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Case report on chronic non-bacterial osteomyelitis (CNO) and review of literature

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Abstract
Introduction: Chronic Non-Bacterial Osteomyelitis (CNO) is a rare inflammatory disorder not related to any infectious disease characterized by focal aseptic inflammation with a self-limiting, relapsing course of disease with female predominance and usually observed in paediatric age groups diagnosed by clinical, radiological and histopathological findings after ruling out all other differentials.
Case Report: A case of 6 year old female which presented with non-specific bone pain in the metadiaphyseal region of proximal humerus. X-rays had osteolytic lesions in the metadiaphyseal region and with a history of trivial trauma and no positive history of autoimmunity.
Conclusion: CNO is difficult to identify and no consensus exist on diagnosis and treatment modality. Multifocal bone lesions with characteristic radiological findings are very suggestive of CNO. But dilemma with unifocal lesion with no corroborative findings. In such cases diagnosis is achieved with exclusion. No data exist on best treatment option after Non-Steroidal Anti-Inflammatory Drugs failure. But excision biopsy with complete curettage in unifocal lesions gives immediate symptom relief and long term good outcome without a background of identifiable auto-immune disease.

Keywords: chronic, non-bacterial, osteomyelitis, CNO

Introduction
Chronic Non-Bacterial Osteomyelitis (CNO) is a rare inflammatory disorder not related to any infectious disease [1] characterized by focal aseptic inflammation with a self limiting, relapsing course of disease with female predominance and usually observed in paediatric age groups diagnosed by clinical, radiological and histopathological findings after ruling out all other differentials. It was first described in 1972 by Giedion *et al*. [2] as a symmetric multifocal bone lesions; later, in 1980, Bjorksten B *et al*. [3] first used the term CNO in order to identify a clinical condition which is characterized by recurring episodes or persisting presence of chronic sterile osteomyelitis. Multiple names have been used in literature to describe this disorder; these include chronic recurrent multifocal osteomyelitis (CRMO) in cases with extended multifocal involvement (often symmetric) and synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome (SAPHO), which usually manifests in adolescent and adult patients and which distinguishes for skin involvement [4]. The terms CRMO and CNO are often used interchangeably. Although CNO is still considered a rare disorder, its incidence is probably underestimated. In fact, in a single center retrospective study, it has been recently demonstrated that the incidence of CNO is similar to infectious osteomyelitis [5]. For these reasons, in absence of standardized diagnostic work out and treatment guidelines, it is important to have and understanding of this disease course.

Materials and Methods
Case: A 6 year old female presented with complaints of pain and swelling of the left shoulder since 4 months. The pain was intermittent and dull aching in nature, localised to the left shoulder joint. His shoulder range of motion was restricted and it responded with NSAIDS. There was a history of trivial trauma few months back with a no significant bony abnormality. No significant personal or family history present for the patient. Physical examination showed tenderness over the area and restricted range of motion at left shoulder joint with rise in local temperature and redness.

Constitutional symptoms of fever, weight loss, polyarthralgia and arthralgia were absent. Patient was having overall good general health with normal weight and paediatric milestones as per age. Laboratory results showed normal blood count with consistent negative CRP and normal ESR repeated every 3-5 days. RA factor and HLAB27 are negative as well. On the first presentation X-ray was performed which revealed an osteolytic lesion over the proximal humerus region with minimally displaced fracture of the neck of humerus. On suspicion of osteomyelitis, a contrast enhanced MRI was done which revealed intra-osseus collection in the head of humerus with cortical defect forming sub periosteal collection and multiple bony cloaca in the meta-diaphyseal region connected to the sub periosteal collection. All these radiographic findings along with the clinical history strengthened the presupposition of chronic osteomyelitis. For histopathological and microbiological evidence, the patient underwent saucerization and curettage under general anaesthesia. An incision made over the deltopectoral region with blunt dissection of soft tissues and periosteum elevated to expose the lesion sparing the physis. Frank pus was drained from the lesion. Samples of bone taken and sent for biopsy and culture sensitivity. Biopsy showed unremarkable cartilaginous and collagenous tissues admixed with chronic lymphocytic inflammatory infiltration and no evidence of caseous necrosis, granuloma, atypia or malignancy. Tissue and pus c/s were negative for any organism. Genexpert for MTB was negative. All these findings validate the aseptic nature of lesions and signifies more towards inflammatory nature of the condition.

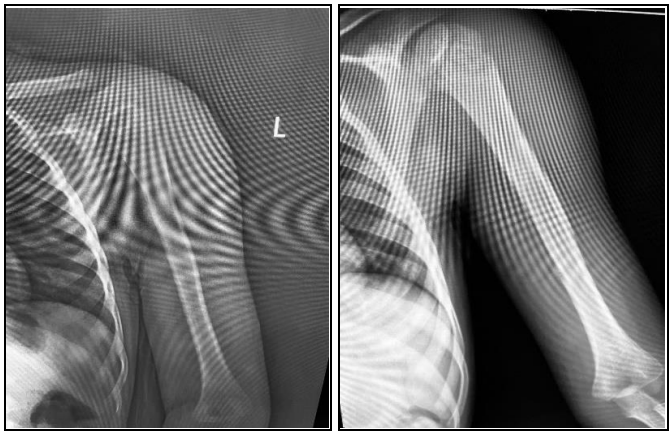


Fig 1: Preoperative X-rays showing osteolytic areas

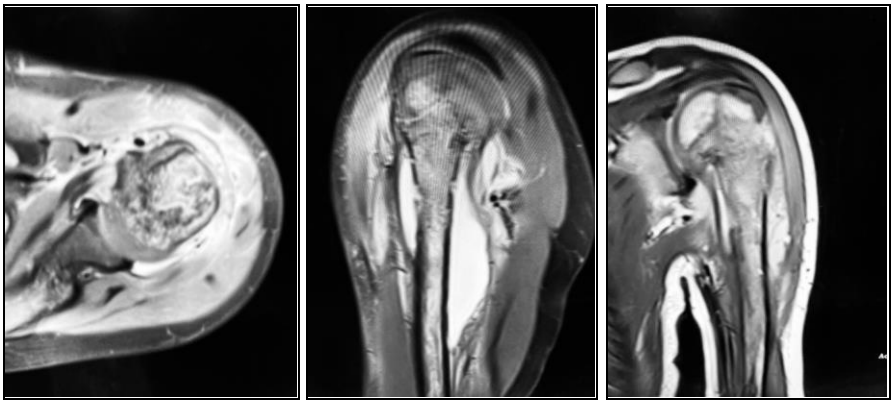


Fig 2: Preoperative MRI-showing the intraossesus and subperiosteal collection with multiple cloaca

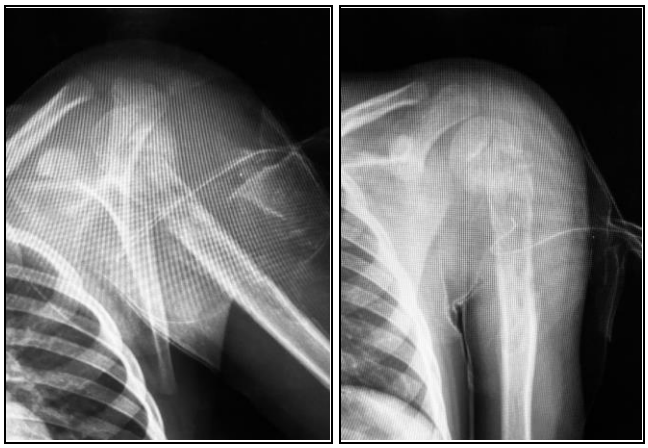
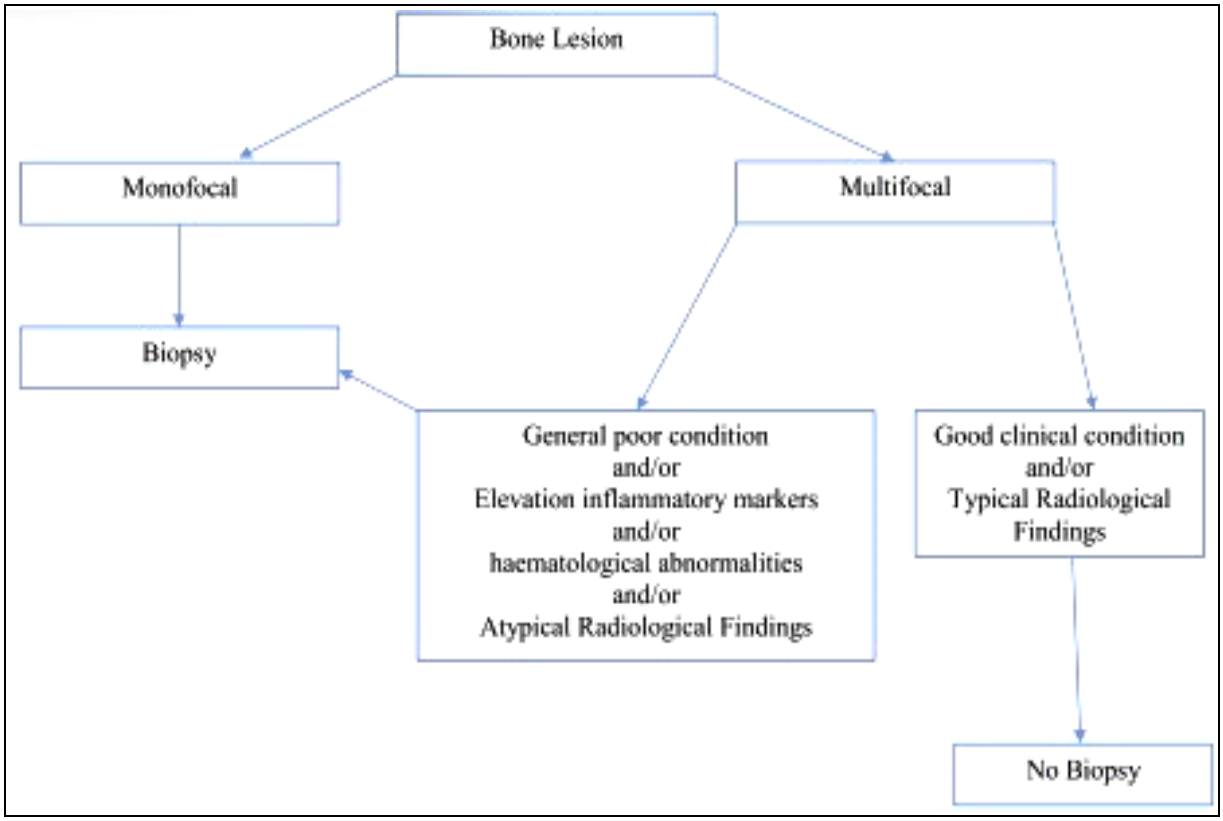


Fig 3: Post-operative X-rays After Excision biopsy and local debridement

Discussion

CNO/CMRO is a diagnosis of exclusion and requires combined clinical, radiological and histopathological data to come to a final diagnosis. Lab tests are nonspecific and may have modest elevation in inflammatory markers like leukocytosis, ESR and CRP. Clinically symptoms may vary from unifocal to multifocal and persistent to relapsing course of the disease. CRMO is frequently associated with other autoimmune disorders like inflammatory bowel disease, peripheral arthritis, sacroiliitis, psoriasis, pyoderma gangrenosum, Takayatsu's arteritis. It is also considered as the paediatric equivalent of SAPHO syndrome [6]. An initial investigation in such cases with bone pain is usually a plain X-ray which at an early stage may not show any significant changes but shows osteolytic or osteosclerotic lesions only in later stages of the disease [7]. On MRI, the investigation of choice, inflammatory lesions are hypointense in T1 and hyperintense in T2/STIR. Bone marrow oedema is also identified through altered marrow signal in contrast enhanced MRI. In culture, aseptic condition in the absence of any antibiotic coverage is necessary to rule out bacterial or fungal osteomyelitis. Genexpert done to rule out tubercular etiology of osteomyelitis. Histopathological findings in CNO are non-specific and usually show inflammatory infiltration. Bone biopsy is done primarily to rule out malignancy or to distinguish it from other condition. The protocol for conducting excision biopsy is demonstrated in flow chart.



There's no existing guidelines to treat CNO at present and empirical treatment is provided to the patient. Generally accepted treatment protocols for CNO do not exist and the treatment of CNO has been largely empiric. A number of retrospective assessments of response to treatment in case reports or small series are available in the literature. Neither Guidelines nor expert consensus treatment do exist for CNO. The first line treatment is usually NSAIDs (mainly naproxen and indomethacin, which have been demonstrated useful for pain control and inducing remission in a percentage of patients and decreasing bone lesions [8] Oral corticosteroids may be used in cases of relapsing symptoms. Bisphosphonates are required in multifocal and spinal lesions. TNF Alpha blockers are used in patients not responding to aforementioned treatments [9]. MRI full body screening is required to visualise any new lesions that may occur.

A long term follow up is required to evaluate for any relapsing symptoms. Case of CNO is quite rare and usually diagnosis is difficult and takes a lot of investigations and long term follow up which are great limitations for research purposes due to migration of patients, loss of follow ups or economic constraints. Sadly, we too have lost follow up of these cases due to the COVID 19 Pandemic. Lack of enough previous literature on the topic has also led to less awareness among the fraternity.

Conclusion

CNO is difficult to identify and no consensus exist on diagnosis and treatment modality. Multifocal bone lesions with characteristic radiological findings are very suggestive of CNO. But dilemma with unifocal lesion with no corroborative findings. In such cases diagnosis is achieved with exclusion. No data exist on best treatment option after Non-Steroidal Anti-Inflammatory Drugs failure. But excision biopsy with complete curettage in unifocal lesions gives immediate symptom relief and long-term good outcome without a background of identifiable auto-immune disease.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest

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