Comparison of magnetic resonance imaging and ^{99m}Technetium-labelled methylene diphosphonate bone scintigraphy in the initial assessment of chronic non-bacterial osteomyelitis of childhood and adolescents

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Abstract

Objectives

To compare sensitivity of bone scintigraphy using ^{99m}Technetium-labelled methylene diphosphonate (Tc-99m MDP) and magnetic resonance imaging (MRI) in the detection of inflammatory bone lesions in patients with chronic non-bacterial osteomyelitis (CNO).

Methods

Tc-99m MDP bone scintigraphy and MRI were performed in 32 CNO patients at the time of diagnosis and compared regarding their sensitivity in detecting inflammatory lesions in symptomatic regions of the body.

Results

Inflammatory lesions could be detected in 40 out of the 54 (74.1%) symptomatic regions by bone scintigraphy and in 53 (98.1%) of these regions by MRI ($p<0.001$). Sensitivity of MRI compared to bone scintigraphy was superior in detecting lesions in the long bones of the thigh and the lower legs (100% vs. 78.4%, respectively, $p<0.05$).

Conclusion

Bone scintigraphy does not seem to display the whole extent of the inflammatory process in CNO. Therefore, depending on clinical relevance, MRI rather than planar bone scintigraphy should be considered for the detection of CNO lesions at diagnosis.

Key words

chronic non-bacterial osteomyelitis, Tc-99m-MDP bone scintigraphy, MRI imaging

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Introduction

Chronic non-bacterial osteomyelitis (CNO) is an inflammatory, non-infectious disorder of the skeletal system with unknown etiology, mainly affecting the metaphyseal regions of long bones in children and adolescents (1-3). Histological and microbiological analyses indicate a chronic inflammation with infiltration of lymphocytes and monocytes and absence of detectable microbial components (4). The extent of CNO may range from a single non-recurrent lesion to the most severe form of CNO, chronic recurrent multifocal osteomyelitis (CRMO), affecting multiple, often symmetric sites of the skeletal system with an undulating time course (2, 5).

Radiological methods covering the whole body are important tools in estimating the extent of inflammatory bone lesions in CNO (6-9). Whole body bone scintigraphy using Tc-99m MDP provides a complete overview of skeletal changes due to inflammatory processes (10). Radiotracer uptake depends on increased bone metabolism, especially due to increased calcium turnover. Detection of inflammation by MRI depends on the presence of bone oedema, increased vascular permeability or increased perfusion. Due to progresses in MRI technology whole body MRI (WB-MRI) might be an alternative approach to bone scintigraphy in the initial work up of CNO, as it also may allow analysing the total lesion load (11).

We compared the sensitivity of Tc-99m MDP bone scintigraphy with MRI in the detection of inflammatory bone lesions in CNO patients at the time of diagnosis.

Patients and methods

A total number of 32 patients (20 female), who had been diagnosed with CNO at the Children's hospital, University of Würzburg, within 5 years, were included in the study. The mean age at diagnosis was 10.9 years (range 2.1–16.6). The mean time between onset of symptoms and diagnosis was 4.5 months (range 0–25 months). CNO in these patients has been suspected due to skeletal pain, which led to radiological work-up. The local ethics committee approved the study. Written consent of the patients and/or parents was obtained.

All patients were clinically assessed using a standardised protocol addressing pain, local swelling or limited motion (12). The body was separated into distinct regions (cranium, clavicle, rib/sternum, arms, vertebral column, pelvis, thigh, lower leg and foot) and symptomatic regions were defined by the appearance of local pain and/or swelling. Symmetrically appearing regions were defined as those presenting with symptoms at the same anatomic site of both half of the body. A diagnostic biopsy including histological and microbial work-up was performed in all patients to exclude malignancy or infection.

MRI as well as Tc-99m MDP bone scintigraphy was perfomed in all patients within 30 days and before biopsy had been performed. Independent physicians blinded to detailed clinical information analysed MRI and bone scintigraphy. None of the patients were on anti-inflammatory/immunosuppressive drugs at the time of imaging.

Bone scintigraphy was performed as a two-phase study (blood-pool and skeletal-phase) with ^{99m}Tc-labelled methylene diphosphonate adapted to bodyweight according to the pediatric dosage card of the European Association of Nuclear Medicine. Early static phase representing the blood-pool phase was acquired 5 minutes and skeletal accumulation phase 120 minutes after injection of the radiolabeled tracer using a large field-of-view dual-detector camera (E.CAM, Siemens). Planar images were performed as whole body acquisition and static images of selected body regions.

Whole body MRI was performed on a 1.5 Tesla scanner (Magnetom Symphony, Siemens). MRI protocol included non-enhanced TSE T1w (TR 690ms, TE 12ms), post-contrast (Gd-DTPA, Magnevist®, Bayer Schering Pharma, 0.2ml/kg body weight) fat saturated TSE T1w and TIRM T2w (TI 120ms, TR 5590ms, TE 75ms) sequences with section thickness of 4mm.

MRI was performed without using sedation in two separate sessions (upper and lower body). The length of time required for each session was 45 minutes in average.

Inflammatory lesions were defined by an increased T2-TIRM signal, a reduced

Table I. Distribution of symptomatic regions.

Symptomatic regions	n. of regions (%)
Visceral cranium	1 (1.8)
Rib/sternum	1 (1.8)
Clavicle	4 (7.4)
Vertebral column	5 (9.3)
Arm	1 (1.8)
Pelvis	15 (27.8)
Thigh	14 (25.9)
Lower leg	5 (9.3)
Foot	8 (14.8)
All	54 (100)

The distribution of symptomatic body regions of 32 patients with CNO is shown.

T-1 signal and a post-contrast lesional signal elevation. In 14 patients, imaging was performed as WB-MRI. In the other 18 patients, MRI analysis has been focused on the symptomatic regions of the body.

Statistical analysis

Categorical variables were compared using chi-square test. *P*-values <0.05 were regarded as statistically significant.

Results

A total of 54 symptomatic regions could be detected in the 32 patients (mean 1.7 per patient, range 1–8), (Table I). Bone scintigraphy indicated at least one lesion in 30 out of 32 patients (93.8%). MRI indicated one or more inflammatory lesions in each of the 32 analysed patients ($p>0.05$). To compare the sensitivity of both imaging techniques, we analysed whether one or more lesions could be detected in the symptomatic regions. Indicators of inflammation could be detected in 40 out of the 54 (74.1%) symptomatic regions by bone scintigraphy and in 53 (98.1%) of these regions by MRI ($p<0.01$). Regarding the localisation of the symptomatic regions, sensitivity of MRI compared to bone scintigraphy was superior in detecting lesions in the long bones of the thigh and the lower legs (Table II). Next, we addressed the question, whether symmetrical appearance of lesions might influence the sensitivity of the imaging techniques. Twenty-four out of the 54 (44.4%) symptomatic regions showed symmetrical appearance. Whereas MRI could detect inflammation in all of these regions, bone scintigraphy detected inflammation in only 17 of these regions (70.8%, $p<0.01$).

MRI could absolutely define 98 different inflammatory lesions. Fifty-two of these lesions (53.1%) could also be detected by bone scintigraphy. We did not identify any lesion that could be found by bone scintigraphy but not by MRI. Inflammatory lesions could also be detected in asymptomatic regions (16 out of 98 lesions, 16.3%). However, the proportion of scintigraphically positive lesions did not differ between asymptomatic (6 out of 16 lesions, 37.5%) and symptomatic MRI lesions (46 out of 82 lesions, 56.1%, $p>0.05$).

Discussion

Radiological imaging techniques covering the whole body and implying high sensitivity for detection of inflammatory skeletal lesions are an indispensable tool in the diagnostic approach of patients suspected with CNO (2, 6-11, 13).

In this study, we compared the sensitivity of planar Tc-99m MDP bone scintigraphy with MRI. Both techniques have been described as a diagnostic tool in CNO in several case reports and small case series (2, 6-11, 13). Although the sensitivity of bone scintigraphy and MRI in detecting malignant bone lesions has been analysed recently (with bone scintigraphy being inferior) (14), a comparative analysis of both imaging procedures in the detection of inflammatory lesions (like in CNO) is missing.

Multifocal involvement of disease can be detected by both imaging techniques. However, inferiority of spatial resolution by planar scintigraphy might indicate fewer inflammatory lesions *per se*. To circumvent this bias, we analysed if the respective imaging procedures could detect signs of bone inflammation in a distinct symptomatic body region. We assumed that clinical symptoms in a biopsy proven CNO patient regard a gold standard for active inflammatory bone lesions.

MRI and bone scintigraphy did not differ in the sensitivity of detecting any number of lesions (one or more) in a patient diagnosed with CNO. However, we could show that the sensitivity of MRI in determining the extent of inflammatory lesions in symptomatic regions of patients with CNO is superior compared to bone scintigraphy. This was most evident for symmetrically appearing lesions of the long bones, *e.g.* in the thigh and lower leg. Since the inflammatory process in CNO is often affecting the metaphyseal regions of the long bones and often has a symmetrical appearance, differentiation between physiological radiotracer uptake of the growth plate and increased uptake of inflammatory lesions at these sites seems to be difficult (Fig. 1). In addition to that, inflammatory reactions of adjacent tissues (periostitis, synovitis, myositis) can often be detected by MRI in CNO patients (7, and own unpublished observations) but cannot be differentiated from osteomyelitis by bone scintigraphy. The MRI protocol in our study included non-enhanced as well as post-contrast sequences. However, all

Table II. Sensitivity of MRI and Tc-99m MDP bone scintigraphy according to the localisation of the symptomatic regions.

Localisation of symptomatic regions	MRI		Scintigraphy		*p*-value
Clavicle	4/4	100%	4/4	100%	n.s.
Vertebral column	5/5	100%	2/5	40%	n.s.
Arm	1/1	100%	1/1	100%	n.a.
Pelvis	14/15	93.3%	12/15	80.0%	n.s.
Thigh/lower leg	19/19	100%	13/19	68.4%	<0.05
Foot	8/8	100%	6/8	75.0%	n.s.
Visceral cranium	1/1	100%	1/1	100%	n.a.
Rib/sternum	1/1	100%	1/1	100%	n.a.

The number of symptomatic regions indicating signs of bone inflammation by MRI or by Tc-99m MDP bone scintigraphy was compared according to their localisation (n.s.: not significant; n.a.: not applicable).

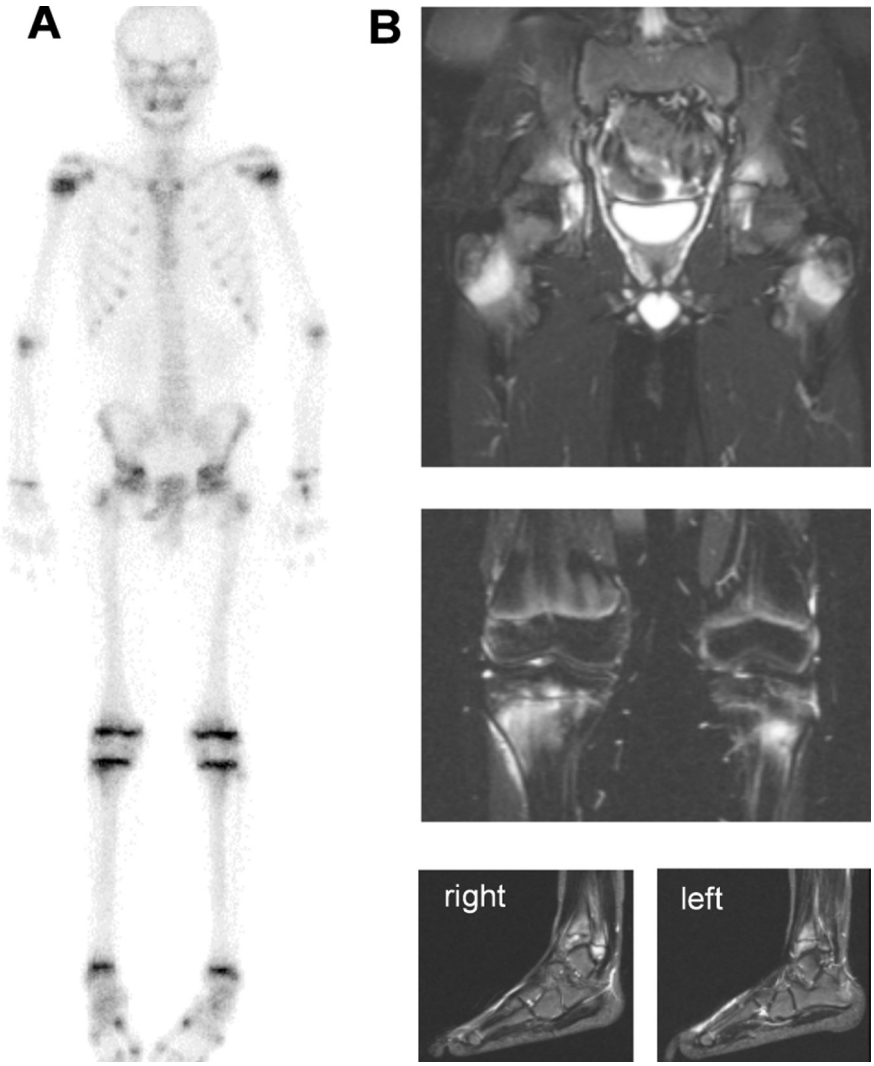

Fig. 1. ^{99m}Technetium-labelled methylene diphosphonate (Tc-99m MDP, A) and TIRM sequences of magnetic resonance imaging (MRI, B) in an 11-year old boy with biopsy proven chronic non-bacterial osteomyelitis (CNO). Bone scintigraphy shows physiological tracer uptake in the metaphyseal regions of the pelvis, proximal and distal femur as well as proximal and distal tibia. MRI shows a symmetrical increased T2-TIRM signal in both sides of the pelvis, proximal and distal femur as well as in the proximal and distal tibia indicative for inflammatory lesion.

inflammatory lesions detected by post-contrast T1 sequences could also be detected by TIRM sequences. Therefore, the use of contrast agents seems to be helpful in the initial assessment of ambiguous bone lesions. However, non-enhanced sequences may be sufficient for follow-up imaging in CNO patients.

Although MRI seems to be more sensitive in the detection of inflammatory lesions in CNO, the question of specificity still remains controversial. Not all the lesions in patients with multifocal disease pattern have been histologically analysed. Additionally, the phenomenon of asymptomatic lesions seems to be a common feature in CNO. Therefore, some controversy about the diagnostic specificity and also clinical relevance of the MRI positive but scintigraphically silent lesions still remains. However, symptomatic as well as asymptomatic lesions were detectable with equal sensitivity by bone scintigraphy, challenging the hypothesis of unspecific MRI findings in asymptomatic regions.

Differences in sensitivity might be explained by imaging of different tissue reactions by the particular imaging technique. Whereas bone scintigraphy indicates changes in bone metabolism (*e.g.* osteoclast/-blast activity, calcium turnover), MRI rather displays interstitial fluid accumulation (oedema) or increased perfusion / vascularisation. Since histological analysis of CNO lesions might show different inflammatory reactions (oedema, cellular infiltrate, sclerosis), each imaging procedure might have advantages in detecting a distinct stage of this inflammatory process. Given that oedema is an early sign of bone inflammation and bone resorption/remodelling might appear in later stages of disease, it is tempting to speculate if bone scintigrapy might yield higher specificity in predicting osteolytic outcome of inflammatory lesions. Further improvement of the sensitivity of bone scintigraphy might be achieved by tomographic instead of planar imaging, *e.g.* by using single photon emission computed tomography (SPECT) or SPECT/CT.

In summary, bone scintigraphy is less sensitive in the detection of the extent of inflammatory lesions in patients diagnosed with CNO, especially in symmetrical lesions of the metaphysis. Thus, depending on clinical relevance, MRI rather than planar bone scintigraphy should be considered for the detection of all CNO lesions at diagnosis.

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