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Influence of Chronic Recurrent Multifocal Osteomyelitis (CRMO) On Densitometry Measurements Obtained by Dual X-Ray Absorptiometry

Danny L Costantini[1,3*], Reza Vali[1,3], Eman Marie[1,3], Mandy Kohli[1], Holly Convery[2], Martin Charron[5], Amer Shammas[1,3] and Ronald M Laxer[2,4]

[1]Department of Medical Imaging, The Hospital for Sick Children, Toronto, Canada
[2]Division of Rheumatology, Hospital for Sick Children, Toronto, Canada
[3]Department of Medical Imaging, University of Toronto, Toronto, Canada
[4]Department of Pediatrics, University of Toronto, Toronto, Canada
[5]Brampton Nuclear Services, Brampton, Canada

Abstract

The incidence of detecting focal chronic recurrent multifocal osteomyelitis (CRMO) lesions on dual-energy x-ray absorptiometry (DXA), and the effect of these lesions on DXA bone mineral density (BMD), bone mineral content (BMC), and their associated Z-scores were retrospectively reviewed. Materials and Methods. The study included 22 patients (14 females, 8 males; median age of 13 years) with CRMO and in whom a total body less head (TBLH) and lumbar spine DXA scan had been obtained. Whole-body bone scintigraphy and MRI were used as the reference standards. Sites involved with CRMO were subsequently detected and DXA measurements were re-measured after removing the sclerotic lesions from the analysis. Results. In total, sclerotic CRMO lesions were detected in 15 of the 22 patients (68%) by DXA, although the number of lesions detected (on a per-lesion analysis) was much less (i.e. 29 of 129 lesions; 19.4%) when compared to MRI and/or bone scintigraphy. Larger lesions had a greater impact on the derived BMD/BMC measurements, and changed the diagnosis in one patient from having normal to abnormal DXA results based on the final Z-score. Discussion. CRMO lesions detected on DXA examinations should be regarded as a potential source of error. Careful inspection and re-quantification of the BMD, BMC and associated Z-score after applying an appropriate correction should be considered in patients with large CRMO lesions identified on DXA examinations.

Introduction

Chronic recurrent multifocal osteomyelitis (CRMO) is a non-infectious auto-inflammatory bone disease of unknown etiology [1]. CRMO typically affects the metaphysis of long bones and spine in children and young adolescents [1]. Radiographically, early CRMO lesions show osteolysis, whereas later stages of the disease may present as hyperostosis and sclerosis [2]. Treatment options include non-steroidal anti-inflammatory agents (NSAIDs), corticosteroids, methotrexate, bisphosphonates as well as anti-TNF therapies [1]. The overall goals of treatment are to slow disease progression and achieve good symptom control while maintaining normal bone growth and range of motion.

Dual-energy X-ray absorptiometry (DXA) is used in CRMO to assess bone mineral density (BMD) and bone mineral content (BMC), particularly in patients undergoing bisphosphonate treatment [3]. In children, total body less head (TBLH) and spine are the recommended DXA sites for bone health assessment [4]. Careful evaluation of the DXA scan image and BMD/BMC data are essential in formulating accurate DXA scan interpretations. Numerous factors can cause spurious bone mineral results, including the presence of focal sclerotic or lytic lesions, degenerative disease, fractures, or artifacts external to the patient [5]. In this retrospective study, we sought to determine the incidence of detecting focal CRMO lesions on DXA examinations in patients diagnosed with the condition, and the effect of these lesions on densitometry measurements.

Subjects and Methods

This retrospective study was approved by our institution's research ethics board (REB no. 1000036874). Patients diagnosed with CRMO who underwent DXA in our department between January 2009 to July 2013 were included (22 patients total). The TBLH and lumbar spine DXA images and densitometry measurements were retrospectively reviewed. The number of osteolytic/sclerotic lesions and the location were independently recorded by two nuclear medicine physicians who were blind to the number and location of bone lesions on MRI/bone scan, but were aware of the diagnosis of CRMO. A consensus was achieved in another session in case of a discrepancy. Findings were correlated with MRI or bone scan which served as the standard of reference when performed within 3 months of the DXA.

All BMD and BMC measurements were made with a General Electric Lunar Prodigy bone densitometer. Each child was scanned twice; once with a total-body scan requiring 3-5 minutes, and then with a dedicated lumbar spine scan (to include L1-L4) similarly requiring 30 seconds to 1 minute [6]. Results were determined as BMD (g/cm^2) and BMC (g) values and age and sex matched Z-score. The height-for-age Z-score-adjusted BMD/BMC Z-scores was not calculated as none of these patients had a short status or a delayed bone age [7].

Sites involved with CRMO were subsequently detected and the BMD/BMC Z-scores were re-measured after removing the sclerotic lesions as an artifact. This was done based on recalculation of the involved limb density (the area with a sclerotic lesion) based on the contralateral limb or just removing the sclerotic lesion as an artifact

Corresponding author: Danny L Costantini, The Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X8, Canada, Tel: 4168136066; Fax: 4168137591; E-mail: dan.costantini@utoronto.ca

Figure 1: A. Total body less head (TBLH) bone mineral density (BMD) and bone mineral content (BMC) Z-scores obtained in a 13-year old female (patient 16) with history of right knee pain and diagnosis of CRMO showing a large sclerotic lesion in the right distal femur. B. MRI T2 STIR sequence of both knees demonstrates patchy area with high signal intensity at the distal meta-diaphysis of the right femur associated with marked periosteal reaction, cortical thickening and bone expansion as well as scalloping along the distal meta-diaphysis. The calculated TBLH BMC Z-score decreased from -1.1 to -2.3, and changed the diagnosis of this patient to 'below expected range for age'.
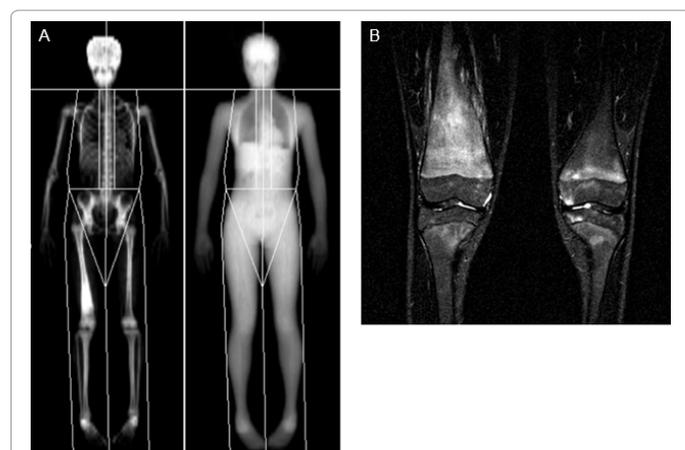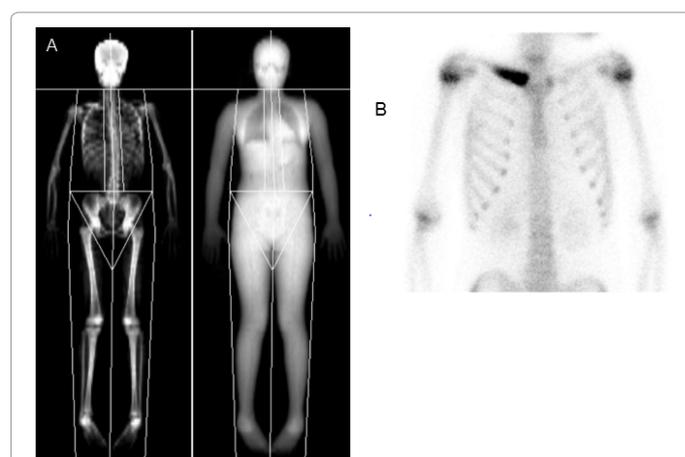

Figure 2: A. Total body less head (TBLH) bone mineral density (BMD) and bone mineral content (BMC) Z-scores obtained in a 9-year old female (patient 22) with right clavicular CRMO involvement. B. Bone scan shows a focal linear increased uptake in the right clavicle. The BMD/BMC and associated Z-score did not change significantly after correction.

in case of a lesion in the spine or clavicle, using the standard software available with DXA scanner. Lumbar spine and TBLH BMD and BMC values were considered clinically significant when a change in the diagnosis was observed. The diagnostic categories "within expected range for age" (i.e. lumbar spine or TBLH BMD/BMC Z-score greater than -2.0) or "below expected range for age" (i.e. lumbar spine or TBLH BMD/BMC Z-score equal or below -2.0) were used according to standard practice guidelines [8] (Figures 1 and 2).

Results

In total, 28 patients with CRMO underwent DXA; 6 were excluded as a TBLH had not been performed. Of the 22 patients who were included (14 females, 8 males; median age of 13 years), 15 (68%) had at least one CRMO-related bone lesion on DXA manifesting as a well-circumscribed area of focally increased density. On a per-lesion basis,

129 CRMO-related skeletal lesions were detected on MRI and/or bone scan and only 25 (19.4%) of these lesions were detected on DXA. Most of the lesions were identified in the distal femoral metadiaphysis [9,10], while other lesions were identified in the proximal tibia [6], lumbar vertebral bodies [3], clavicle [4], and mid/hind foot bones [2].

Overall, no significant change in the average derived Z-scores was observed after removing the CRMO lesion from the analysis of BMD and BMC (BMD Z-score; -0.607 versus -0.593, and BMC Z-score -0.292 versus-0.386, before and after applying the correction, respectively). On a per patient basis, an absolute change in the TBLH BMD/BMC Z-score of ≤ 0.5 or > 0.5-1.0 was observed in 9 and 5 patients, respectively, whereas 1 patient had a Z-score change of ≥ 1.0 after applying the correction (Table 1). In one of these patients (patient 16), the Z-score decreased from -1.1 to -2.3, and changed the diagnosis of this patient to 'below expected range for age' (according to standard clinical practice guidelines [8]). In the remaining patients, no CRMO lesion was detected by DXA and as such a corrected Z-score could not be calculated.

Discussion

The lumbar spine and TBLH are generally considered to be the most accurate and reproducible skeletal sites for measuring BMD and BMC in children and adolescents [4]. For the lumbar spine, the L1-L4 region is used unless focal artifacts or structural changes (e.g. fracture or end plate sclerosis) require exclusion of individual vertebra. In such cases, one vertebral body can be removed from the analysis, and the BMD/BMC measurements are still considered reliable [9]. No similar consensus exists for the TBLH as to what should be excluded when artifacts are present [4,8]. As such, our method of analysis may be limited as it is not known what effect removing CRMO lesions from the TBLH has on the accuracy of the obtained BMD/BMC and associated Z-score. Moreover, our technique of correcting for the CRMO lesion was limited based on the available software. Exclusion of the bony site involved with CRMO changed the obtained TBLH BMD/BMC values and associated Z-score >0.5-1.0 in 23% (5/22) of the patients studied. Larger lesions had a greater impact on the derived measurements, and changed the diagnosis in one patient from having normal to abnormal DXA results based on the final Z-score. To our knowledge this is the first report to identify CRMO lesions as potential sources of error in the interpretation of DXA examinations. Careful visual inspection of images and re-quantification of the densitometry measurements after removal of sites involved with CRMO should therefore be considered, particularly in situations where a change in the diagnostic classification may occur.

CRMO is a challenging diagnosis to make because of its complex presentation and varying appearance on imaging. The differential diagnosis is extensive and its final diagnosis requires ruling out other possibilities including infection, inflammation and neoplastic etiologies. Whole-body bone scintigraphy and MRI are generally complementary in the evaluation of CRMO by demonstrating the extent of the skeleton involved [2]. Moreover, whereas bone scintigraphy has the advantage over MRI in detecting cortical-based osseous lesions, MRI is more advantageous in demonstrating marrow infiltration/edema. DXA similarly has the advantage of providing a whole-body skeletal assessment with very low radiation dose (0.2 μSv to 0.4 μSv) that is orders of magnitude less compared to pediatric bone scintigraphy (3500 μSv) and plain film analysis (1 μSv to 5 μSv per film exposure) [3,10,11]. Although the lower sensitivity of DXA precludes its use in the initial imaging assessment of CRMO, baseline and sequential follow up DXA examinations not only provides an assessment of bone

Patient no.	Age, gender	Lesions detected		Location	BMD Z-SCORE		BMC Z-SCORE	
		MRI/BS	DXA		Before	After	Before	After
1	13, F	6	2	L4	-1.4	-1.4	-1.5	-1.5
				distal femur				
2	6, F	4	2	L1	-0.1	-0.1	N/A	N/A
				distal femur				
3	14, F	12	none	-	-	-	-	-
4	8, F	2	1	distal femur	1.2	1.1	1.2	1.0
5	10, F	14	3	distal femur	-0.7	-0.6	-0.8	-0.7
				left tibia				
				right foot				
6	9, F	4	1	right proximal tibia	0.1	0.1	0.5	0.5
7	11, M	1	1	right distal femur	0.2	0.2	0.4	0.3
8	15, F	1	none	-	-	-	-	-
9	14, M	3	2	right distal femur	0.2	0.2	0.4	0.3
				left proximal tibia				
10	15, M	7	3	right distal femur	-1.5	-1.6	-1.4	-1.3
				right distal femur				
				left tibia				
11	17, F	8	1	left clavicle	0.3	0.3	0.9	0.9
12	15, M	2	none	-	-	-	-	-
13	6, M	5	none	-	-	-	-	-
14	13, F	6	none	-	-	-	-	-
15	13, F	10	2	left clavicle	-1.5	-1.4	0	0
				left tibia				
16	13, F	12	2	right femur	-1.5	-1.7	-1.1	-2.3[†]
				right tibia				
17	10, M	8	none	-	-	-	-	-
18	17, M	2	1	right femur	0	0	0.9	0.9
19	10, F	10	2	left clavicle	-1.6	-1.4	-0.8	-0.7
				left foot				
20	6, F	1	1	L3	-2.1	-2.1	-2.3	-2.3
21	13, M	9	none	-	-	-	-	-
22	12, F	2	1	right clavicle	-0.7	-0.8	-0.3	-0.4

Table 1: Patient demographics and DXA derived BMD/BMC Z-scores. Bone mineral density (BMD) and bone mineral content (BMC) Z-scores obtained from the total body less head (TBLH) before and after removing the CRMO lesion from the analysis. In patient 20, the Z-score was obtained from the lumbar spine. MRI/BS – Magnetic resonance imaging / bone scintigraphy. [†] Removing the CRMO lesion resulted in a new diagnosis of 'below expected range for age'.

density, but may also help to provide pathophysiological information by assessing the pattern of osteolytic/sclerotic change that may occur in these lesions over time throughout the course of treatment. Scanning only specific skeletal sites with suspected CRMO involvement rather than obtaining a TBLH may also help to improve the detection rate of lesions by DXA. A prospective study to further evaluate the sensitivity of focused DXA scanning and its potential role in assessing treatment response in CRMO is planned.

DXA may be particularly useful in children with chronic systemic disease requiring long-term systemic steroid treatment and frequent DXA evaluation, for example in children with inflammatory bowel disease in which an association with CRMO has been described [12,13]. The incidental finding of a focal sclerotic bone lesion on DXA, for example, may prompt the suggestion of CRMO as a potential differential diagnosis in the appropriate clinical context. DXA in children with CRMO undergoing cyclical bisphosphonate treatment may also have the added benefit of identifying dense metaphyseal bands which are typically associated with prolonged bisphosphonate treatment and correspond to alternating areas of increased and normal bone mineralization. Since dense metaphyseal bands have been implicated in increasing fracture risk by creating mechanical stress-rises [13], their visualization on a DXA scan in a patient with CRMO may prompt a change in the type (or duration) of therapy.

In summary, our results demonstrate that focal sclerotic CRMO lesions can be detected on DXA scans and can potentially falsely elevate BMD/BMC, particularly in patients with large lesions. As such, careful inspection of DEXA images and re-quantification of the BMD/BMC after applying an appropriate correction should be considered. Further prospective studies are needed in order to evaluate the role of DXA in assessing bone health in response to treatment in patients with CRMO.

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