



Chronic nonbacterial monoarticular osteomyelitis of the elbow

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Chronic nonbacterial osteomyelitis (CNO) is an exceedingly rare autoinflammatory bone condition with a prevalence of 1–2 cases per 1 million people.⁵ Commonly affecting children and adolescents, CNO is characterized by insidious onset chronic bone pain that waxes and wanes for months to years. CNO was initially described by Giedion in 1972 and was previously considered a relatively mild disease.¹² Subsequent cases confirmed the morbidity and sometimes devastating nature of the condition as it frequently limits sleep and can cause pathologic vertebral body fractures.²⁹ CNO represents a clinical spectrum from mild, asymptomatic unifocal bone pain to severe, recurrent multifocal bone lesions involving the metaphysis and epiphysis of the long bones.⁴ When the latter occurs, the term chronic recurrent multifocal osteomyelitis (CRMO) is used to characterize the disease.¹⁵ Other commonly affected bones include the spine, pelvis, shoulder, clavicle, and jaw. Other organs may also be involved, such as the skin: synovitis, acne, pustulosis, hyperostosis, and osteomyelitis.¹⁶ The exact pathophysiology of CNO remains unknown, but the interleukin 10 and interleukin 1 cytokine pathways may play a role.¹⁷ Emerging data have allowed some guidance as to the best way to diagnose and treat CNO. Because of its variable clinical manifestations and similarity to other pathology, CNO is essentially a diagnosis of exclusion. Treatment of CNO is mainly empiric, most commonly using nonsteroidal anti-inflammatory drugs (NSAIDs) as first-line and implementing corticosteroids, tumor necrosis factor (TNF) inhibitors, and bisphosphonates only when needed.³⁰ To the best of the authors' knowledge, unifocal CNO of the elbow has yet

to be described. Herein, we present an interesting case of CNO of the elbow in a 15-year-old. This experience expands the anatomic sites of involvement and reinforces the important diagnostic and treatment options unique to this case that will contribute to better understanding of the existence and treatment of this poorly understood pathologic condition.

Case presentation

A 15-year-old right-hand dominant male presented to the clinic with about 3 years of atraumatic and episodic left elbow pain. His pain began in the 7th grade and was mainly on the posterior elbow, and he also complained of nighttime pain that woke him on occasion. The patient played recreational football, and excessive activity worsened his pain. On examination, the elbow revealed a 30-degree flexion contracture and full flexion. Palpation elicited pain in the enthesis of the triceps on the olecranon without osseous pain. The patient was maximally tender in the region of the medial epicondyle. Notably, the ulnar nerve was also tender, although he did not have radicular symptoms. The elbow was stable, lacked an effusion, and was not warm or erythematous.

A complete blood count with differential demonstrated no abnormalities other than a mildly elevated hemoglobin of 15.1 g/dL, and the patient's prothrombin and international normalized ratio were normal as well. Radiographic imaging denoted nonspecific localized sclerosis and irregularity along the posterior margin of the olecranon at the triceps insertion, indicating triceps enthesitis without periostitis or osteolytic lesions (Fig. 1). On magnetic resonance imaging (MRI), there was osseous edema about the olecranon process not extending into the coronoid process (Figs. 2 and 3). Acute enthesitis at the triceps insertion was also noted, but there were no changes suggesting osteoid osteoma or a neoplastic or active infective process.

A presumptive diagnosis of CNO was made, and because this condition has not been previously identified in this anatomic

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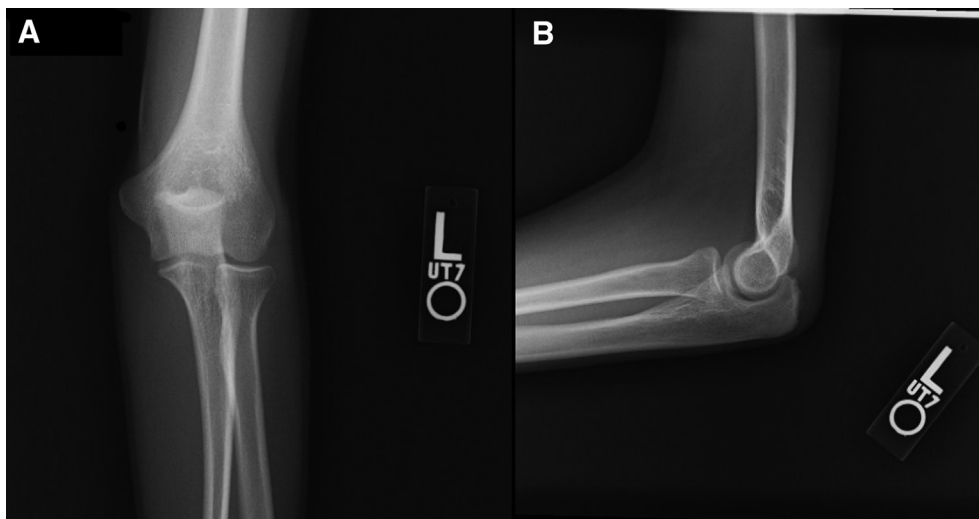


Figure 1 Anteroposterior (A) and lateral (B) radiographs of left elbow 3 years after onset of pain. There is subtle sclerosis and cortical irregularity along the posterior margin of the olecranon at the triceps insertion with likely associated with enthesitis.



Figure 2 Sagittal (A) and coronal (B) T2W MRI demonstrating extensive olecranon edema and tendinopathy of the triceps insertion at the olecranon taken 1 month after plain films. Note the process does not cross the joint and does not extend into the coronoid. MRI, magnetic resonance imaging.

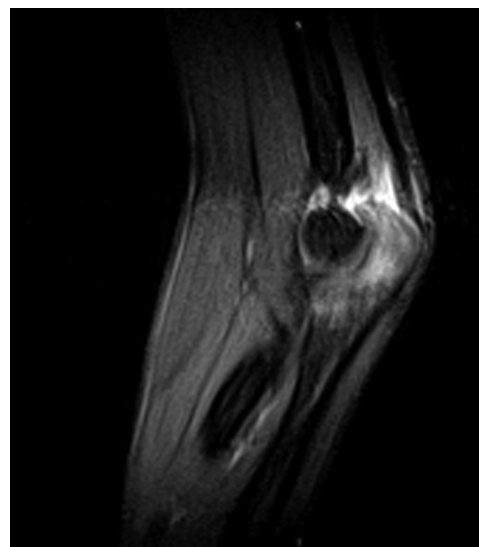


Figure 3 Sagittal gadolinium enhanced T1 MRI view demonstrating intraosseous edema of the olecranon. MRI, magnetic resonance imaging.

part, a surgical biopsy was undertaken and was consistent with chronic osteomyelitis of the elbow. However, as expected, the cultures of the osseous tissue failed to reveal an organism. The biopsy did also rule out a neoplastic processes. The patient then began a regimen of the anti-inflammatory agent Naproxacin sodium. At one and a half years surveillance, the pain had resolved, and he had no restrictions of routine daily functions. Direct palpation of the olecranon produced mild pain, but the patient was able to sleep through the night. Of interest, his range of motion was similar to that at the time of presentation between 25 and 30 degrees of extension to 155 degrees of flexion (Fig. 4). This loss of motion did not interfere with any activity according to the patient. The patient took the anti-inflammatory medication for one and a half years before essentially discontinuing it and using it as needed. The MRI at the final follow-up confirmed near-complete resolution of the osseous edema and triceps enthesitis (Figs. 5 and 6). Surveillance is ongoing.

Discussion

CNO is an elusive and rare disease with an incidence as low as 1 million children or 2%-5% of all osteomyelitis cases.^{1,8} The present report describes important clinical features of CNO when it presents in the elbow. To the best of the authors’ knowledge, mono-articular elbow CNO has yet to be described in the literature. Along with classic signs and symptoms of CNO in other joints, elbow CNO, in particular, may manifest with a persistent flexion contracture as seen in our patient. Atraumatic and noninfectious pain from the elbow coupled with a flexion contracture can portend a challenging differential diagnosis. In addition to considering benign and malignant bone tumors, osteochondritis dissecans, olecranon apophysitis, olecranon bursitis, atypical infections, chronic stress fractures, and little league elbow warrant consideration with presentation at the elbow.

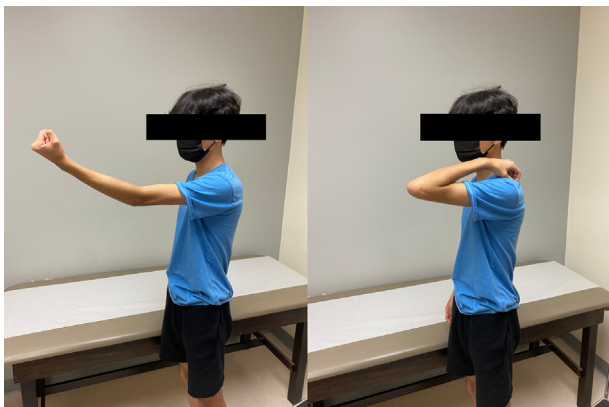


Figure 4 Patient at final follow-up demonstrating an arc of motion between 25 and 30 degrees of extension and 155 degrees of flexion.

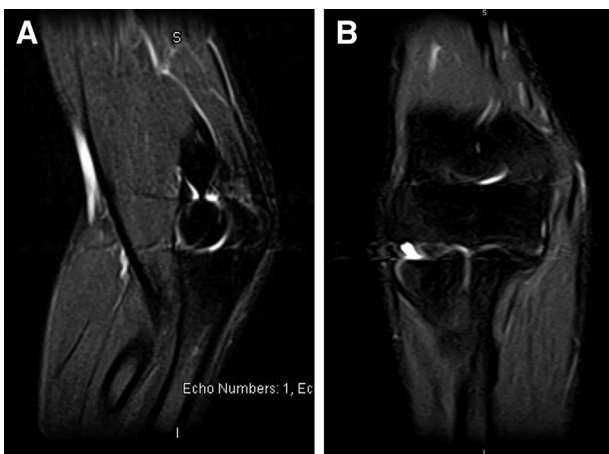


Figure 5 Sagittal (A) and coronal (B) T2W MRI at final follow-up demonstrating resolution of olecranon edema. MRI, magnetic resonance imaging.

This case underscores the utility of a thorough clinical and physical examination, MRI, and surgical biopsy to rule out other disease processes effectively. Diagnosing CNO requires first an awareness of the condition and a high index of suspicion but remains a diagnosis of exclusion. Diagnostic criteria for CNO have been proposed, although none have been prospectively tested and validated.^{19,24,30} Ruling out infectious, neoplastic, or other rarer bone pathology requires clinical, radiographic, and histological findings. Insidious and atraumatic onset with recurrent bouts of bone sensitivity and pain occurring at night are typical of CNO. A chronic olecranon stress fracture was considered but ruled out in our patient due to the lack of trauma before the onset of pain, the presence of nighttime pain, and the lack of corroborating findings on MRI. The stability of the patient’s elbow strengthened our suspicion because of the associated ulnar collateral ligament instability with a stress fracture. The clinical course of CNO varies widely and may spontaneously remit over 1-20 years.¹⁰ Unifocal or multifocal bone pain exacerbated by pressure or activity can arise in any bone, although pain presents more frequently in the metaphysis of long bones in children.⁴ When multifocal lesions are present over an extended period, patients are diagnosed with CRMO. Infrequently, regional swelling and warmth may occur over the affected bone(s) in conjunction with fever, malaise, and weight loss.⁶ Inflammatory biomarkers are elevated in about half



Figure 6 Sagittal gadolinium enhanced T1 MRI view at final follow-up demonstrating near-complete resolution of intraosseous edema of the olecranon and of the enthesopathy of the triceps attachment. MRI, magnetic resonance imaging.

of patients, and about one-third of affected individuals have additional autoimmune diseases.^{7,13} Radiographs are generally non-specific for the diagnosis of CNO, as they can be normal or have sclerotic or lytic lesions.²¹ MRI plays a significant role in the diagnosis of CNO and is generally the preferred imaging tool. MRI spares children of the associated radiation with computed tomography (CT) and is more sensitive than CT, radiographs, or bone scintigraphy in detecting inflammatory signs such as edema.^{11,20} There is a paucity of data on Tc-99 scintigraphy and CNO, yet MRI may be more sensitive to the presence of the condition as well as more accurate in defining the extent of the disease process.²² Whole-body MRI offers information regarding the extent of bony and organ involvement. Whole-body MRI may also be used to screen for clinically silent lesions and exclude differential diagnoses.²⁹ However, whole-body MRI is expensive, and because these lesions are typically symptomatic, targeted MRI of symptomatic areas may be the most sensitive and pragmatic approach. Bone biopsies are undertaken in 60%-80% of patients because they provide additional information for excluding diagnoses such as malignancy, Langerhans cell histiocytosis, infection, and fibrous dysplasia.^{14,29} Histologic findings of CNO include infiltrates of normal bone, immune cells, bone lysis, or fibrosis.¹⁵ Bone biopsies are particularly helpful in distinguishing CNO from atypical infections because they present similarly. Atypical infections can be indolent and resemble the pain experienced with CNO, but a more pronounced inflammatory presentation is usually present with infections. Radiologic findings are nonspecific in this setting, and a culture of the causative microorganism along with clinical findings can lead clinicians toward this diagnosis over CNO.

The report highlights the significant improvement in symptoms by treating this condition with NSAIDs. Although the range of motion remained the same, consistent use of medication has improved the patient’s function, and he does not complain of limitations because of the contracture. Ongoing surveillance is planned to determine if the contracture is permanent or spontaneously resolves, as after osteoid osteoma treatment. There is a lack of consensus regarding ideal treatment guidelines for CNO because

of the rarity of the disease and paucity of prospective trials. Therefore, the management of CNO is mainly empiric and based on collective insight from case reports, case series, and expert opinion. Surgery is often not indicated, as NSAIDs such as Naproxen or Indomethacin are an effective and safe first-line approach for patients with CNO that can provide symptomatic relief in approximately 80% of patients with CRMO.^{7,29} Because of this, there is a paucity of data regarding surgical management of CNO. Surgery of the jaw may be done in cases when CNO is misdiagnosed as bacterial osteomyelitis or for contour reduction.^{2,4} Drugs beyond NSAIDs should be considered in patients with minimal relief.²⁸ In this setting, oral steroids may be used with caution, knowing that they can quickly control bone inflammation yet fail to produce long-lasting relief.²⁶ Intravenous bisphosphonates offer another alternative in refractory cases.¹⁸ They may be used in conjunction with or independent of NSAIDs because they inhibit osteoclasts and inflammatory bone loss. Symptoms and radiological improvement typically ensue after the first infusion.^{23,27} However, bisphosphonates may limit growth, and their prolonged half-life produces hesitation over NSAIDs as first-line options in children.²⁵ TNF inhibitors have been proposed as another potential treatment option in refractory cases because of the increased serum concentration of the pro-inflammatory cytokine TNF-alpha in patients with active disease. The role of TNF inhibitors has been limited due to their cost, although most reports have shown promising results regarding symptom and radiological improvement.⁹ Guidance on treatment duration protocol remains unknown because of the lack of clinical trials.

Conclusion

In our patient, a combination of clinical, MRI, and biopsy findings was key to the diagnosis of CNO. The unique location of CNO in the elbow coupled with the flexion contracture expands our understanding of how this challenging disease can manifest. Treatment with Naproxen sodium, in our case, demonstrates how this can provide symptom relief in this subset of patients. Timely identification and diagnosis are paramount, as this disease can progress to arthritis, structural damage, and spondyloarthropathy.^{3,25} The elbow contracture is usually resolved after removing the nidus of the osteoma, yet there is not enough data to support the same conclusion with CNO in the elbow. Finally, further studies are necessary to understand the long-term consequence of this disease as a function of anatomic site of involvement.

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