Chronic Recurrent Multifocal Osteomyelitis: Clinical Outcome Following Two Different Treatment Plans with Long Term Follow-Up

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Abstract

Chronic recurrent multifocal osteomyelitis (CRMO) is a rare, inherited auto-inflammatory disease with an unknown genetic cause which predominantly affects children, and is characterized by the insidious onset of periodic bone pain, with or without fever. Diagnosis is difficult and is dependent on the clinical course, imaging, pathology, and microbiology. A large number of drug treatments have been tried with variable success, and medical management includes nonsteroidal anti-inflammatory drugs (NSAIDs), bisphosphonates, azithromycin, tumor necrosis factor α–blocker (infliximab), interferon, and oral steroids. Antibiotics are now thought to have a limited role in light of the inflammatory rather than infective nature of the disease. Surgical treatment has been reported, but its role is not yet clearly defined. Here we report two patients who were diagnosed with CRMO presenting to a District General Hospital. Despite receiving differing drug treatments, one of which included the use of antibiotics, both made a good clinical recovery.

Key words: Chronic recurrent multifocal osteomyelitis, chronic nonbacterial osteomyelitis, sterile osteomyelitis.

Introduction

Chronic recurrent multifocal osteomyelitis (CRMO) is a rare condition affecting approximately one per million of the population. It is an inherited auto-inflammatory disease with an unknown genetic cause. There are many other terms used in the literature to describe disorders in which sterile osteomyelitis predominates as the primary clinical feature; these include Chronic nonbacterial osteomyelitis (CNO), sterile osteomyelitis, or nonbacterial osteitis. CRMO is described as chronic due to the fact that it takes a long time to resolve, recurrent as it is cyclical between active and dormant stages, and multifocal as it can occur at multiple sites at any one time. Each episode can affect a different part of the body. The disease affects those from age 4 to 14, with the median age being 10 years. It is primarily a female disease with a 5:1 ratio [1-3]. Clinical features include nonspecific complaints of pain, swelling, tenderness, and limited ranges of movement at one or more sites. Symptoms can present over a time period of days to years. Most patients present complaining of symptoms at one site, but further sites are usually identified with clinical history and
radiological imaging. CRMO has been associated with skin lesions, and Schultz et al. report their presence to be as high as 25%, with pustulosis being the most common, followed by psoriasis [4].

The most common diagnostic tools are plain radiographs and MRI. Typical imaging findings of CRMO include lytic and sclerotic lesions in the metaphysis of long bones and the medial clavicle which may show an ‘onion skin’ appearance. CRMO is the most common disease process to involve the medial third of the clavicle in all age groups, and is the most frequent non-oncological pathology to affect the clavicle in people aged under 20 years old. [5] However, any site in the skeleton can be involved, with the tibia, femur, pelvis, and spine being the most commonly affected areas [6]. MRI is the most sensitive imaging modality to delineate the extent of the lesions, but the findings are non-specific and do not differentiate from acute bacterial osteomyelitis.

Laboratory tests usually reveal non-specific evidence of inflammation with normal or only minor alterations in CRP, erythrocyte sedimentation rate or full blood count. Cultures of blood and bone are almost always negative.

CRMO is treated empirically with non-steroidal anti-inflammatory drugs (NSAIDs) as a first line, which are reported to be effective in reducing pain, swelling and restricted mobility [7-10]. Historically, antibiotics were routinely prescribed, as in our case; however, studies have shown this to be ineffective. With recently improved knowledge about the inflammatory nature of the disease, other anti-inflammatory medication including corticosteroids, methotrexate, sulfasalazine, colchicine, azithromycin and, more recently, anti-TNF agents has been used for frequent relapses and is reported to be beneficial [11-15] Prognosis for patients with CRMO is good, with most having complete resolution of clinical symptoms with no physical impairment.

We present two cases of chronic recurrent multifocal osteomyelitis (CRMO) treated in two different ways along with their clinical presentation and outcome from a district general with a catchment population of 310,000.

**Case 1**

An 11-year-old boy initially presented as an emergency admission with a 12-month history of acute, chronic left humeral pain and swelling but no specific bony tenderness on clinical examination of the left arm. The patient had a normal appetite and no weight loss. He did not have a history of night sweats, fever or rigors. There was no history of trauma. X-rays taken on admission (Fig. 1) demonstrated an aggressive lesion affecting the diaphysis of the left distal humerus with cortical erosion. The working diagnosis at this time was that of Ewings sarcoma. He underwent a CT scan of the chest and abdomen, which showed borderline axillary lymphadenopathy and no distant metastases. He was then transferred to the regional specialist center for MRI scanning (Fig. 2) and a bone biopsy. Histology reports showed chronic osteomyelitis. Bone scans and plain films were performed, which identified changes on the right distal femur and the left 12th rib. The diagnosis was therefore made of chronic multifocal osteomyelitis; at this point he was commenced on oral Flucloxacillin.

He went on to have recurrent flares of his pain. Elbow flexion has been well maintained with only a loss of the last 5 degrees. Shoulder movements are entirely normal. He has now had follow-up till the age of 20, is participating in fulltime education at college, and is enjoying sporting activities.

![Figure 1. X-ray left humerus](https://example.com/image1.jpg)
Case 2

An 11-year-old girl presented to the orthopedic department complaining of a lump in the region of her left clavicle which had arisen over a 4-month period. Radiographs taken at the time of the referral showed no abnormality. The symptoms had increased in severity in the 3–4 weeks prior to the orthopedic appointment. She was complaining of night pain and difficulty performing physical activities at school. At the time of first review, the child did not complain of any systemic upset, fever or rigors. There had been no history of trauma.

Clinical examination demonstrated a fusiform swelling along the line of the left clavicle which was locally tender. The shoulder range of movement was uninhibited. X-rays taken in the clinic (Fig. 3) demonstrated an expansile, sclerotic lesion in the mid-clavicle which was poorly defined and with loss of the normal bony architecture.

She was discussed with the regional soft tissue and sarcoma expert who advised an MRI of her clavicle to supplement her routine baseline investigations including inflammatory markers. Her CRP was 12, WCC 7.2, and she had normal bone biochemistry. MRI of the left clavicle (Fig. 4) showed gross abnormality of the medial and middle thirds of the left clavicle with exuberant periosteal reaction, expansion and cortical disruption. There was no nearby lymphadenopathy or soft tissue infiltration. The lateral third of the clavicle was spared, as was the sterno-clavicular joint.

She was then transferred to the specialist center for percutaneous core biopsy, which showed benign changes consistent with sterile osteomyelitis, and the diagnosis of chronic recurrent multifocal osteomyelitis was made. At follow-up 3 months later, her clavicle pain was diminishing with the use of non-steroidal anti-inflammatory medication. Clinically, the clavicle is less tender and the lesion appeared to be consolidating on X-rays. Her physical function has also improved.
Discussion

These two cases demonstrate the rare presentation, in a rural district general hospital, along with two differing treatment options for CRMO and the long-term clinical outcome in the first case. Recent evidence suggests that antibiotic therapy is not the treatment of choice, but this has provided relief and clinical improvement in our first case which has been maintained into adulthood. Recent literature supports the use of biological agents which have not been used in either of these cases and may be something to report at a later date. CRMO is a rare disease, which is generally a diagnosis of exclusion. In light of the two presentations within a district general hospital, it is important for clinicians to be mindful of the condition and include it in their differential diagnosis when a patient presents with these symptoms or signs and other more sinister pathologies have been fully excluded.

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References