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Chronic nonbacterial osteomyelitis involving the mandible: A case report[☆]



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ABSTRACT

INTRODUCTION: Chronic nonbacterial osteomyelitis (CNO) or chronic recurrent multifocal osteomyelitis (CRMO), is a very rare condition of unknown aetiology. It is characterised by focal sterile inflammatory disease with prolonged, self-limiting and recurrent episodes.

CASE PRESENTATION: We report the discovery of this very rare disease following a mandibular abscess in a 10-year-old female. We initially focus on the difference between the preoperative orthopantomography and the maxillofacial computed tomography and magnetic resonance images obtained, and then on the improvement of strategies for correct diagnosis and treatment of this disease.

DISCUSSION: Bone pain and localised swelling can occur in a single bone or can spread to soft tissue and adjacent bone; areas commonly affected by CMRO include the metaphyseal plates of the long bones, as well as the spine, clavicle and, rarely, the maxillofacial area. The clinical presentation of CMRO includes pain, functional impairment, and swelling, similar to our case.

CONCLUSIONS: We report a very rare case of this unifocal mandibular disease in a child who presented for an abscess and was then diagnosed and treated for CNO.

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1. Introduction

Chronic recurrent multifocal osteomyelitis (CMRO), or chronic nonbacterial osteomyelitis (CNO), is a very rare idiopathic non-infectious inflammatory disorder, characterised by bone lesions with pain and swelling, and periods of exacerbations and improvement in different locations over the course of several months to years [1,2]. CRMO primarily affects children, with a female-to-male ratio of 4:1, and the mean age at onset is 10 years [3,4]. The diagnosis of this disorder is based on clinical, radiological, and histological features [5].

Relatively few cases of CMRO have been reported since the first description in 1972 by Giedion, who described the disease as an unusual form of multifocal bone lesions with subacute and chronic symmetrical osteomyelitis [6]. This was followed by Bjorksten's report in 1978, which coined the term 'chronic recurrent multifocal osteomyelitis'. The term CRMO is used to describe the multifocal form of CNO [7].

CNO is poorly characterised in the maxillofacial surgery literature due to the use of inconsistent terminology [8].

Many authors agree that chronic osteomyelitis involving the jawbone may be divided into two major categories: suppurative and non-suppurative. We use the Marx classification [24] to emphasise the difference between CNO and other lesions.

Mandibular lesions are found in 1.5–3% of disease foci in patients with CRMO [9] and the bone most commonly affected by unifocal disease is the mandible [10].

Here, we describe a case of this very rare disease, which was discovered during a frequently-occurring mandibular abscess in a 10-year-old female.

2. Case report

A 10-year-old girl with a recurrent mandibular abscess was referred to the Outpatient Unit of the Department of Maxillofacial Paediatric Surgery, Children's Hospital, ASST degli Spedali Civili, Brescia, Italy. Physical examination revealed only left mandibular swelling and pain with trismus (Fig. 1). The parents revealed that this was the third presentation of the abscess within the last year. Vitaly tooth tests were positive and the percussion test negative. Blood examination revealed only that the C-reactive protein (CRP)

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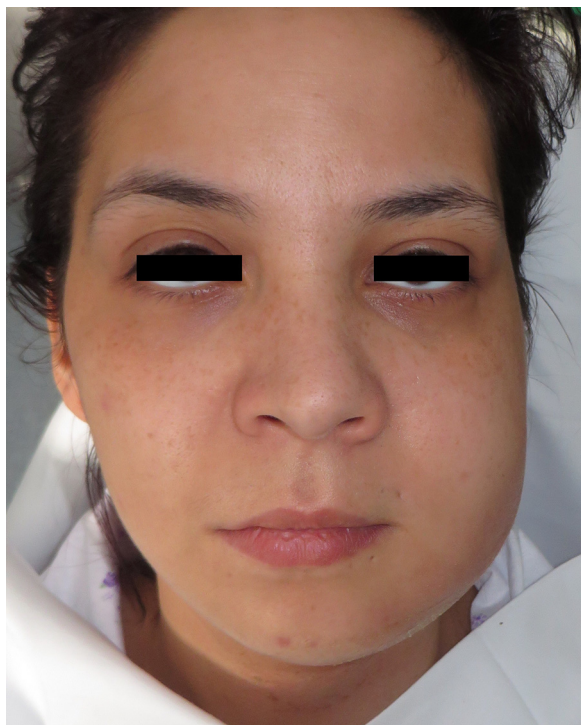


Fig. 1. Clinical view of the patient.



Fig. 3. The CT axial view of the mandibular lesion.

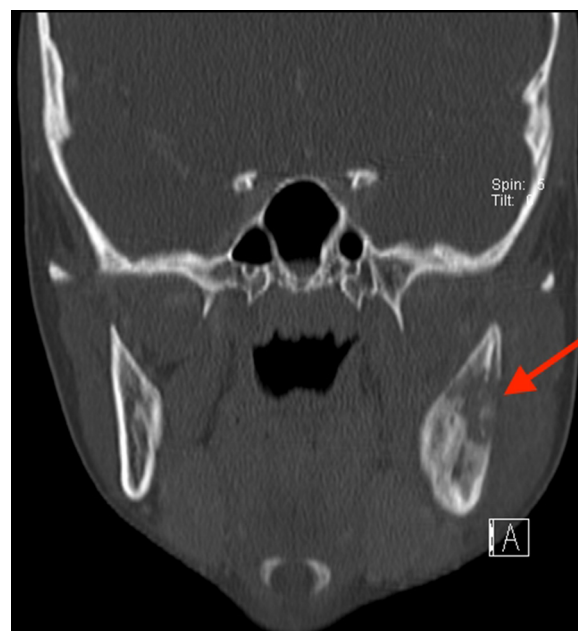


Fig. 4. The CT coronal view of the mandibular lesion.

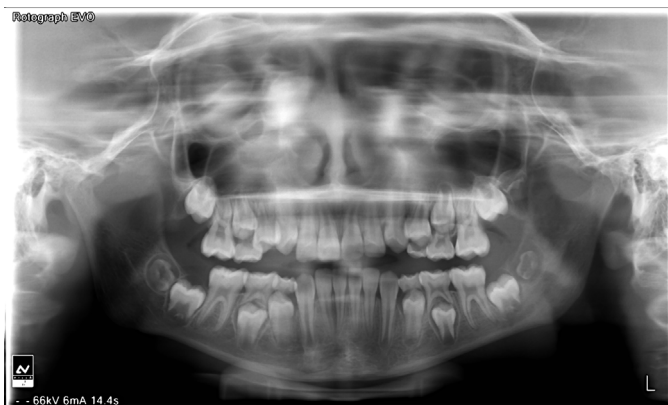


Fig. 2. The preoperative orthopantomogram.

level was elevated to >30 g/L; the blood count was normal and she was in good general health.

Orthopantomography revealed mixed dentition with nothing of note in the mandible or maxilla (Fig. 2). The patient had no history of trauma, previous medication, gingival bleeding, or caries.

To treat the abscess, the patient was immediately started on intravenous antibiotic treatment with rocefin 1 g per day and metronidazole 500 mg every 6 h.

As, clinically, abscess neoformation was evident, we decided to commence broad-spectrum antibiotic therapy [25].

One day later, it was decided to perform a contrast-enhanced computed tomography (CT) maxillofacial scan to better understand the causes of this recurrent problem.

The CT showed remarkable results. The left masseter muscle was diffusely swollen by oedematous imbibition and was also associated with nuanced imbibition of the surrounding subcutaneous soft tissue, down to the muscle itself and in contact with the mandibular angle bone surface. There was a significantly thin, soft, hypodense component, with a thickness of about 5–6 mm and an anteropos-

terior extension of approximately 2 cm. The seat of the cortical bone of the left mandibular branch was interrupted (maximum 1 cm extension) and the structure of the underlying cancellous bone appeared to be particularly inhomogeneous (2 cm cranio-caudal extension) and showed the presence of multiple areas of osteolysis (Figs. 3–5).

Two days later, on the suspicion of mandibular osteomyelitis, the patient underwent contrast-enhanced maxillofacial magnetic resonance imaging (MRI), which revealed diffuse structural alteration of the left vertical mandibular branch and horizontal branch in the molar region (Figs. 6–8). The alteration consisted of:

- an irregularity of the cortical focal profile with continuation into the cortical branch of the vertical branch on both sides;
- widespread alteration of the cancellous bone signal, characterised by an intermediate T2 signal with moderate impregnation (the alteration also extended to the coronoid);

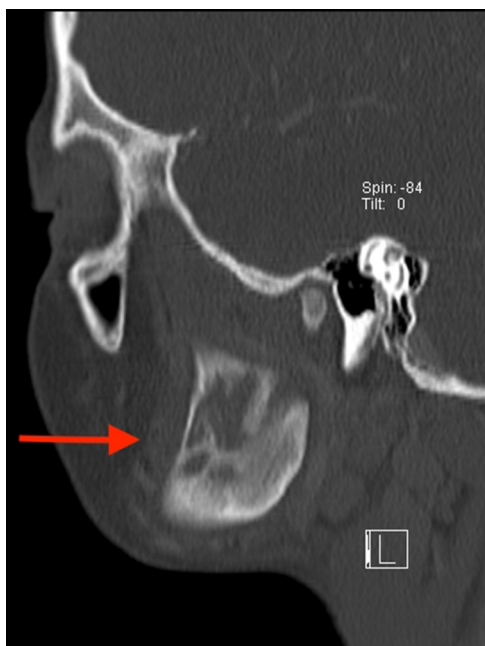


Fig. 5. The CT sagittal view of the mandibular lesion.

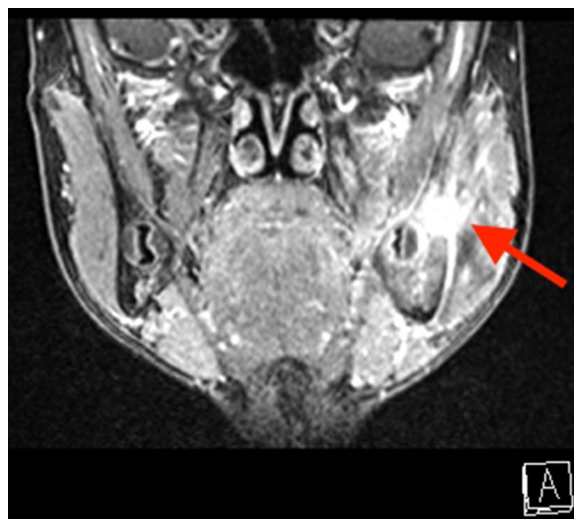


Fig. 7. The MR coronal view of the mandibular lesion with diffuse structural alteration of the left vertical mandibular branch and horizontal branch in the molar region.



Fig. 6. The MR axial view of the mandibular lesion with diffuse structural alteration of the left vertical mandibular branch and horizontal branch in the molar region.

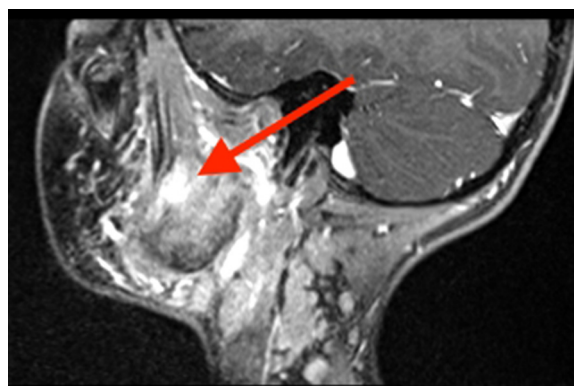


Fig. 8. The MR sagittal view of the mandibular lesion with diffuse structural alteration of the left vertical mandibular branch and horizontal branch in the molar region.

- close to the 38 not-yet-erupted teeth, the external cortical surface was focally interrupted and showed a nodular area of impregnation about 8 mm in extent;
- diffuse alteration of the soft tissues of the masticatory space, much more evident in the masseter muscle whose total volume was significantly higher than the contralateral.

These findings, even considering the clinical evolution, supported the initial hypothesis of osteomyelitis.

The next step was to biopsy the lesion. The biopsy was performed under general anaesthesia using nasotracheal intubation. Local anaesthesia (mepivacaine 0.2% with 1:100,000 adrenaline) was then used in the left mandibular region and an intraoral approach was performed (Fig. 9). An incision was made along the left external oblique line, the periosteum was elevated, and the

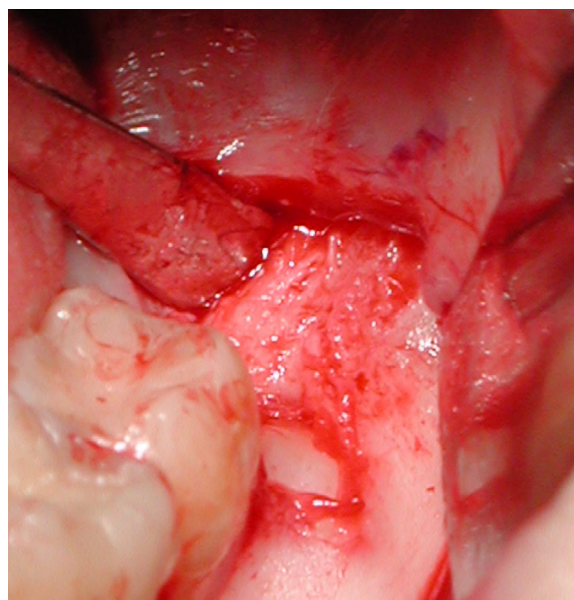


Fig. 9. Intraoperative view.

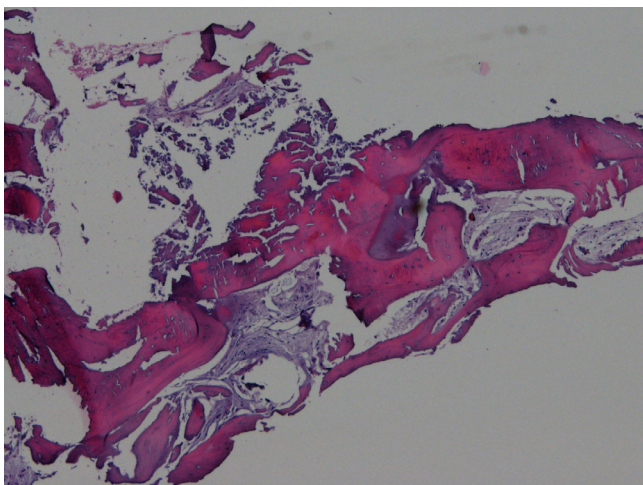


Fig. 10. Histological view of the lesion showing bone spicules that were largely necrotic, with disappearance of the osteoblastic contour and an absence of inflammatory infiltrate and bacterial or fungal colonies.

bone was dissected until the lesion was exposed; thus, a biopsy specimen comprising cancellous and cortical bone was obtained.

Microscopically, the lesion showed small fragments consisting of bone spicules that were largely necrotic, with disappearance of the osteoblastic contour. An absence of inflammatory infiltrate and bacterial or fungal colonies confirmed the aseptic nature of the lesion (Fig. 10). The histopathological and radiological findings, in association with the clinical findings, finally resulted in a diagnosis of CNO.

To discriminate the presence of multifocal disease, a whole body MRI was performed after the biopsy.

We decided to perform MRI rather than a bone scan to minimize the amount of radiation delivered to the young patient. Given the extent of prior radiological investigations, we did not consider it necessary to perform scintigraphy.

The MRI scan was negative, indicating that disease was confined to the mandible.

3. Discussion

According to Roderick et al. [5], various inclusion criteria are used for the diagnosis of CRMO: the presence of typical clinical findings, such as bone pain and/or localised swelling without significant local or systemic features of inflammation or infection, and of typical radiological findings, such as bone marrow oedema and/or bone expansion, lytic areas and periosteal reaction, and either more than one bone without significantly raised C-reactive protein (CRP) or, if unifocal disease or a CRP level greater than 30 g/l, a bone biopsy showing inflammatory changes with no bacterial growth while not on antibiotic therapy. Otherwise, Beretta-Piccoli et al. [1] advise that CRMO can be diagnosed if the following criteria are fulfilled: 1) disease course at least 3 months in duration, 2) bioptical evidence of chronic bone inflammation with the exclusion of other diseases, and 3) failure to cultivate an organism.

CRMO is a very rare disease characterised by recurrent flare-ups of inflammatory bone pain related to aseptic osteomyelitis [9]; lesions can be unifocal (CNO) or multifocal (CRMO) [11]. The rate of unifocal disease ranges from 10 to 56% [10–12].

The mechanism of CRMO remains unknown and under debate; one theory is that a low-virulence micro-organism that cannot be detected is responsible [13,14]. However, others consider that mutations in the genes encoding TNF-alpha and IL1RA may be pathophysiological [29].

On radiograms, we found osteolysis in the early stages, hyperostosis and sclerosis in the later stages, and periosteal reaction occurring at any stage [15]. The disease occurs within a wide variety of bones, such as the metaphyses of the long bones, in particular the distal femoral metaphyses [1,16]; other sites include the clavicles, vertebrae, pelvis, and ribs, while involvement of the sternum, scapula, or spine is less common [1,16]. Lesions involving the mandible are rare [17].

CRMO can occur in males and females, with a 4–1 predominance in females. The median age at onset of the first symptom is 9 years (range: 1–13 years) and the median age at diagnosis is 11 years (range: 1–17 years) [5].

The clinical presentation of CRMO most frequently includes pain, functional impairment, tenderness, and swelling of the affected region. Clearly, the clinical manifestation depends on the affected area [18]. CT and MRI play crucial roles in the radiographic characterisation of CRMO. CT is used to delineate the extent of osteolysis and provide adequate bone detail [8]; MRI provides greater anatomical and morphological detail [18].

Typical histological findings show non-specific abnormalities, of the type seen in acute osteitis, and are observed with lymphocytic infiltrate, polynuclear cells, and areas of fibroblastic fibrosis with sterile cultures [19]. The differential diagnosis includes infectious osteomyelitis, osteosarcoma, Ewing sarcoma, and Langerhans cell histiocytosis [8,27].

The proper course of treatment for CNO remains unclear and no standard therapy is available; current treatment modalities include non-steroidal anti-inflammatory drugs, which are now the first-line therapy [2,15,17,20,21]. Tumour necrosis factor-blocking agents have also been used [22], as well as bisphosphonate [17]. Surgical intervention is reserved for contour reduction [8].

It remains unclear whether CRMO and SAPHO are parts of the same disease spectrum or separate entities; some authors believe that CRMO is the pediatric presentation of SAPHO syndrome [28]. We could not confirm the presence of SAPHO syndrome in our patient. We performed a biopsy only after careful radiography to exclude malignancy; we sought to understand the nature of the lesion more fully. We preferred an intraoral approach given the site and size of the lesion, the fact that the lesion was intraorally accessible, and because we considered external access excessive in a 10-year-old girl, even though the literature describes such an approach [26].

In our case, the patient underwent pharmacological therapy with non-steroidal anti-inflammatory drugs and bisphosphonates including pamidronate [17].

At present, the follow-up period for this disorder is 3 months; we are currently waiting slightly longer than this before performing other radiographs. No new abscess has developed and the CRP level is <30 g/L.

This case report was written according to the Surgical Case Report guidelines [23].

4. Conclusion

We present a rare case of CNO with mandibular localisations to emphasise that any disease that appears to be simple can lead to the discovery of something that is unexpected and extremely rare. Therefore, in this article, we wish to emphasise the extreme rarity of the case, focusing on the large difference between the preoperative panoramic radiograph and CT and MRI images obtained before the first surgical procedure.

Conflicts of interest

No conflict.

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Ethical approval

No.

Consent

The consent has been given.

Authors contribution

All authors have contributed in study concept, data collection, data analysis and interpretation and in writing the paper.

Guarantor

Gabriele Bocchialini.

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