counts. Statistical analysis between the groups of volunteers, and the different patient groups was done using non parametric Kruskal-Wallis \(H\) test and Mann-Whitney U test (SPSS Inc.).

Results:

MR images showed no significantly different diagnostic value between the T1 SE and the op GE sequence. Hypointense lesions in T1 SE corresponded in all cases with focal hyperintensities in op GE. Visually there was no advantage of one sequence over the other. After G-CSF stimulation 6/17 examinations of the lumbar spine and 11/17 of the femoral bone marrow were assessed as pathologic showing focal inhomogenieties in 4 (8) cases and diffuse signal alterations in 2 (3) cases. The images were similar to those of malignant disease especially compared with the „salt and pepper“ pattern of diffuse malignant plasmocytoma.

After successful bone marrow stimulation the spectroscopically measured water content increased in 7/10 G-CSF patients in the lumbar spine and in 6/10 in the femoral region significantly. The mean increase in water content was 34% in the region of the femur shaft and 21% in the lumbar spine. All patients without a peripheral blood count increase (n=3) had a decreased bone marrow water content during the course of therapy. There was no correlation between the amount of the increase in peripheral blood count and bone marrow water/fat fraction.

The mean water content of the lumbar spine vertebra after G-CSF therapy was significantly higher than in healthy volunteers (82% vs. 72%). Cellularity increased to an amount comparable to malignant tumorous bone marrow infiltration (82-86%), especially diffuse multiple myeloma (82%).

In the limited number of patients we studied, T2 values were not of diagnostic or prognostic value. Correlation to clinically successful therapy or spectroscopically measured water/fat fraction of the bone marrow was only poor.

Discussion:

This study demonstrates that the effect of G-CSF on central and peripheral bone marrow can be monitored by MRI and MRS. Imaging and spectroscopic changes consistent with reversion to hematopoietic tissue were observed in initially fatty marrow of the lumbar spine or femur in 7/10 patients treated clinically successful with G-CSF. The changes under therapy are more pronounced peripherally than centrally. In oncologic patients the differential diagnosis between therapeutically induced bone marrow changes and metastatic disease has to be thought of [3]. MRS quantifies the degree of water/fat fraction shift under G-CSF therapy. From our preliminary data it is not possible to decide whether MRS of the bone marrow or peripheral blood counts are a better prognostic factor for G-CSF therapy. The spectroscopic data also demonstrate that the cellularity of the bone marrow of healthy volunteers and patients after G-CSF differ significantly. In contrast, there is a broad overlap between water/fat fractions of the bone marrow in patients after G-CSF therapy and patients with malignant bone marrow infiltration.

References:

