Muskuloskeletal

Late bone marrow changes in Hodgkin’s disease patients: a characterization with proton chemical shift imaging


Abstract. Our aim was to measure, by quantitative chemical shift imaging (CSI), the late therapy-induced changes in bone marrow (BM) of Hodgkin’s disease (HD) patients. Fifteen HD patients treated with radiotherapy alone and radiochemotherapy (age at treatment between 11 and 50 years, post-treatment interval between 15 and 127 months, applied dose 25.5 to 50 Gy), were studied with a 1.5 T MR imager. For the fat-water separation in phase and opposed-phase (SE 1200/22) images were generated according to the Dixon method, with a modified post-processing. Long-term fatty replacement was seen in the irradiated BM only. The radiation fields were visualized as areas of high signal intensity in the T1-weighted images. There was a marked increase of the relative fat-signal fraction in quantitative CSI without time, dose and age-dependent recovery within the investigated ranges.

Fatty replacement of the irradiated BM is a long-term effect in HD patients, probably induced by an obliteration of the microvasculature with consecutive fatty metaplasia.

Key words: Bone marrow – Hodgkin’s disease – Radiotherapy – Quantitative CSI

Introduction

The pattern of red and yellow marrow distribution changes physiologically. With completion of the process of red to yellow marrow conversion, the adult pattern of marrow distribution is achieved. In the human adult, 40% of active bone marrow (BM) is in the pelvis, 25% in the lumbar and thoracic vertebrae, the other red marrow fractions are residing in the skull, proximal humeri and proximal femura [1]. With advancing age the fractional balance of red and yellow marrow changes with an increase in the percentage of fatty marrow.

The myelo-ablative effect of radiotherapy is an often discussed problem in the literature [2–14]. The threshold dose, however, causing irreversible myelo-ablation in fractionated radiotherapy is not clearly defined. Doses between 30 and 45 Gy are stated, a dependence on volume and age is described as well as a time-dependent recovery. According to Rubin et al. [9], for small fields, when less than 10–15% of BM volume is irradiated, permanent ablation is achieved with fractionated doses beyond 30 Gy. For large fields, when between 25–30% of the BM is exposed, permanent ablation occurs at similar dose levels. Subtotal BM irradiation, however, involving 50–75% of the total active BM, allows a regeneration after application of 35–40 Gy.

Most of the results are based on scintigraphic (i.e. functional) investigations using 111InCl, 52Fe, 59Fe and 99mTcS [5, 6, 9, 10].

Magnetic resonance imaging (MRI) is a proven sensitive method for the diagnosis of malignant BM infiltration [15]. By making use of proton chemical shift imaging (CSI) the diagnostic accuracy of MRI can be improved with an increased sensitivity, however, a low specificity. The clinical relevance of CSI becomes obvious in pathological processes effecting a change of the fat and/or water content of the tissue [15].

Therefore we have investigated the radiation-induced changes after fractionated radiotherapy by means of conventional MRI and CSI and the dependence on the age at treatment, the applied dose, the irradiated volume and the post-therapy interval.

Methods

We examined 15 patients with Hodgkin’s disease (HD), all of whom were clinically in complete remission. The age at the time of treatment ranged from 11 to 50 years and the post-therapy interval from 15 to 127 months. All patients received radiotherapy, 13 in combination with multi-agent
Chemotherapy. Radiotherapy was applied with megavoltage equipment (60Co source, 43 MV Betatron Siemens, Erlangen, FRG, 6-MV linear accelerator) using large field techniques. In 11 patients the supra- and infra-diaphragmatic lymph node areas had been irradiated, thus exposing approximately 70% of the active BM to the radiation fields. Four patients received irradiation of the infradiaphragmatic lymph nodes only, involving about 30% of the active BM. The applied doses ranged from 25.5 to 50 Gy with a daily dose of two Gy.

Imaging was performed on a 1.5 T imager (Magnetom, Siemens, Erlangen, FRG) using the body coil. All patients were examined using the same imaging protocol. We studied only the infra-diaphragmatic areas because of the better image quality; the images of the supra-diaphragmatic areas showed movement artefacts of the heart and great vessels. T1-weighted, SE images (TR = 600 ms, TE = 10 ms, 4 acquisitions) were generated in the coronal and sagittal orientations. The field of view (50 cm, matrix size 256 × 256 pixels) extended from the proximal femora to the lumbar part of the spinal column. Thirty contiguous 5-mm slices were obtained using a multi-slice technique. For the fat-water separation, in a selected slice with the best visualization of the BM in phase (SE 1200/22) and opposed phase (SE 1200/22), images were generated according to the Dixon method [16]. The fat-water separation (Fig. 1) was carried out according to a modified Dixon method developed by our group [17].

We first evaluated the T1-weighted images visually. In addition to the visual assessment fat and water signals were analyzed in the irradiated BM areas (L2-5, user-defined regions of interest, mean number of pixels 138). The gluteus muscle tissue and subcutaneous fat tissue served as reference. For widely eliminating the influence of inhomogeneities in the excitation profile, the relative fat signal fraction, F, and the relative water fraction, W, were calculated from the fat signal, SF, and the water signal, SW. To visualize the results of the quantitative evalu-