

## CASE REPORTS

## Recurrent Osteomyelitis Refractory to Antimicrobial Therapy?

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## ABSTRACT

### Introduction

Juvenile mandibular chronic osteomyelitis (JMCO) is a rare non-suppurative, non-infectious, chronic inflammatory bone disease of unknown etiology that primarily affects the mandible in children and adolescents. JMCO presents similarly to infectious osteomyelitis with recurrent mandibular pain, swelling, and trismus. JMCO should be suspected when there is an absence of pus, repeatedly negative cultures, and no response to antimicrobial therapy.

### Case Report

A 29-year-old African-American female with history of recurrent left jaw pain presented with 3-day history of worsening left jaw pain associated with inability to open her mouth. Her pain was intermittently relieved by non-steroidal anti-inflammatory drugs (NSAIDs). She denied fevers, chills, rhinorrhea, congestion, otorrhea, sore throat, cough, trouble with hearing, swallowing, or changes in speech. She denied any recent medication or herbal supplement use, recent trauma, childhood dental problems, or family history of dental problems.

The patient reported multiple tooth extractions starting in her teenage years; however she was unable to provide further details. In the 18 months leading to presentation, she experienced recurrent episodes of left-sided jaw pain, up to 3-4 times per month, resulting in the left lower wisdom tooth and multiple left mandibular molars to be extracted. During this period she completed three courses of clindamycin for presumed dental infection without relief of symptoms.

On presentation to the emergency department, she was afebrile and hemodynamically stable. Examination revealed a large unilateral edematous area over the left masseter muscle extending over the left angle of the mandible. There was severe tenderness to palpation, but the area was not warm, erythematous, or fluctuant. There was no stridor or respiratory distress, and she spoke in full sentences.

Upon evaluation by dentistry and otolaryngology, the extra-oral exam was notable for less than one finger trismus. The intra-oral exam was limited; however it revealed an edentulous alveolar ridge at the original insertion sites of the mandibular third molars

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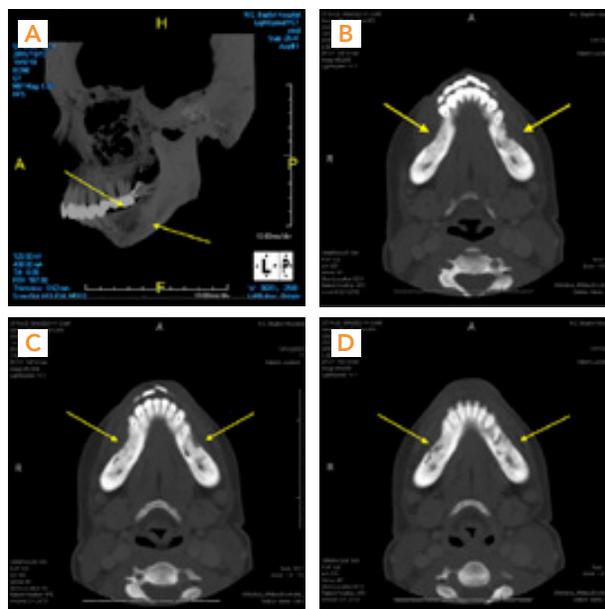
(17, 32), second molars (18, 31), first molars (19, 30), and second premolars (20, 29). Posteriorly, there was no exposed bone, swelling, or tenderness to palpation. The mandibular left first premolar (21) was tender to percussion and exhibited mild mobility (class I).

Labs were notable for leukocytosis (WBC 13.4) and elevated inflammatory markers (ESR 79, CRP 17.6). Preliminary results of the computed tomography (CT) of face and sinuses and orthophantomogram favored extensive chronic osteomyelitis (OM) of the left mandibular ramus, with adjacent myositis involving the muscles of mastication. Additionally, there was a large periapical lucency noted on the mandibular left first premolar (bicuspid), and multiple missing teeth. No acute surgical intervention was indicated due to lack of drainable abscess. Clindamycin was initiated for presumed infectious OM.

The final imaging reports favored a diffuse lytic and sclerotic process involving the mandible (left greater than right), most prominent at the left mandibular body and ramus, with edema and enlargement of the surrounding muscles of mastication reflecting extensive inflammatory changes. The findings of an acute odontogenic inflammatory process with chronic changes (Figure 1 and 2) were compatible with JMCO.

Following discussion between the primary team, otolaryngology, dentistry, and radiology, the patient was suspected to have JMCO, not infectious OM, and clindamycin was discontinued. Though the patient was not specific about the age of onset of her symptoms, the combination of her history of multiple tooth extraction in her teenage years along with head CT performed one year ago showing chronic changes in the mandible, supported that the disease was juvenile in onset.

The patient underwent extraction of the mandibular left first premolar (21) and incisional biopsy of the left body of the mandible. Intraoperatively, the patient was found to have pulpal pathology of the mandibular left first premolar (21). No pus or other evidence of infection was noted in the mandibular region.



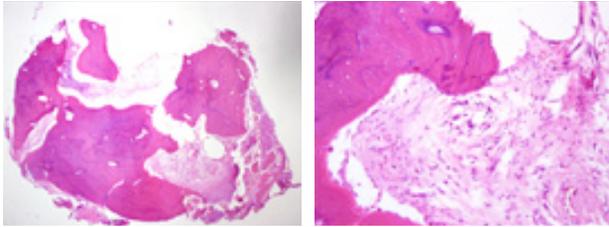
**Figure 1:** Radiographic findings. (A) CT face and sinuses with contrast revealed a left mandibular lesion with multiple left mandibular molars missing. (B, C, D) CT face and sinuses with contrast, consecutive helical images, revealed lytic and sclerotic lesions in the mandible bilaterally (left greater than right).



**Figure 2:** Orthophantomogram revealed a diffuse sclerotic and lytic process in the left mandible.

The final pathologic diagnosis of the left body of the mandible (location of tooth 18) was reactive bone and fibrous tissue, no malignancy identified (Figure 3). Two blood cultures from admission were negative.

During the hospitalization, the patient also complained of left knee pain. There was concern for multifocal disease



**Figure 3:** Left mandibular bone biopsy revealed reactive bony trabeculae in a loose fibrous stroma with associated chronic inflammatory cells.

involvement; however a plain radiograph of the left knee revealed no acute fracture, malalignment, joint space abnormality, or effusion.

The clinical and radiographic findings of a chronic non-suppurative inflammatory process, with no evidence of infectious, neoplastic, or dysplastic processes on tissue biopsy, and negative cultures, together with the patient's age at presentation, mandibular focality, and historical non-response to clindamycin, led to a diagnosis of JMCO. NSAID therapy was initiated and the patient was discharged. On follow-up, the patient reported improvement in jaw pain, and extra-oral and intra-oral exam revealed improvement of trismus and no signs of infection.

## Discussion

Chronic osteomyelitis (OM) more commonly occurs secondary to infection, and less commonly as a primary process.<sup>1</sup> In 1893 Swiss surgeon Carl Garré first described primary chronic OM as a non-suppurative sclerosing type of OM characterized by distension and thickening of the bone. Unfortunately, there have been no clear classification criteria for primary chronic OM in the literature. Subsequently, a variety of names have been used for this entity: Garré sclerosing OM, chronic non-suppurative sclerosing OM, periostitis ossificans, among others.<sup>2</sup> In recent literature, the most commonly used term “diffuse sclerosing OM” (DSO) is used to describe the manifestation of chronic recurrent multiple OM.<sup>2</sup> However, DSO is non-specific and is often sub-categorized based on age at presentation as well as focality. The suggested term for DSO occurring in the mandible

in pediatric populations is “juvenile mandibular chronic osteomyelitis”.<sup>3</sup>

Juvenile mandibular chronic osteomyelitis (JMCO) is a rare type of primary chronic OM.<sup>2,3</sup> It is a strictly non-suppurative, chronic inflammatory bone disease of unknown etiology that primarily affects the mandible in children and adolescents.<sup>1,3,4</sup> Few cases have been reported in the literature due to low incidence.<sup>2</sup> The median age at presentation is 9.6 years, and ranges from 3 to 17 years.<sup>5,6</sup> JMCO appears to have a female predominance, with a ratio of females to males of 4:1 reported in a case series.<sup>2,7</sup>

The exact etiology and pathophysiology of JMCO remains unknown. Despite limited supporting evidence, a number of disease mechanisms have been proposed including hyperactive or hypoactive immune response, complete impairment of the immune system, low virulence infection, or bacterial toxin(s).<sup>3,4</sup> The idea of an infectious etiology has been challenged by multiple studies failing to isolate and culture organisms or show a clinical response to antibiotic therapy.<sup>8</sup>

Clinically, JMCO has an insidious onset developing over the course of a few days to several weeks.<sup>2</sup> The disease course may be cyclical with periods of exacerbation and remission.<sup>9</sup> Patients with JMCO may present with similar symptoms to infectious OM, including recurrent mandibular pain, swelling, and trismus, however there should be an absence of pus.<sup>10,11</sup>

Expected laboratory findings include elevated inflammatory markers (ESR, CRP) and negative cultures.<sup>1-3,10</sup> In the appropriate clinical setting, positive cultures should raise suspicion for oral contamination during the surgical procedure.<sup>3,12</sup>

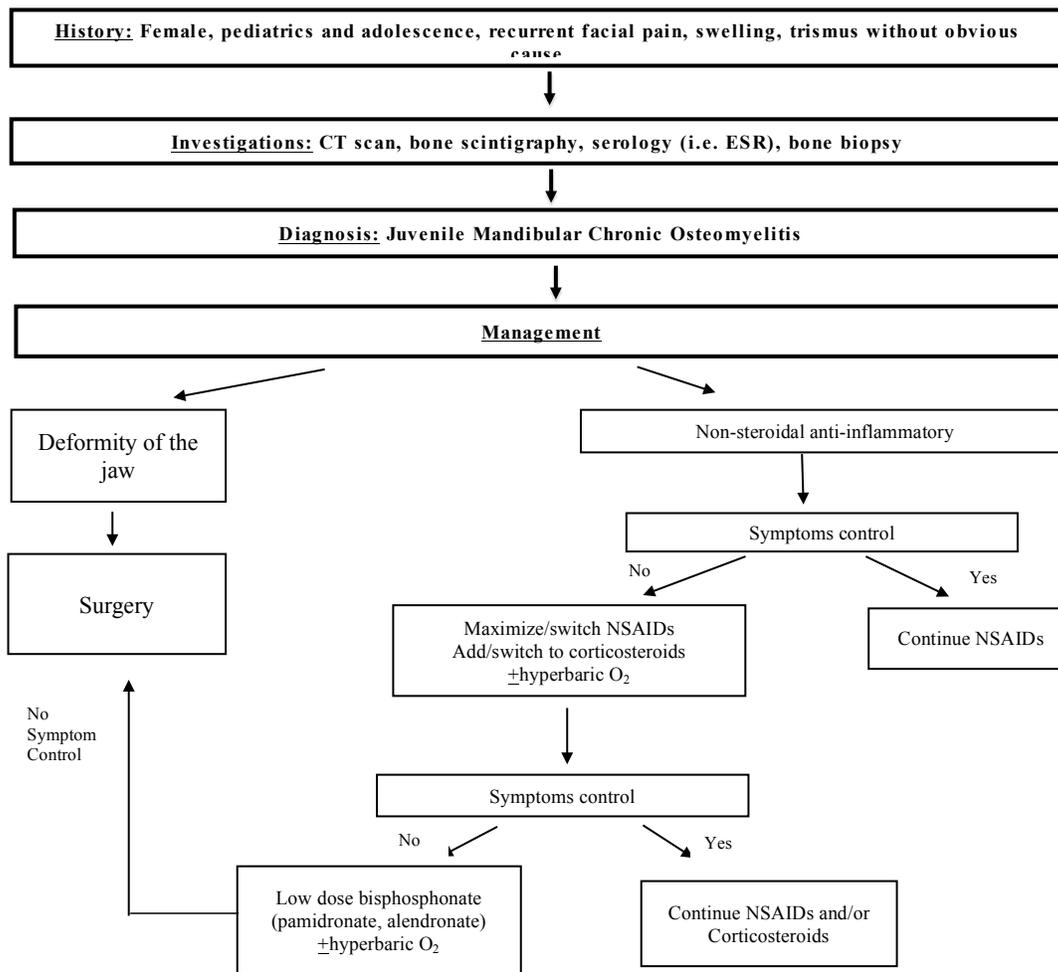
Numerous imaging modalities, including panoramic radiograph, MRI, bone scintigraphy, and CT scan, have been utilized to aid in diagnosis. JMCO lesions have mixed sclerotic and osteolytic elements with associated periosteal reaction, giving the appearance of a widened mandible.<sup>2,7</sup> Features of chronic infectious OM should be absent.

Tissue biopsy can be a helpful diagnostic adjunct, as it may help distinguish malignant, dysplastic, and infectious processes with similar presentation to JMCO.

The differential diagnosis includes malignant processes such as Ewing sarcoma, chondrosarcoma, and osteosarcoma, dysplastic and neoplastic processes such as fibrous dysplasia and non-ossifying/ossifying fibroma, and infectious processes.<sup>1,13</sup> If JMCO is suspected and the above diagnoses have been ruled out, a diagnostic evaluation consisting of imaging and biopsy is recommended (Table 1). The diagnosis

of JMCO should be made based on the combination of clinical, radiologic, and histopathologic findings.<sup>2</sup>

Many authors suggest NSAIDs as first line treatment for symptomatic control.<sup>1-3,14</sup> In patients who have poor symptomatic control or disease relapse with NSAID therapy, the use of corticosteroids showed symptomatic improvement during exacerbation periods and disease regression in some case series.<sup>1,14</sup> Bisphosphonate derivatives, such as alendronate or pamidronate, have also been used and showed favorable response in clinical and



**Table 1:** Proposed schematic diagram of the approach to investigation and management of juvenile mandibular chronic osteomyelitis (Modified from Heggie).

radiographic parameters.<sup>14-16</sup> However, the long-term effects of bisphosphonate use were not evaluated in these studies. Because of the risk of jaw osteonecrosis, bisphosphonate therapy should be used with caution and should only be utilized when conventional treatments are not effective. The use of other forms of treatments have also been reported including hyperbaric oxygen therapy, interferon, TNF alpha, and methotrexate.<sup>1,6,10,14,17</sup> It is important to note that there is no evidence in the literature to recommend antibiotic treatment in patients with JMCO.<sup>1,12</sup>

In addition, surgery has been suggested as an option in patients with severe facial asymmetry secondary to mandibular deformity or in patients with severe cases refractory to pharmacological treatment. However, studies show inconsistent or only short-term success with surgical intervention. Heggie et al reported recurrence of symptoms after decortication or partial resection.<sup>3</sup> These recurrences were thought to be due to inadequate resection margins.<sup>3</sup> In another case series, Baltensperger et al found no or only short-term success with surgery. Therefore, some authors recommend conservative treatment as the primary therapy for patients with JMCO, with careful consideration of the risks and benefits of surgical intervention.<sup>1,3,10,18</sup>

## Conclusion

Juvenile mandibular chronic osteomyelitis (JMCO) is a rare non-suppurative chronic inflammatory bone disease primarily affecting the mandible in children and adolescents. JMCO has a similar clinical presentation to infectious osteomyelitis. Clinicians should suspect non-infectious etiologies, such as JMCO, in patients with repeatedly negative cultures and no response to antimicrobial therapy so that they receive the appropriate management.

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