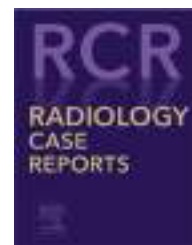


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Case Report

Evolution of chronic recurrent multifocal osteomyelitis in a child shown by MRI

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ABSTRACT

Chronic recurrent multifocal osteomyelitis (CRMO) is a rare idiopathic inflammatory disease that mainly affects children and young adults. The clinical signs and symptoms are nonspecific, hindering and delaying the proper diagnosis.

We report a case of CRMO in a child with chronic pain in the cervical and thoracic spine. Investigations of the pain revealed a diagnosis of osteomyelitis in the biopsy, indicating a course of antibiotic treatment. After a year, there was progressive worsening of the pain, and it soon spread to the left wrist and right ankle. Magnetic resonance imaging of the left wrist and right ankle revealed morphostructural changes. A new biopsy was performed on the wrist and ankle, and osteomyelitis was pinpointed again.

In view of the clinical, radiological, and histopathological findings, the patient was diagnosed with CRMO. The following treatment consisted of nonsteroidal anti-inflammatory drugs, methotrexate, and pamidronate.

The strength of this case is the fact that there was extensive imaging and more than one biopsy, and the patient was followed. Magnetic resonance imaging was valuable in assessing the extent and activity of a lesion.

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Introduction

Chronic recurrent multifocal osteomyelitis (CRMO) is a multifocal nonpyogenic skeletal disorder of unknown etiology occurring mainly in children and teenagers, with a male-to-

female ratio of 1:2.1 [1,2,3] and a true estimated prevalence of more than 1 in 10,000 [4]. However, it has been described in infants as young as 6 months and in adults as old as 55 years [2,5]. It is diagnosed by exclusion [1,3,6], based on certain criteria, which are a prolonged clinical course; an unusual location of lesions compared to those of infectious osteomyelitis, such as involvement of the clavicle; multiple foci of osteolysis with associated sclerosis or hyperostosis; lack of abscess formation, fistulas, or sequestra; lack of response to antibiotics; and comorbid inflammatory disorders such as psoriasis, palmoplantar pustulosis, or inflammatory bowel disease [5].

The histopathological study of this disease usually reveals inflammatory lesions with signs of reabsorption and necrosis [7]. Accurate diagnosis of CRMO is challenging because the clinical examination findings, laboratory evaluation data, and radiography are nonspecific or insensitive [8].

Treatment generally involves anti-inflammatory agents. In nonresponders, corticosteroids, bisphosphonate, colchicines, interferon-alfa, interferon-gamma, and gamma-globulin have been shown to be effective [3,9–13].

The clinical, radiological, and nuclear scintigraphy findings can mimic subacute and chronic infectious osteomyelitis, histiocytosis, hypophosphatasia, leukemia, Langerhans's cell histiocytosis, lymphoma, osteosarcoma, Ewing's sarcoma, neuroblastoma, rhabdomyosarcoma, osteoid osteoma, and osteoblastoma, resulting in a complex diagnostic challenge [6,10,14,15]. Therefore, histopathological study has been proven essential for the conclusion of the investigations [5,16].

We present a case of CRMO with a 3-year follow-up with adequate treatment that evolved partial resolution of the radiological findings in magnetic resonance imaging (MRI). Therefore, the objective of this report is to demonstrate the diagnostic importance of MRI in matters of CRMO, allowing an adequate study of the evolution of the disease and the possible optimal outcomes.

Case presentation

An 11-year-old female patient consulted with a rheumatologist due to nonspecific pain in the cervical and thoracic spine. The patient was previously healthy, with no history of fever, chills, or weight loss. There were no reports regarding previous surgery, trauma, risk factors for immunosuppression, or a family history of bone or joint disorders.

A T5 lamina thoracic spine biopsy revealed bone tissue with remodeling and medullary spaces and soft tissues containing polymorphonuclear inflammatory cell proliferation alongside xanthomatous histiocytes and epithelioid histiocytes. However, an immunohistochemistry demonstrated CD68 positive markers and CD1a negative and S100 negative proteins, ruling out the possibility of histiocytosis X. The patient received several antibiotics for the diagnosis of osteomyelitis, evolving with periods of improvement followed by the exacerbation of pain.

After a year, there was progressive worsening of pain and extension in the patient's left wrist and right ankle. A left wrist radiograph was performed, which found morphostructures in the metaphysis of the radius, characterized by mildly delimit-

ed osteolytic foci and adjacent periosteal reaction. A right ankle radiograph showed poorly delimited osteolytic lesions in the distal metaphysis of the right tibia. An MRI of the left wrist showed a metaphyseal infiltrative lesion in the distal radius, with decreased signal intensity on T1-weighted images, scattered increased signal intensity on T2-weighted images, postcontrast enhancement, and a significant periosteal reaction at the distal radius to the outer cortex (Fig. 1). Gallium scintigraphy was performed, confirming disease activities in the right posterior costal arcs, right ankle, and left wrist. An MRI of the chest wall was also performed after this finding in scintigraphy, showing scattered increased signal intensity on STIR-weighted images in the medullary cavity of the right posterior costal arcs (Fig. 2).

A new biopsy was conducted without the wrist and ankle revealing lamellae of the ebony bone and conjunctival foci and mixed exudation of the inflammatory cells with predominance of neutrophils, compatible with osteomyelitis (Fig. 3).

In view of the clinical, radiological, and histopathological findings, the patient was diagnosed with CRMO and treated with nonsteroidal anti-inflammatory drugs, methotrexate, and pamidronate. After 12 months, MRI exams were performed (Fig. 4) that showed partial regression of the findings.

Discussion

Little is known about the evolution and possible factors that may influence in sequels and partial or complete remissions regarding CRMO disease. Solid periosteal reaction and bone marrow edema are the primary findings in MRI, and these may vary in extent and severity. Although radiographic imaging is also very useful for detecting the periosteal reaction, MRI can provide a broader view of the disease involvement, such as extension and activity.

After the bone tissue is damaged, vascular proliferation and thickening of the periosteum occur in varying degrees, which results in edema, enhancement, periosteal reaction, periostitis, and soft tissue inflammation, with T1 hypointensity and T2 hyperintensity on MRI. Such results might be found in several diseases, such as tumors, trauma, infection, and venous stasis, among others. What will draw attention to CRMO is the age group, usually in children [3], and the disease outbreak and remission cycle, a process that may extend for years [9]. There is no pathological agent in the biopsies, which are negative. Laboratory findings are nonspecific. Findings such as bone sequestration, abscesses in soft parts, and fistulas refer more to an infectious diagnosis.

CRMO usually affects the metaphyseal region and occurs in more than one site simultaneously; its most common sites of involvement are the lower limbs, spine, and clavicle [1,2,9,13,14]. In some cases, it might extend to the physis, which increases the chances of sequelae deformities [2]. The clavicle is uncommon in hematogenous osteomyelitis, and CRMO is the most common non-neoplastic process involving this site in patients younger than 20 years of age [2]. The involvement of the diaphyseal and epiphyseal regions might occur, although this is less common. The fact that this disease occurs in more than one site makes whole-body MR a fun-

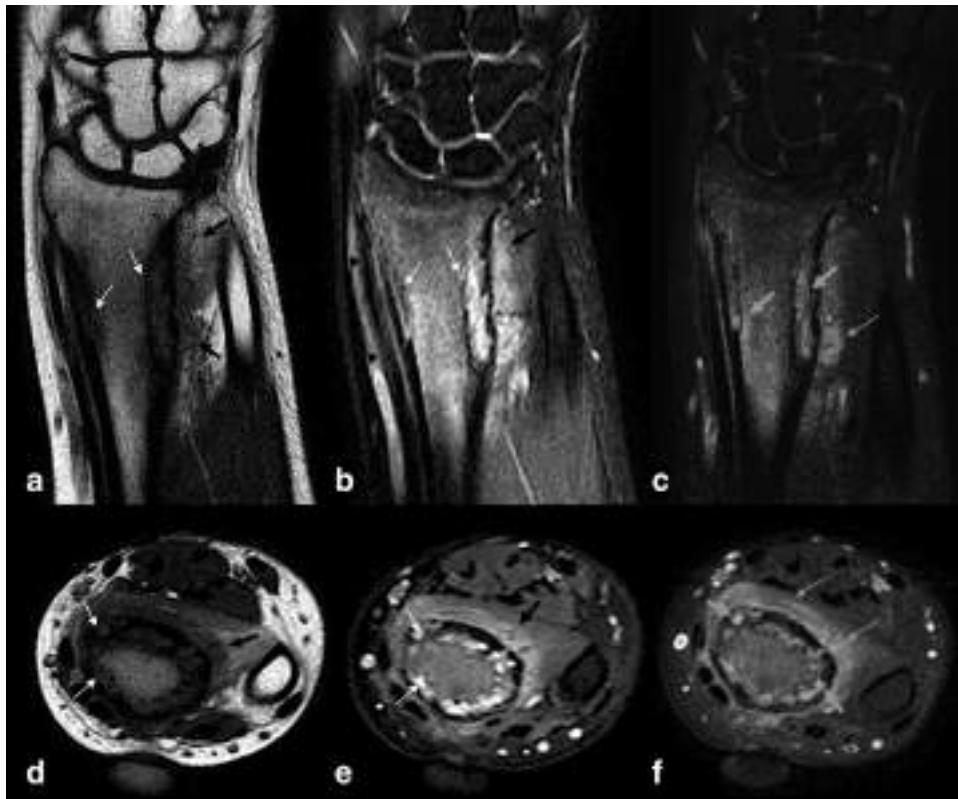


Fig. 1 – Coronal and axial reconstructions of the wrist. The images demonstrate metaphyseal infiltrative lesion in the distal radius, with decreased signal intensity on T1-weighted images (A and D), scattered increased signal intensity on T2-weighted images (B and E), and significant periosteal reaction and cortical thickening at the distal radius to the external face in all sequences (white arrows). There was concomitant surrounding soft tissue edema (black arrows) presenting as a high signal intensity rim, but no abnormalities suggesting abscess formation. After gadolinium (C and F), there was intense enhancement of the marrow periosteum (thick gray arrows), with some enhancement also seen in the bordering musculature (thin gray arrows).

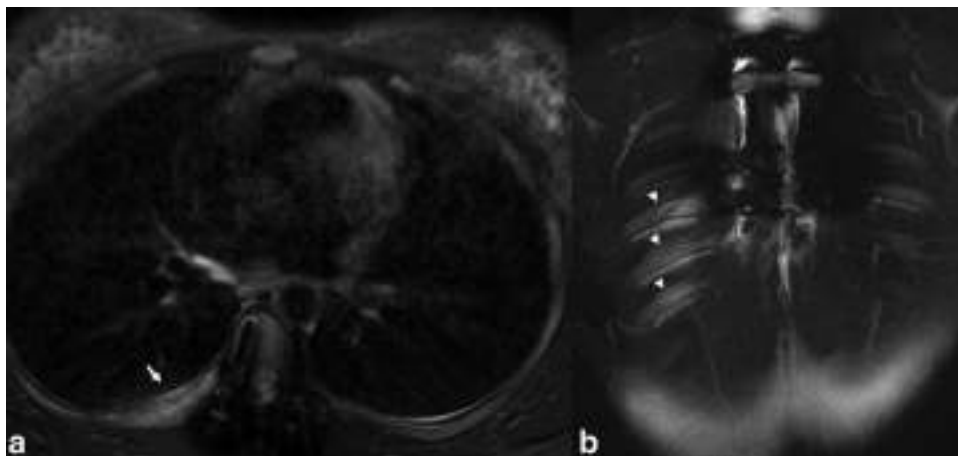


Fig. 2 – Axial (A) and coronal (B) STIR-weighted images of the chest wall showing scattered increased signal intensity in the medullary cavity (white arrowheads), periosteal reaction, and cortical thickening (white arrow) of right posterior costal arcs.

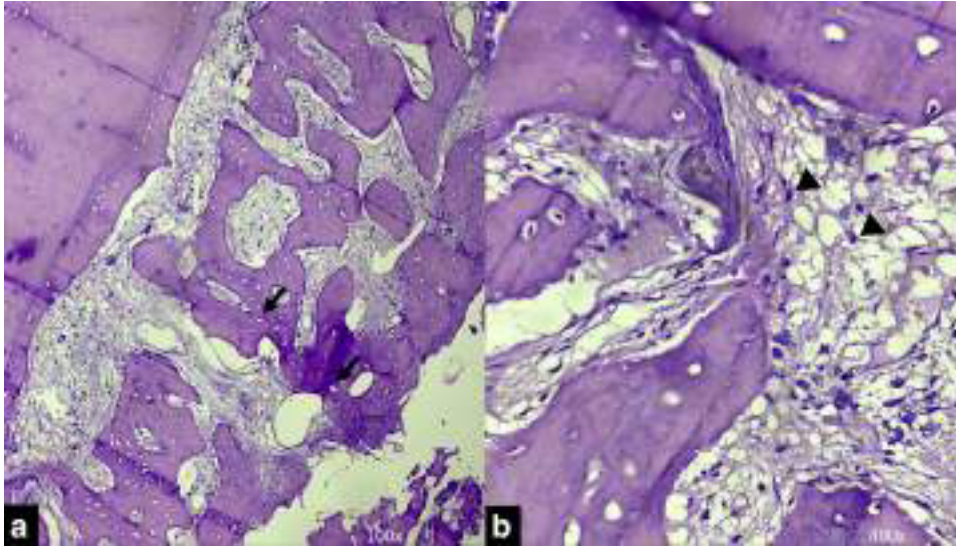


Fig. 3 – Bone needle-biopsy. (A) Islands of bone remodeling, with outbreaks of osteonecrosis and empty osteocyte lacunae (black arrows). (B) Intertrabecular fibrosis with lymphoplasmacytic infiltrate (black arrowheads) of a reactionary pattern.



Fig. 4 – Coronal (A, B, and C) and axial (D, E, and F) reconstructions of the wrist MRI after 12 months showing that the increased bone marrow signal intensity on T2-weighted (black arrows) and post-contrast enhancement on T1-weighted (black arrowheads) images partially disappeared followed by regeneration of the normal marrow signal intensity on T1-weighted images (white arrows).

damental diagnostic tool for research into this entity, which can demonstrate a characteristic periphyseal, multifocal pattern [8].

Repetitive outbreaks can cause morphostructural deformities due to hyperostosis. But there are also cases of complete remission, especially in skeletally immature children

[2,4]. Some patients may evolve with sequelae, such as the premature closure of physes, bony deformity, limb-length discrepancy, kyphosis secondary to fracture compression of the vertebral body, and diffuse demineralization, which may predispose patients to fractures [2,3]. Other manifestations that might be found include thoracic outlet syndrome in the clav-

icle and the flat vertebra. Image findings in the spine may resemble spondylodiscitis, but this disease does not usually affect the disc space.

Our case demonstrated the occurrence of CRMO imaging findings in rare sites such as the radius, found in approximately 1%-5% of all lesions [2,4], and the ribs, which are also rarely affected. MRI was fundamental in the follow-up of the outbreaks and in the evolutionary evaluation of this patient, who has shown partial remission.

In conclusion, our study suggests that further long-term follow-up studies of CRMO are required to show the real incidence and evolution of the imaging findings. As much as the follow-up of patients is difficult because the long course of the disease, it is also imperative so that we might understand more clearly what leads to complete and partial remission and possible deformities. The accompaniment of case data is also necessary so we can confirm the risk factors for severe and persistent disease in order to have the quickest and most accurate diagnosis, and, consequently, attempt the most effective treatment.

Ethical approval

All of the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent

Informed consent was provided by the patient and her legal guardians.

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