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Commentary

Commentary on: radiological diagnosis of chronic recurrent multifocal osteomyelitis using whole-body MRI-based lesion distribution patterns

L.-S. Ording Müller [a,*], P. Humphries [b]

[a] *Division of Radiology and Nuclear Medicine, Department of Paediatric Radiology, Oslo University Hospital, Rikshospitalet, Oslo, Norway*

[b] *Department of Radiology, Great Ormond Street Hospital, London, UK*

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At present, interpretation of the findings on whole-body magnetic resonance imaging (WBMRI) in children is by large based on the individual radiologist's personal experience and opinion, causing diverging research results and practice. The study by Andronikou *et al.*, in this edition of *Clinical Radiology* is welcome as it describes two distinct patterns of bone marrow signal change in children with chronic recurrent multifocal osteomyelitis (CRMO)/chronic non-bacterial osteomyelitis (CNO); namely tibial/appendicular involvement and clavicular/spinal involvement.[1] Recognising these patterns of distribution may be useful in guiding the interpreting radiologist towards a diagnosis of CRMO/CNO, rather than alternative diagnoses such as neoplasia or bacterial infection. There are, however, some caveats that should be born in mind.

The technique is already embraced for clinical use in children by many centres, although to date, there is no evidence of the method's precision, accuracy and clinical validity.[2–5] WBMRI is a relatively new assessment tool for multifocal skeletal pathology. WBMRI enables depiction and characterisation of diseases at an early, and sometimes pre-clinical stage, without the use of ionising radiation. Skeletal involvement is seen in numerous diseases in childhood and multifocal skeletal manifestations are more frequently encountered in children compared to adults. Children relatively lack the ability to express and localise symptoms in the skeleton, and in addition, the skeleton is difficult to examine clinically. Diagnosing skeletal disease in children is therefore challenging. WBMRI is regarded as a promising tool for depiction of multifocal skeletal pathology in children having a high sensitivity to skeletal involvement of disease.

One of the target groups for WBMRI is CRMO/CNO.[6] CRMO/CNO is an auto-inflammatory bone disease of unknown origin, primarily affecting children and adolescents. Some lesions may be asymptomatic. Uncontrolled CRMO/CNO is associated with premature fusion of the growth plates, growth disturbances, and pathological fractures; hence, the findings of additional clinically silent lesions in the skeleton will direct the clinical decision-making and several studies suggest that WBMRI is more sensitive than

* Guarantor and correspondent: L.-S. Ording Müller, Division of Radiology and Nuclear Medicine, Department of Paediatric Radiology, Oslo University Hospital, Rikshospitalet, Oslo, Norway. Tel.: +47 92828097.
E-mail address: lilsofie.ording@googlemail.com (L.-S. Ording Müller).

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other methods in detecting both symptomatic and asymptomatic bony lesions in patients with CRMO/CNO.[6,7]

When considering the growing skeleton, using definitions derived from research in adults may lead to erroneous interpretations and misdiagnosis. This has been demonstrated in several recent studies, e.g., in juvenile idiopathic arthritis (JIA)[8–14] and highlight one of the most important mantras in paediatric medicine; that definitions derived from research in adults cannot automatically be used in children. This knowledge has changed the existing clinical practice, and fuelled demands for further research.

Although recognition of patterns of marrow change distribution on WBMRI in CRMO/CNO is welcome and helpful to suggest the diagnosis, there are challenges that need to be met. Currently, there is no consensus between centres regarding protocols for WBMRI, leading to divergent approaches and limiting comparison between centres.[4] This exacerbates a major shortcoming in the investigation of paediatric disease, namely accruing significant numbers of patients for studies to be meaningful on a population level. Greater collaboration between paediatric centres is needed to homogenise WBMRI protocols in meaningful way.

The other major challenge is defining thresholds for normality versus pathology in children. During childhood, cellular red bone marrow is replaced by fatty marrow, and the remaining red marrow undergoes maturation changes. In addition, there is an evolving ossification process, turning the cartilaginous growth zone into bone. Moreover, the skeleton in children is softer and more hypervascular than in adults.[15] Pathological signal on MRI is caused by the high water content in highly cellular- or hyper-vascular tissue, such as inflammation or tumours. This signal is non-specific and simply represents increased proton density as compared to the surrounding tissue. Therefore, normal maturation processes may influence the MRI signal in a similar way to pathology. For obvious reasons, biopsy cannot be performed of all the lesions; therefore, the rate of false-positive findings on WBMRI in children is unknown.

There remains a significant gap in our knowledge regarding the variation in MRI signal changes on WBMRI during normal skeletal maturation. To this end, further study is needed in healthy childhood cohorts to differentiate normal maturation/variation from pathology in addition to examining signal change patterns in cohorts of patients with known diagnoses, as described by Andronikou *et al.*, which aid recognition of disease entities.

Conflicts of interest

The authors declare no conflict of interest.

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