Case Report / *Olgu Sunumu*

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# Chronic Recurrent Multifocal Osteomyelitis in the Youngest Patient

## Kronik Rekürren Multifokal Osteomiyelit: En Genç Pediyatrik Olgu

Kübra Nur Erdoğan[1](İD), Mustafa Gençeli[2](İD), Özge Metin Akcan[2](İD), Buğra Kaya[3](İD), Ülkü Kerimoğlu[4](İD), Sıdıka Fındık[5](İD)

[1] *Department of Pediatrics, Necmettin Erbakan University Meram Faculty of Medicine, Konya, Türkiye*
[2] *Division of Pediatric Infectious Diseases, Department of Pediatrics, Necmettin Erbakan University Meram Faculty of Medicine, Konya, Türkiye*
[3] *Department of Nuclear Medicine, Necmettin Erbakan University Meram Faculty of Medicine, Konya, Türkiye*
[4] *Department of Radiology, Necmettin Erbakan University Meram Faculty of Medicine, Konya, Türkiye*
[5] *Department of Medical Pathology, Necmettin Erbakan University Meram Faculty of Medicine, Konya, Türkiye*

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**Abstract**

Chronic recurrent multifocal osteomyelitis (CRMO) is a rare idiopathic inflammatory disease characterized by non-bacterial osteomyelitis. Diagnosis is established after excluding other potential causes. The disease typically manifests between the ages of 5 and 10 years, with bone pain being the most common presenting symptom. We present a case of a three-year and 11-month-old patient who presented with inability to walk and was subsequently diagnosed with CRMO, representing the youngest patient reported in the literature. In cases of multifocal osteomyelitis not attributed to infectious causes or unresponsive to antibiotic therapy, CRMO should be considered within the differential diagnosis.

**Keywords:** Inflammation, child, non-bacterial osteomyelitis, bone pain

**Öz**

Kronik rekürren multifokal osteomiyelit (KRMO), bakteriyel olmayan osteomiyelit ile karakterize nadir görülen idiyopatik enflamatuvar bir hastalıktır ve tanısı diğer tanılar dışlanarak konur. Bu hastalık genellikle 5 ile 10 yaşları arasında ortaya çıkar. En sık başvuru nedeni kemik ağrısıdır. Bu çalışmada, yürüme güçlüğü ile başvuran ve KRMO tanısı alan üç yaş 11 aylık olan literatürdeki en genç hasta sunulmaktadır. Multifokal osteomyelitin ayırıcı tanısında, antibiyotik tedavisine yanıt alınamayan ve enfeksiyöz kaynaklı olmayan olgularda KRMO olasılığı göz önünde bulundurulmalıdır.

**Anahtar Kelimeler:** Enflamasyon, çocuk, bakteriyel olmayan osteomiyelit, kemik ağrısı

## Introduction

Chronic recurrent multifocal osteomyelitis (CRMO) is an uncommon idiopathic inflammatory condition characterized by non-bacterial osteomyelitis. The diagnosis of CRMO is complex and requires excluding other potential causes of bone inflammation, such as infections, tumors, and other autoimmune diseases. About 400 cases of CRMO have so far been documented in the literature. The true prevalence of CRMO is likely underestimated due to the non-specific nature of symptoms, which makes establishing a definitive diagnosis challenging (1,2). Patients with CRMO typically present with bone pain and swelling at the affected site. On average, three or four lesions are observed, often affecting the long bones of the lower extremities, pelvis, vertebrae, and clavicles (3,4). Symptoms may relapse, remit, and migrate

**Correspondence Address / Yazışma Adresi**
**Kübra Nur Erdoğan**
Department of Pediatrics,
Necmettin Erbakan University
Meram Faculty of Medicine,
Konya, Türkiye
**E-mail:** kubranurerdogan29@gmail.com

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to different bones over time (5). Here we report a case of a three-year and 11-month-old patient who presented with inability to walk and was ultimately diagnosed with CRMO, representing one of the youngest such cases documented in the literature to date.

## Case Report

A previously healthy three-year and 11-month-old female presented to another medical facility with complaints of abdominal pain, back pain, and difficulty walking. Ceftriaxone was initiated under the provisional diagnosis of pyelonephritis. However, due to the negative urine culture and lack of symptom improvement with antibiotic therapy, pyelonephritis was ruled out, and magnetic resonance imaging (MRI) was performed. Subsequently, the patient was referred to our clinic with a preliminary diagnosis of osteomyelitis. At admission, the patient reported persistent back pain and inability to walk. These complaints were not associated with any recent trauma or febrile infection. The patient's pain was present both during the day and throughout the night. A thorough review of the patient's medical history revealed no other pertinent findings. Physical examination revealed tenderness to palpation at the proximal side of the right clavicle and sacral region. The remainder of the physical examination findings were unremarkable. Laboratory findings were as follows: White blood cell count= 6.9 x $10^3$/μL (reference range 4-10 x $10^3$/μL), hemoglobin= 10.3 g/dL, platelet count= 450 x $10^3$/μL, erythrocyte sedimentation rate (ESR)= 11 mg/h, and C-reactive protein (CRP)= 5.4 mg/L (reference range 0-5 mg/L). Peripheral blood smear test detected no atypical cells or blasts. Brucella agglutination and tuberculin skin tests yielded negative results. Abdominal ultrasonography and urine vanillylmandelic acid levels were within normal limits. Immunologic evaluation revealed no significant abnormalities. Chest radiography showed no signs of mediastinal enlargement or lymphadenopathy, however a lytic and sclerotic lesion was observed on the clavicle (Figure 1).

To rule out infectious osteomyelitis and malignancy, as well as to identify any other potential areas of concern, positron emission tomography/computed tomography (PET/CT) imaging was performed. The PET/CT scans revealed lytic lesions with surrounding soft tissue components showing increased uptake of 18F-Fluorodeoxyglucose (FDG) at the proximal end of the right clavicle [standardized uptake value $(SUV)_{max}$= 3.38] and in the middle part of the sternum ($SUV_{max}$= 3.66) (Figure 2). Besides, focal FDG uptake was observed in the left half of the sacrum ($SUV_{max}$= 1.98), left ischium ($SUV_{max}$= 1.20), and the trochanteric region of the right femur (SUV max= 2.09). These findings suggested the presence of active inflammation in these areas.

Bone biopsy samples were obtained from both the medullary and cortical regions to further characterize the lesions and to differentiate a diagnosis of Langerhans cell histiocytosis (Figure 3). Comprehensive microbiological examinations, including culturing, were performed on the biopsy specimens to exclude infectious causes. The combined results of these investigations, along with the patient's clinical presentation, led to the definitive diagnosis of CRMO. Naproxen therapy was initiated, and the patient exhibited significant improvement in symptoms following the treatment.

## Discussion

Chronic recurrent multifocal osteomyelitis is a rare inflammatory bone disease of unknown etiology, believed to have an autoimmune origin. Diagnosis is based on integrated clinical, laboratory, and radiological findings, after the exclusion of alternative diagnoses. This condition typically manifests in children aged five to 10 years old (6). Our case stands out due to the patient's remarkably young age, as she is the youngest reported patient in the current literature.

Bone pain is typically the primary reason for seeking medical care. Our patient presented with bone pain and inability to walk. While non-specific laboratory abnormalities such as

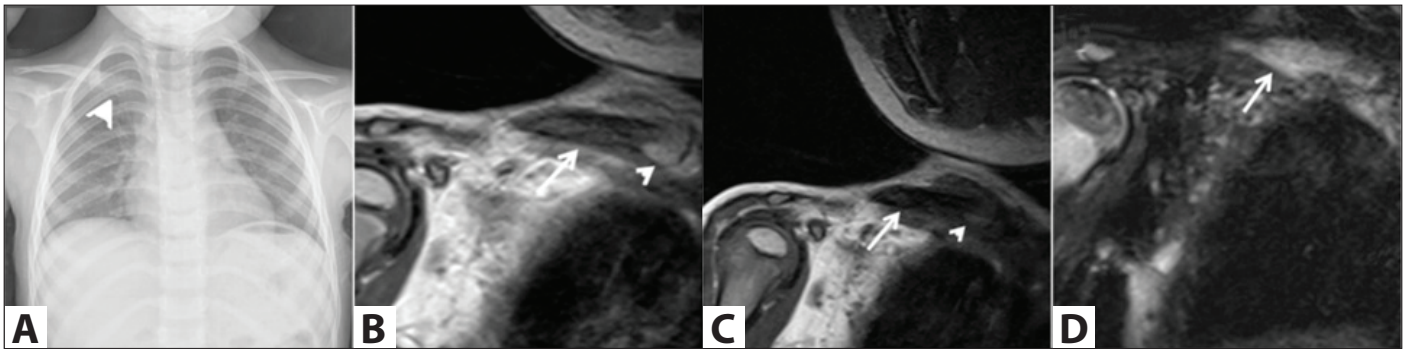


**Figure 1. A.** Lytic and sclerotic lesion on the right clavicle on X-ray (arrowhead). **B.** Coronal T2 weighted fat saturated image demonstrates medullary edema of clavicle (arrow). **C.** Coronal T1 weighted image obtained before administration of contrast material demonstrates hipointensity (arrow) in the medulla of clavicle related to sclerosis as well as increased soft tissue intensity (arrowhead) and capsular distension of sternoclavicular joint. **D.** Coronal T1 weighted image obtained after administration of contrast material demonstrates marked enhancement of the medulla (arrow) and joint (arrowhead) secondary to inflammation.

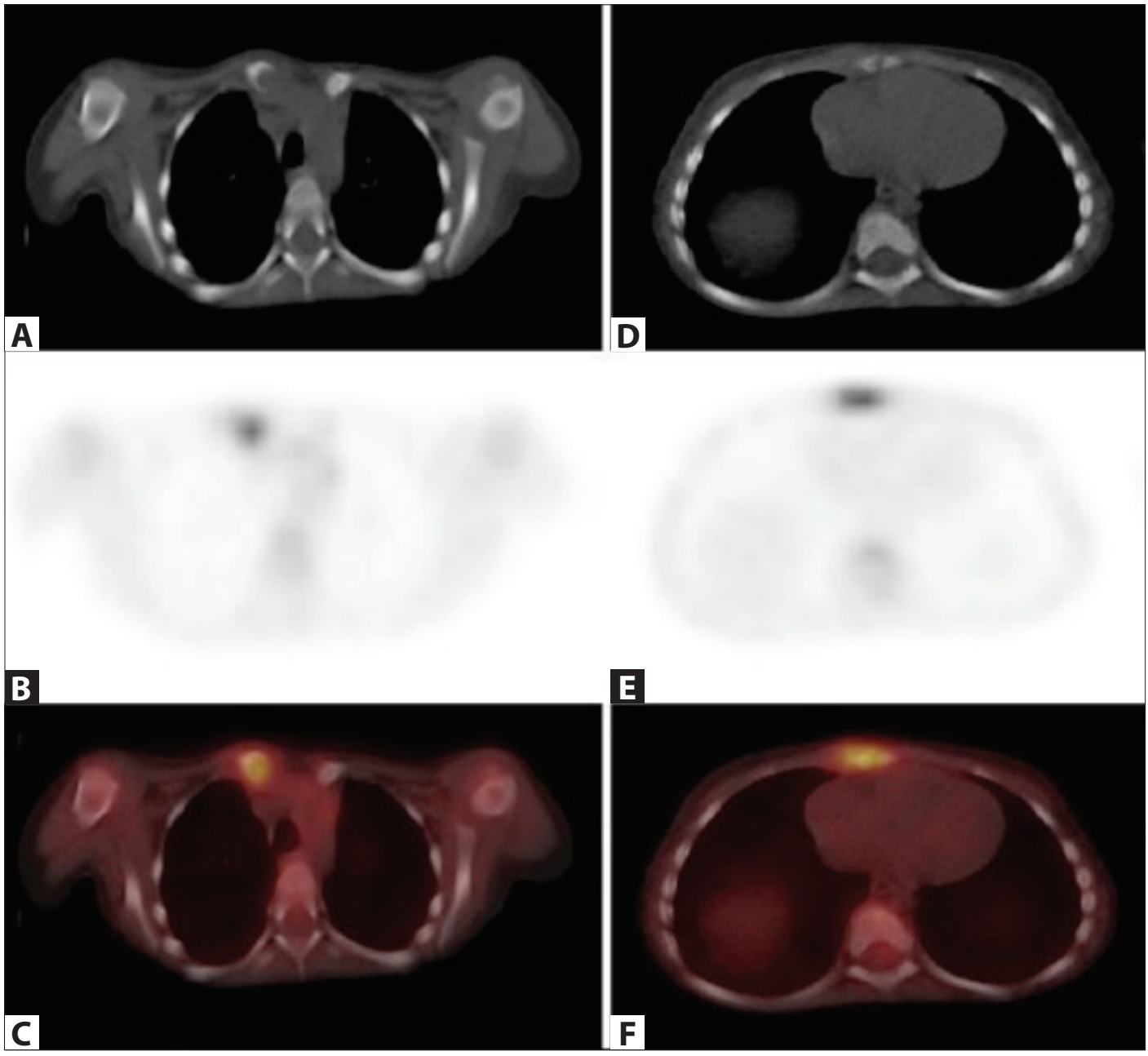


**Figure 2.** FDG uptake at the proximal end of the right clavicle (**A.** CT, **B.** PET and **C.** PET/CT) and in the middle part of the corpus sterni (**D.** CT, **E.** PET and **F.** PET/CT).

leukocytosis and mildly elevated ESR can occasionally be observed, findings are usually unremarkable. Laboratory results for our patient were consistent with this. Radiologically, CRMO can be difficult to distinguish from bone neoplasms (7). Positron emission tomography/computed tomography scans can be helpful in identifying active inflammation and differentiating CRMO from other conditions. Histological analysis of bone lesions helps rule out malignant processes, though the appearance of CRMO may mimic acute and secondary chronic osteomyelitis caused by microbial infection (8).

Chronic recurrent multifocal osteomyelitis can exhibit a variety of appearances on plain radiographs, including purely osteolytic, osteolytic with a sclerotic rim, mixed lytic and sclerotic, and purely sclerotic, as described in literature (9). In our patient's chest X-ray, a lytic and sclerotic lesion was evident on the clavicle. However, it is crucial to note that MRI remains the most sensitive imaging modality in differential diagnosis. MRI findings in patients with CRMO typically demonstrate increased intensity of the short time inversion recovery (STIR) signal within the

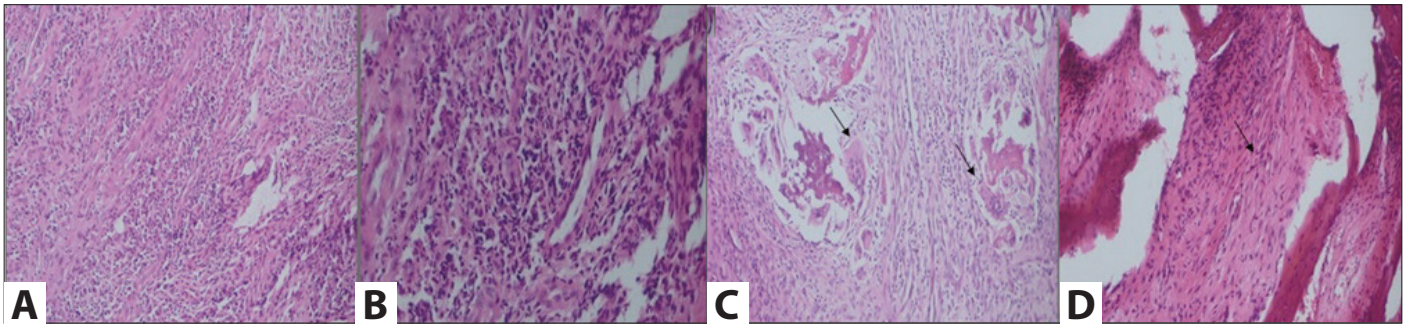


**Figure 3. A,B.** Hematoxylin and eosin (H&E) (x100 and 200) stained bone biopsy in the early phase of CRMO. Neutrophils are the predominant cell types. **C.** H&E stained bone biopsy showing chronic inflammation in CRMO with monocytes, lymphocytes and plasma cell infiltration. Black arrows show the osteoclastic giant cells in fibrosing stroma. **D.** H&E stained biopsy of the late chronic fibrosing stage in CRMO.

bone marrow and surrounding tissues, along with bone expansion (10). The imaging findings in our case are consistent with those described in the literature. Specifically, we observed increased sclerosis in the right clavicle and infiltrative signal changes in the focal area of the medulla adjacent to the sternoclavicular joint. In order to identify lesions that exhibit FDG uptake throughout the body, a PET/CT scan is performed as a comprehensive imaging modality for a thorough assessment of such lesions. In our case, we observed lytic lesions with surrounding soft tissue components exhibiting FDG uptake. They were localized to the proximal end of the right clavicle and in the middle part of the sternum. Focal FDG uptake was also detected in the left half of the sacrum, left ischium, and the trochanteric region of the right femur. Given the non-infectious nature of CRMO, antibiotics are not employed as a treatment modality. Instead, non-steroidal anti-inflammatory drugs (NSAIDs) serve as the first-line therapeutic approach. In our patient's case, naproxen, an NSAID, was administered, resulting in a significant improvement in her clinical presentation. In patients showing an inadequate response to NSAIDs, there is no universally established second-line treatment strategy for CRMO. A variety of medications have been employed in this context, including corticosteroids, methotrexate, sulfasalazine, bisphosphonates, anti-tumor necrosis factor agents, and interleukin-1 receptor antagonists (2). The choice of second-line therapy is often guided by individual patient factors and specific characteristics of their CRMO presentation.

Several reports in the literature describe patients with similar symptoms who were ultimately diagnosed with CRMO. For instance, a 10-year-old female presented with persistent right shoulder pain that had lasted for a year. A comprehensive clinical evaluation, including laboratory tests, radiographic imaging, and a bone biopsy, led to the diagnosis of CRMO (11). Another case highlights potential for misdiagnosis and the need for comprehensive investigation. A 4.5-year-old female was initially treated with long-term antibiotics for six months under the presumption of chronic bacterial osteomyelitis. However, further evaluation confirmed the diagnosis of CRMO and she was successfully treated with NSAID therapy (12). In another instance, a 13-year-old female presented with left thigh swelling. Initial imaging raised concerns about malignancy, but a biopsy revealed non-specific osteomyelitis. A subsequent biopsy confirmed CRMO, and during hospitalization, she developed a secondary lesion in the left humerus, further solidifying the diagnosis (13). This case, in particular, highlights the potential for CRMO to mimic other conditions and complicate the diagnosis.

## Conclusion

In conclusion, the non-specific nature of symptoms and the potential for misdiagnosis make it imperative for healthcare providers to maintain an acute clinical awareness, conduct thorough evaluations, and consider a broad differential diagnosis in cases of multifocal osteomyelitis, especially when there is no evidence of infection and antibiotic treatment is ineffective.

**Informed Consent:** Patient consent was obtained.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - KNE, ÖMA; Design - MG; Supervision - ÜK; Resource - BK; Data Collection and/or Processing - KNE, SF; Analysis and/or Interpretation - SF; Literature Search MG; Writing - KNE; Critical Review - ÖMA, ÜK.

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