

Chronic Recurrent Multifocal Osteomyelitis Involving the Mandible – A Rare Case Report

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Chronic recurrent multifocal osteomyelitis (CRMO) is an uncommon, aseptic, autoinflammatory condition characterized by multifocal bone lesions with pain, swelling, and frequent exacerbations and remissions. It is noteworthy that these lesions occur without any identifiable etiology or microbiologic finding. The clavicle and metaphyses of the long bones are often involved whereas involvement of the mandible is considered rare. It is usually diagnosed by exclusion of other diseases. As it shares most of its features with the more commonly occurring infective osteomyelitis, patients are often unnecessarily subjected to prolonged courses of antibiotics, serial radiation exposures, and repeated bone biopsies.

We present a case of CRMO involving the mandible. Our primary objective is to demonstrate the clinical features of this uncommon disorder, highlighting the radiographic appearance. Familiarity with this condition among radiologists greatly increases the likelihood for early diagnosis and formulating an appropriate treatment plan.

Keywords: Chronic multifocal osteomyelitis, Multifocal osteomyelitis, chronic osteomyelitis,

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INTRODUCTION

Chronic recurrent multifocal osteomyelitis (CRMO), first described in 1972 by Giedron *et al*, is an uncommon, autoinflammatory condition affecting the bone.¹ Multifocal bone lesions with pain and swelling and frequent exacerbation and remission over a period of time are characteristics of this disorder.² The etiology of the disease is unknown and upon histological evaluation there is a lack of microbiological findings. The clavicle and metaphyses of the long bones are the most commonly involved sites.²⁻⁴ Involvement of the mandible is rare.² CRMO is considered to be a subtype of SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) syndrome.⁵ The diagnosis of CRMO is primarily by exclusion of other diseases. Since the presenting features are similar to infective osteomyelitis, it can be easily misdiagnosed thereby subjecting patients to prolonged and unnecessary courses of antibiotics, serial radiation exposures, and repeated bone biopsies.

We present a case of CRMO involving the mandible. Our primary objective is to present the clinical features, and the radiographic appearance of this disorder. Recognition of this rare entity may prevent misdiagnosis and initiate appropriate therapy.

Case report

A 13-year-old male patient presented to our emergency department complaining of left-sided facial pain and swelling. The patient’s medical history was significant for CRMO and hospitalization for recurrent right facial swelling and chronic right ankle pain. Multi-detector computed tomographs (CT), magnetic resonance imaging (MRI), and nuclear medicine bone scans acquired during previous hospitalizations were reviewed. The prior CT revealed mild osteopenia in the right mandibular body surrounded by soft tissue swelling and effacement of fat planes. There was also soft tissue density in the right mandibular foramen (Fig. 1). A contrast enhanced and fat suppressed T1-weighted image revealed a high signal intensity in the right mandibular marrow spaces accompanied by surrounding muscle edema (Fig. 2). Bone scintigraphy

Figure. 1: Axial MDCT soft tissue window showing soft tissue density in the right mandibular foramen (solid black arrow).



Figure. 2: MRI T1 fat-suppressed: shows a high signal in the marrow space of posterior right mandible (Solid black arrow) and muscle edema (black arrow).



with 99mTechnetium-labeled methylene diphosphonate depicted increased tracer uptake in the right mandibular body, right ankle, and the epiphyses of most of the long bones during the blood pool and delayed phases (Fig. 3A, 3B). Bone biopsies and culture from the right retromolar trigone, buccal fat pad and right ankle were inconclusive. There was a marked elevation of the erythrocyte sedimentation rate and C-reactive protein, suggestive of an ongoing inflammatory process. Recurrent tenderness in the above mentioned sites was present since the initial visit. The pain was self-limiting or reduced in intensity with non-steroidal anti-inflammatory drugs (NSAID). There was no history of fever, HIV or skin lesions. The patient was on Naproxen sodium 250 mg twice daily and his symptoms were controlled until his most recent hospital visit.

During the most recent visit to the Emergency Department, multiple extra-oral radiographs were obtained to evaluate for a bony or dental abnormality (Fig.4A-C). The radiographs show normal finding except for a soft tissue swelling which was noted overlying the left mandible (Fig. 4B). An MRI was subsequently performed for better evaluation.

The most recent MRI (Fig. 5) revealed improvement of the lesion in the right mandible. In comparison with the prior MRI (Fig. 2), there was persistent high signal in the marrow of the right ramus and mandibular body, but with a resolution of surrounding intramuscular edema on T2 weighted images. Additionally, there was also a new hyperintense signal in the marrow of the left mandibular body around the molar roots and in the mandibular foramen which led us to conclude that this was a new active CRMO site (Fig. 5).

DISCUSSION

CRMO is a rare condition with a female predominance. Approximately 70% of cases affect younger individuals, the mean age being 9 to 10 years.⁶ The clavicle, and proximal and distal tibia are the most frequently affected sites, followed by the femur, spine, and lastly mandible.²⁻⁴ Multifocality and symmetric involvement are key features in the diagnosis.⁷ In our case the patient was a male and mandible was involved symmetrically, however, the lesions on one side showed resolution of the signs and symptoms when the lesions started to develop on the other side.

The pathogenesis of CRMO remains unclear. Some suggest that a low-virulence micro-organism may be responsible for the condition.^{2, 8} This concept contradicts the fact that CRMO is unresponsive to antibiotic. Another postulate is that a micro-organism could be a triggering factor for the inflammatory response, which later becomes independent of the agent and continues to be a noninfectious process.² Another theory suggests an imbalance between the pro-inflammatory cytokines, tumor necrosis factor and anti-inflammatory cytokines.⁹ Autoimmunity has also been proposed as a cause as it is seen in conjunction with other diseases such as SAPHO syndrome, inflammatory bowel disease, etc.^{2, 9}

Patients report pain and swelling of insidious onset that run a prolonged time with periods of exacerbations and remissions. Signs and symptoms may recur at the same site or may involve new regions.⁴ In the present case, the lesions were first noticed in the right mandible and right ankle. Later, these lesions resolved while new lesions developed in the left mandible.

Figure. 3: (A) Phase 2 bone scan showing increased uptake on the wrists, right foot, and right mandible. (B) Phase 3 bone scan showing increased uptake on the wrists, right foot, and right mandible.

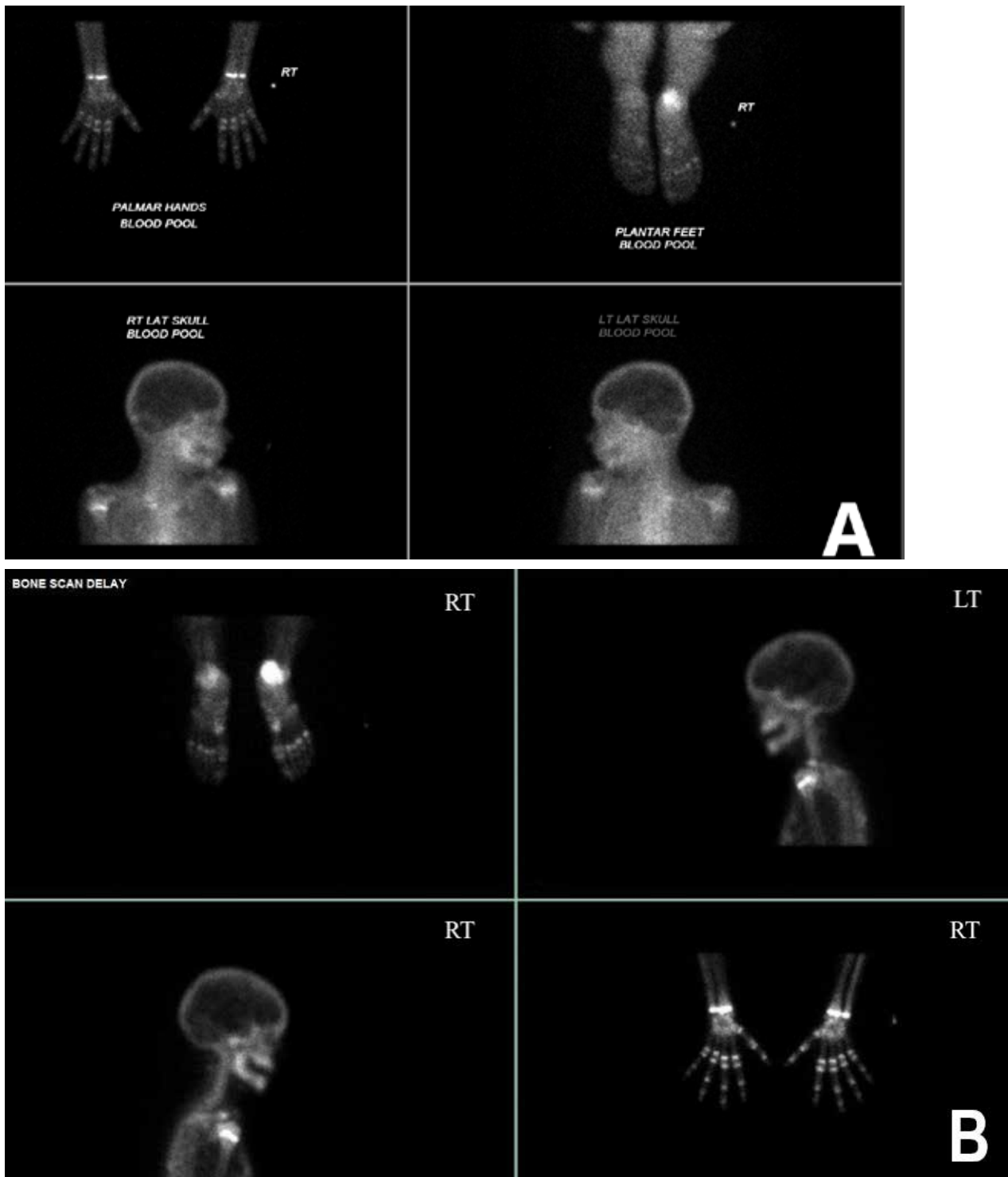


Figure 4: (A) Lateral cephalometric open mouth shows a normal bone pattern in the mandible. (B) posteroanterior view shows a normal bone pattern in the mandible and a soft tissue swelling overlying the left side of the mandible. (solid black arrow). (C) Lateral oblique shows a normal bone pattern in the mandible.

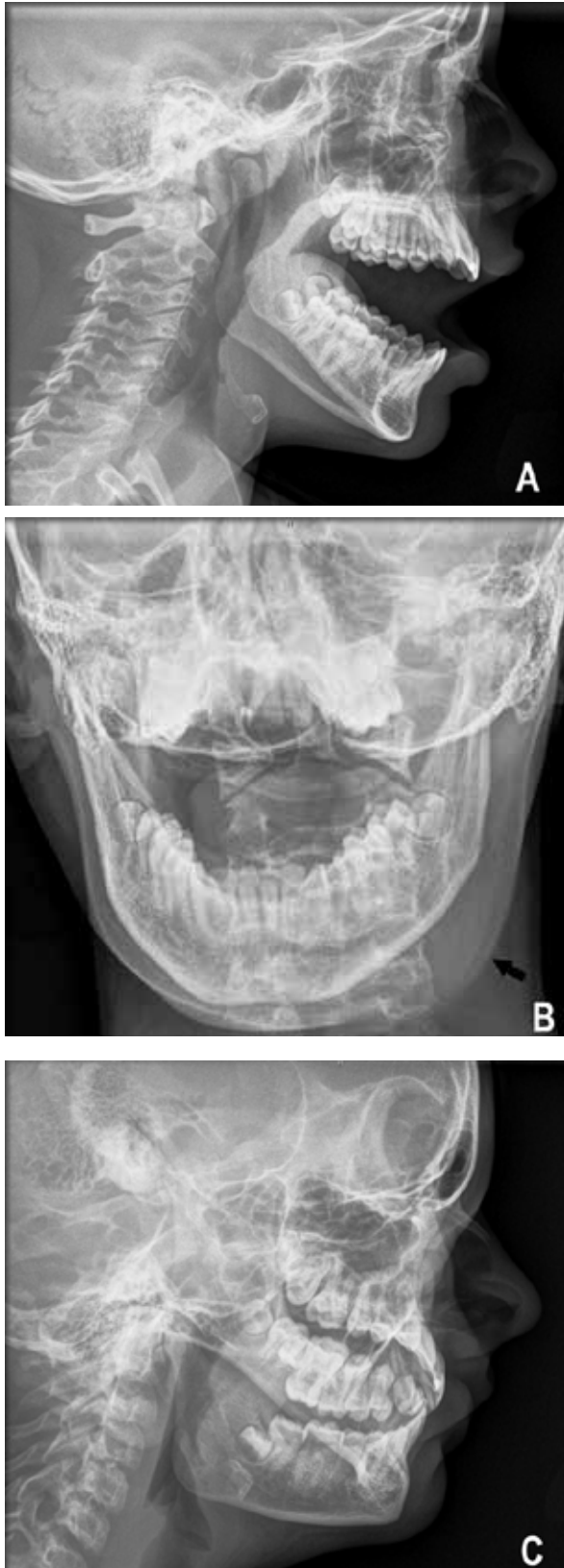


Figure 5: Previous post-contrast MRI: T1 with fat saturation (axial section) showing marrow edema in the mandible on the right (solid black arrow) with overlying muscular edema (Black arrow).



CRMO is essentially considered a disease of exclusion. In our case, the differential diagnoses that were considered are infectious osteomyelitis and inflammatory arthritis like rheumatoid arthritis. Infectious osteomyelitis was ruled out as the culture from the affected site was negative. Laboratory tests were not positive for RA factor which excluded Rheumatoid Arthritis. Neoplasms such as Ewing's sarcoma were excluded as the lesions were multifocal and the lesion in the mandible had soft tissue edema.

Conventional radiographs of the affected sites generally do not reveal any pathognomonic change in the early stages. Nevertheless, they form the first-line of investigations in younger populations where radiation exposure is a concern. In the later stages, they typically show sclerotic reactive bone.⁸ The role of CT in establishing the diagnosis of CRMO was limited in our case. However, it may be useful to rule out any other conditions. The involvement of the mandibular canal can also be demonstrated, as in our case. MRI and bone scintigraphy were our modalities of choice for confirming the CRMO lesions, especially as they were multifocal. A confounding problem is that sometimes the bone scan shows false negative results, typically in early stage lesions.^{8,9,11} In these scenarios the clinical presentation plays a vital role. Moreover, MRI in early stages can detect bone edema and asymptomatic bone lesions before other radiographic signs become evident. CRMO lesions usually appear hypointense in T1 weighted images and hyperintense with T2 weighted images.⁹ The active lesions may also show surrounding intramuscular edema which appear hyperintense with T2 weighted images. Our MRI findings correlated well with the literature.

There is no definitive protocol for the management of CRMO. In a study by Huber et al with 45 CRMO cases, the long-term clinical outcome was generally good.¹⁰ Most lesions are self-limiting, but symptomatic lesions have to be treated.¹¹ NSAIDs form the first line of drugs for this condition.^{2,8,9} Our patient was treated by NSAIDs. Oral corticosteroids form the next line of therapy if the patients do not respond to NSAIDs. Sulfasalazine, methotrexate, bisphosphonates, TNF- α inhibitors and Anti-interleukin-1 beta have been tried with varying outcomes.⁹

CONCLUSION

CRMO is an auto-inflammatory disease with presentation in the mandible that is uncommon. It mimics infective conditions like osteomyelitis and certain malignancies, and is typically a disease of exclusion. MRI is the imaging modality of choice. From the treatment point of view, it is of best interest for the clinician to exclude infective conditions as there exists a difference in their management.

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