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ORIGINAL ARTICLE

Incidentally detected diffuse signal alterations of bone marrow on MRI: is bone marrow biopsy indicated?

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ABSTRACT

Background: Advanced imaging techniques as magnetic resonance imaging (MRI) are increasingly performed in the diagnostic workup of patients. Incidentally, diffuse signal alterations of the bone marrow are detected because MRI visualises various components of the bone marrow. The clinical significance of these signal alterations is unknown.
Objective: The main goal of this study was to determine the diagnostic value of a bone marrow biopsy in patients with incidentally found diffuse signal alterations of the bone marrow.
Methods: We retrospectively examined all bone marrow biopsies performed from 1 January 2007 to 31 December 2013 (n = 1947). Patients were included when the biopsy was obtained following an MRI with a diffuse abnormal bone marrow signal. Patients who underwent MRI for suspected malignancy were excluded. Histological and cytological results of the bone marrow examinations were analysed.
Results: 15 of the 1947 bone marrow biopsies (0.77%) were performed because of diffuse signal alterations on MRI. In seven of these 15 bone marrow biopsies (47%) a clinically important haematological disorder was found. Eight patients had a normal bone marrow evaluation.
Conclusion: Based on this retrospective study, a bone marrow examination in patients with incidentally detected diffuse signal alterations should be considered to exclude haematological pathology. Prospective studies have to be performed to further investigate the best diagnostic strategy.

KEYWORDS

Bone marrow reconversion, bone marrow hyperplasia, diagnostic value, hematologic diseases, magnetic resonance imaging

INTRODUCTION

Advanced imaging techniques as magnetic resonance imaging (MRI) are increasingly performed in the diagnostic workup of patients. As a consequence, unintentionally the bone marrow is also visualised on MRI. Bone marrow contains osseous trabeculae and a cellular component. This cellular component consists of haematopoietic cells (red marrow), fat tissue (yellow marrow) and reticulum cells. The difference in composition of yellow and red marrow, the latter containing more water and less fat, explains the appearance of the bone marrow on MRI. Changes in this composition can thus be noticed and might be the first sign of disease.[1-3] Incidental abnormalities in signal intensity of the bone marrow are frequently observed in routine imaging. Several patterns of marrow change are recognised, including marrow depletion, infiltration and replacement. Another important change in distribution is the reconversion from fatty to cellular marrow.[4,5]
Throughout childhood, a physiological conversion from haematopoietic to fatty marrow is seen. This conversion occurs in a predictable pattern ending in the proximal humeral and femoral metaphyses in early adulthood.[6-9] Bone marrow reconversion, when yellow marrow is replaced with active red marrow, also known as haematopoietic hyperplasia, could be noticed in several conditions, such as anaemia and marrow replacement disorders. Smoking, obesity, obstructive sleep apnoea syndrome and endurance sports are also identified as factors that are associated with reconversion.[10-15]
The clinical significance of incidentally detected signal alterations of the bone marrow on MRI is unknown. There are no studies available on the diagnostic value of modern MRI for the detection of haematological diseases and there is a growing need for data to develop guidelines. The main goal of this study was therefore to determine the

diagnostic value of a bone marrow examination in patients with incidentally found diffuse signal alterations on MRI. Furthermore, we aimed to define a diagnostic strategy for patients with these incidental abnormal findings of the bone marrow on MRI.

MATERIAL AND METHODS

We retrospectively identified all patients who underwent a bone marrow examination in Maxima Medical Center Eindhoven/Veldhoven, a large teaching hospital in the south of the Netherlands, from 1 January 2007 to 31 December 2013. The files of all these patients were examined. Patients were included when the bone marrow examination was obtained following an MRI with an abnormal bone marrow signal. All MRIs were performed because of musculoskeletal symptoms. There was no clinical suspicion of a haematological disorder. An abnormal bone marrow signal on MRI was defined by the radiologist and included complete and diffuse reconversion of the yellow bone marrow to haematopoietic (red) bone marrow, haematopoietic hyperplasia, recognised by a diffusely T1-weighted hypointense signal and a hyperintense signal relative to muscle on short inversion time inversion recovery and fat-suppressed T2-weighted images.[16] Patients who underwent MRI for a suspected malignancy and patients with a known haematological disorder or malignancy were excluded. All bone marrow examinations were performed within two months after the MRI. At the same time the following laboratory tests were done: erythrocyte sedimentation rare (ESR), C-reactive protein (CRP), haemoglobin, leucocytes, differentiation and platelets. Histological and cytological results of the bone marrow biopsy were analysed.

RESULTS

Characteristics of the study population

From 1 January 2007 to 31 December 2013, a total of 1947 bone marrow examinations were obtained. In 20 patients the biopsy was performed after detection of an abnormal bone marrow signal on MRI. Five patients were excluded because the indication for the preceding MRI was a suspected malignant disease (*figure 1*). Fifteen patients (0.77%) were included for further analysis (*table 1*). Of these 15 patients, eight were male (53%). The median age was 51.6 years (range 22-76). Thirteen patients were Caucasian (87%). The MRIs performed were of the spine, shoulder, knee and pelvis. In 12 patients (80%) abnormalities in the peripheral blood were seen.

Figure 1. *Flow chart of patient inclusion*

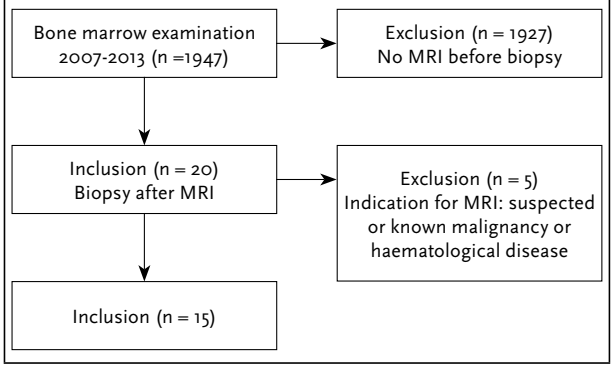

Table 1. *Patient characteristics*

Patient characteristics (n = 15)	
Age – years Median (range)	48 (22 to 76)
Male sex – no. (%)	8 (53)
Caucasian – no. (%)	13 (87)
MRI – no. (%) Spine Shoulder Pelvis Knee	 10 (67) 2 (13) 2 (13) 1 (7)
Abnormal peripheral blood – no. (%)	12 (80)
BMI – kg/m^2 Median (range)	 26.7 (19.6-29.9)
Smoking – no. (%)	4 (26)

Prevalence of haematological disorders

In seven patients (47%) clinically significant haematological disorders were found. One patient was diagnosed with acute myeloid leukaemia (AML), one with myelodysplastic syndrome, one with multiple myeloma, one with monoclonal gammopathy of unknown significance, one with essential thrombocytosis (ET), one with classical Hodgkin's lymphoma and one with congenital spherocytosis. In every case, the diagnostic criteria formulated by the World Health Organisation were met. Eight patients had normal bone marrow histology and cytology. No differences in characteristics were observed between the patients with or without a haematological disorder (*table 2*). In the laboratory tests in patients with no haematological disorder, six patients had a mild leukocytosis, leukopenia, thrombopenia, thrombocytosis, target cells or anaemia. In the patients with a haematological disorder, in six patients a mildly increased ESR and leukopenia (patient with AML), a mild

Table 2. *Patient characteristics, with haematological disorders and with normal bone marrow*

	Haematological disorder	Normal bone marrow
Total patients – no. (%)	7 (47)	8 (53)
Age – years Median (range)	45 (22-67)	52 (31-76)
Male sex – no. (%)	3 (43)	5 (63)
Caucasian – no. (%)	7 (100)	6 (75)
BMI – kg/m² Median (range)	26.5 (19.6-28.9)	27 (22.2-29.9)
Smoking – no. (%)	2 (28)	2 (25)
MRI – no. (%) Spine Shoulder Pelvis Knee	 3 (43) 1 (14) 2 (29) 1 (14)	 7 (87) 1 (13)
Abnormal peripheral blood – no. (%)	6 (86)	6 (75)

thrombocytosis and mildly increased haematocrit (patient with ET), a mild anaemia or a mildly increased CRP (patient with Hodgkin) was found. All abnormalities found in the peripheral blood were mild and not disease specific. Statistical analysis was not performed because of the small patient population.

DISCUSSION

This retrospective study showed haematological disorders in 47% of patients with incidentally detected diffuse signal alterations of bone marrow on MRI. Remarkably, there were no differences in baseline characteristics in the two groups, especially concerning physical examination, peripheral blood results, body weight or smoking, which could have predicted the outcome. The haematological disorders diagnosed are various and clinically relevant, requiring follow-up or medical treatment. The signal alterations of the bone marrow detected on MRI were not characteristic for any specific disease and could not distinguish between the patients with normal bone marrow and with a haematological disorder.

Although we increasingly see patients with incidentally detected diffuse signal alterations of the bone marrow on MRI in clinical practice, no recent studies are available in the literature. In 1989 Deutsch *et al.* reported ten asymptomatic patients who received a routine MRI of the knee that showed diffuse bone marrow abnormalities. Based on peripheral blood results in nine patients and bone marrow biopsy in five with a follow-up period of 4-15 months, it was concluded that the abnormalities seen on MRI were most likely benign.[17] The difference in outcome with our study can be explained in several ways. Firstly, in our study data of the bone marrow were available in all patients, in contrast with the study by Deutsch *et al.*, suggesting that haematological disorders could have been missed. Secondly, in our population more patients had an abnormal blood count, which increases the prior chance of a pathological outcome. However, we did not find any differences in ESR, haemoglobin, leucocytes, differentiation and platelets between patients with and without haematological disorders. Furthermore, the signal alterations detected in the study by Deutsch *et al.* might not be completely comparable with the signal alterations we detected, as the alterations in our patients were seen on other locations than the knee and involved modern MRI technology. Finally, our study design is different, as we started to analyse bone marrow results instead of MRI results. In this way, we were not able to allocate the patients in our hospital who might have had an abnormal signal of the bone marrow on MRI, but were not referred to a haematologist or internist. As a large part of the group had an abnormal blood count, this too might have been decisive for the physician to perform a bone marrow examination. Therefore, a selection bias in our study increases the pre-test probability of finding haematological abnormalities. The real incidence of haematological disorders will be lower than 47%. However, of all 1927 other patients who underwent bone marrow examination in the study period, not a single patient had a previous MRI examination with signal alterations of the bone marrow. To decrease the risk of any selection bias, a prospective study should be performed. The value of MRI is increasingly investigated in patients with haematological disorders. MRI is very sensitive in the staging of lymphoma patients, but it still requires bone marrow biopsy, although positron emission tomography scan might replace bone marrow biopsy for staging in the near future. In early stage myeloma and monoclonal gammopathy of unknown significance, findings on MRI correlate with earlier onset of more aggressive disease, especially using dynamic MRI techniques.[18-21] Early detection of bone marrow abnormalities might be important for determining treatment strategies and improvement of prognosis and outcome.

CONCLUSION

In conclusion, 47% of patients with incidentally detected diffuse signal alterations of bone marrow on MRI were diagnosed with a haematological disorder. Although physical examination and laboratory tests did

not discriminate between patients with and without haematological diseases, a thorough physical examination and blood tests might increase the pre-odds likelihood before a painful bone marrow biopsy is performed. Until data of prospective studies are available, a bone marrow examination in patients with incidentally detected diffuse signal alterations should be considered to exclude haematological pathology.

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DISCLOSURES

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REFERENCES

1. Vande Berg BC, Malghem J, Lecouvet FE, Maldague B. Magnetic resonance imaging of normal bone marrow. Eur Radiol. 1998;8:1327-34.
2. Vande Berg BC, Lecouvet FE, Michaux L, Ferrant A, Maldague B, Malghem J. Magnetic resonance imaging of the bone marrow in hematological malignancies. Eur Radiol. 1998;8:1335-44.
3. Moulopoulos LA, Dimopoulos MA. Magnetic resonance imaging of the bone marrow in hematologic malignancies. Blood. 1997;90:2127-47.
4. Vande Berg BC, Malghem J, Lecouvet FE, Maldague B. Classification and detection of bone marrow lesions with magnetic resonance imaging. Skeletal Radiol. 1998;27:529-45.
5. Ollivier L, Gerber S, Vanel D, Brisse H, Leclere J. Improving the interpretation of bone marrow imaging in cancer patients. Cancer Imaging. 2006;6:194-8.
6. Zawin JK, Jaramillo D. Conversion of bone marrow in the humerus, sternum, and clavicle: changes with age on MR images. Radiology. 1993;188:159-64.
7. Ricci C, Cova M, Kang YS, et al. Normal age-related patterns of cellular and fatty bone marrow distribution in the axial skeleton: MR imaging study. Radiology. 1990;177:83-8.
8. Laor T, Jaramillo D. MR imaging insights into skeletal maturation: what is normal? Radiology. 2009;250:28-38.
9. Shah LM, Hanrahan CJ. MRI of spinal bone marrow: part I, techniques and normal age-related appearances. AJR Am J Roentgenol. 2011;197:1298-308.
10. Altehoefer C, Schmid A, Buchert M, Ghanem NA, Heinrich L, Langer M. Characterization of hematopoietic bone marrow in male professional cyclists by magnetic resonance imaging of the lumbar spine. J Magn Reson Imaging. 2002;16:284-8.
11. Caldemeyer KS, Smith RR, Harris A, et al. Hematopoietic bone marrow hyperplasia: correlation of spinal MR findings, hematologic parameters, and bone mineral density in endurance athletes. Radiology. 1996;198:503-8.
12. Cosentini T, Le Donne R, Mancini D, Aleandri AR, Colavita N. Magnetic resonance imaging evaluation of bone marrow changes in obstructive sleep apnoea syndrome in adults. Radiol Med. 2006;111:572-84.
13. Shellock FG, Morris E, Deutsch AL, Mink JH, Kerr R, Boden SD. Hematopoietic bone marrow hyperplasia: high prevalence on MR images of the knee in asymptomatic marathon runners. AJR Am J Roentgenol. 1992;158:335-8.
14. Vande Berg BC, Lecouvet FE, Galant C, Simoni P, Malghem J. Normal variants of the bone marrow at MR imaging of the spine. Semin Musculoskelet Radiol. 2009;13:87-96.
15. Poulton TB, Murphy WD, Duerk JL, Chapek CC, Feiglin DH. Bone marrow reconversion in adults who are smokers: MR Imaging findings. AJR Am J Roentgenol. 1993;161:1217-21.
16. Hanrahan CJ, Shah LM. MRI of spinal bone marrow: part 2, T1-weighted imaging-based differential diagnosis. AJR Am J Roentgenol. 2011;197:1309-21.
17. Deutsch AL, Mink JH, Rosenfelt FP, Waxman AD. Incidental detection of hematopoietic hyperplasia on routine knee MR imaging. AJR Am J Roentgenol. 1989;152:333-6.
18. Dutoit JC, Vanderkerken MA, Verstraete KL. Value of whole body MRI and dynamic contrast enhanced MRI in the diagnosis, follow-up and evaluation of disease activity and extent in multiple myeloma. Eur J Radiol. 2013;82:1444-52.
19. Kwee TC, Kwee RM, Nievelstein RA. Imaging in staging of malignant lymphoma: a systematic review. Blood. 2008;111:504-16.
20. Kwee TC, Kwee RM, Verdonck LF, Bierings MB, Nievelstein RA. Magnetic resonance imaging for the detection of bone marrow involvement in malignant lymphoma. Br J Haematol. 2008;141:60-8.
21. Alyas F, Saifuddin A, Connell D. MR imaging evaluation of the bone marrow and marrow infiltrative disorders of the lumbar spine. Magn Reson Imaging Clin N Am. 2007;15:199-219, vi.