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BMH Med. J. 2025;12(3):34-39. **Case Report**

A Child With Puzzling Pain And Swelling Of Bones - Chronic Recurrent Multifocal Osteomyelitis

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Abstract

Chronic Recurrent Multifocal Osteomyelitis (CRMO) or Chronic Non-bacterial Osteomyelitis (CNO) is primarily a skeletal disorder of obscure etiology affecting children and adolescents. It is characterized by episodic bony pain and swelling over several years. Unfortunately, pediatricians are not very familiar with this rare inflammatory disorder. If it is not diagnosed and treated promptly, it may subsequently lead to bone destruction. The objective of this case report is to give an overview of this extremely rare disease and to make pediatricians aware of it.

Keywords: Chronic recurrent multifocal osteomyelitis, Autoinflammatory bone diseases, Pustulosis palmoplantaris, MRI

Case report

A young girl, the third child of non-consanguineous parents, immunized up to age, and with normal development, presented with complaints of recurrent pain and swelling of bones for 7 months. It started insidiously in the left lower leg associated with difficulty in walking apparently after she participated in a running race at school, and it subsided in a week with analgesics alone. Two months later, she developed pain over the lower left thigh and difficulty in walking. Her vitamin D level was found to be low by her general practitioner and she was given vitamin D supplements, and analgesics, and her symptoms subsided in a week.

Three months later, she developed similar pain over the left thigh and hence was investigated. Her Hb was 11.7g/dL, TLC 10800/mm^3 (polymorphs 59%, lymphocytes 37%, E 4%) ; RBC 4.5 million/mm^3 and platelet 4.6 lakh/mm^3 . Her peripheral smear was normal except for mild neutrophilia , ESR was 66 mm/1st hour and CRP 38 mg/L. CK was normal (170 U/L).

She was put on prednisolone and analgesics for one week following which her symptoms gradually subsided. One month later, she developed fever, pain and minimal swelling over her right elbow

with mild restriction of movements, followed by pain in the right ankle joint. After a few days, she also developed pain and swelling over the medial end of the left clavicle and pain in the sacrococcygeal area. This time her pain was excruciating and disturbing her sleep, and she even had to be carried to the toilet. She also developed a few vesiculopustular lesions over both palms. There was no history of similar illness in the family. Investigations showed normal leukocyte count with mild neutrophilic predominance(TLC 8910/mm^3, P 55%, L 45%, E 5%); platelet 4.6 lakh/mm^3. ESR was 75mm/1st hour and CRP 55 mg/L. Peripheral smear showed a normochromic normocytic blood picture; there was no evidence of leukemia. PT, INR and aPTT were normal. As her ASO titre was 740 IU/mL she was diagnosed with rheumatic arthritis and put on aspirin. Her repeat ASO after one week was only 50 IU/mL. Transaminases, T4 and TSH were normal. Serum calcium was 9.5 mg/dL and serum vitamin D was 20 ng/mL (normal 20-40 ng/mL). As she was not improving, she was referred to us for further evaluation.

She looked very sick and was carried to our OP by her father. Her vitals were stable. Temperature was 99 degrees F. Her weight (20.5 kg), was below the 3rd centile and height (128cm) was between the 3rd and 10th centiles. She had mild pallor. Her submandibular and left supratrochlear lymph nodes were enlarged, firm and tender. There was a firm tender swelling over the medial end of the left clavicle (**Figure 1**) and the right ankle joint. Both palms showed erythematous, scaly plaques suggestive of pustulosis palmaris (**Figure 2**). There were no cutaneous manifestations of rheumatic fever such as erythema nodosum, erythema marginatum or subcutaneous nodules. Her liver and spleen were not palpable. Heart sounds were normal and there was no murmur. Liver function tests were essentially normal except for mild elevation of alkaline phosphatase (420 IU/L). HIV, anti-HCV and HBsAg were negative. ANA screening was positive but ANA profile and RF were negative. Ultrasonography of abdomen and color Doppler echo of heart were normal. A radiograph of the pelvis showed subchondral marrow edema of left S2-S5 sacral alae and sacrococcygeal region (**Figure 3**). MRI screening showed diffuse bilaterally symmetrical, multifocal areas of marrow edema in the medial ends of clavicles, right humeral metaphysis, distal ends of both tibia, right fifth metatarsal bone, right sacral ala and sacrococcygeal region (**Figure 4**).

Based on the long history, atypical location of lesions, and dermatologic and imaging findings, a provisional diagnosis of CRMO, possibly active stage of the disease, was made. She was started on ibuprofen 40 mg/kg/day in 3 divided doses and pantoprazole. She responded well to treatment, and her pain and swelling gradually subsided. She became active and gradually could walk, run and climb stairs with ease. She was discharged after 10 days on ibuprofen and kept under follow-up and subsequently, the dose of ibuprofen was tapered to 10 mg/kg/day. Her acute phase reactants came down (ESR 18, CRP 8). She did not have any relapse even on this low dose for the next 8 months. However, a few months later, her parents stopped the medication of their own and within a week she again developed similar swellings and severe excruciating pain over right clavicle and right ankle. Investigations revealed high acute phase reactants. She was restarted on full dose ibuprofen but was subsequently lost for follow-up.

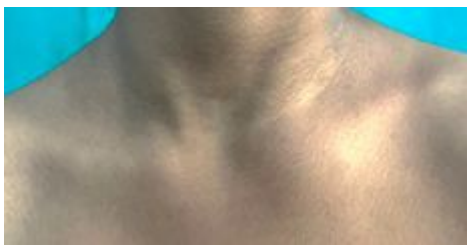

Figure 1. Swelling of medial end of left clavicle

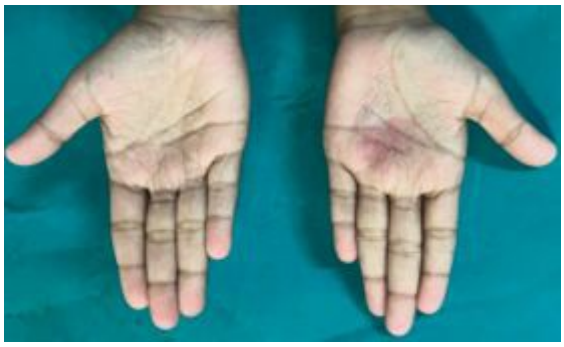

Figure 2. Bilateral pustulosis palmaris

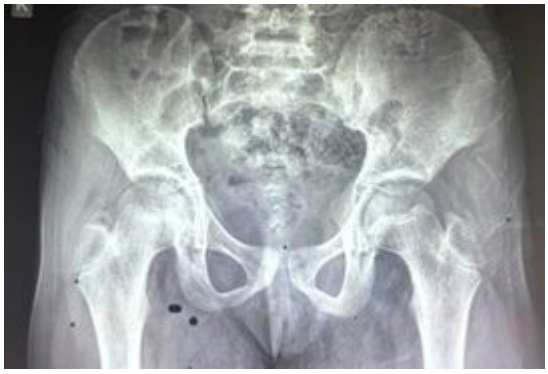

Figure 3. Subchondral marrow edema of left S2-S5 sacral alae and sacrococcygeal region

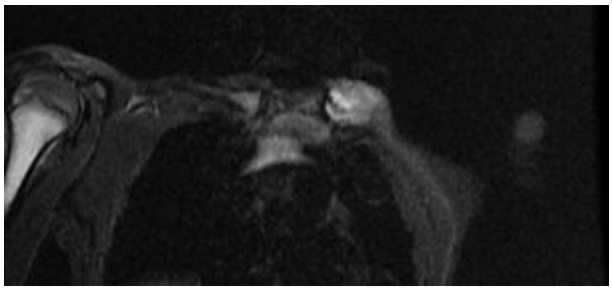

Figure 4. MRI showing diffuse STIR hyperintense marrow edema of the metaphysis of the right humerus and medial ends of both clavicles

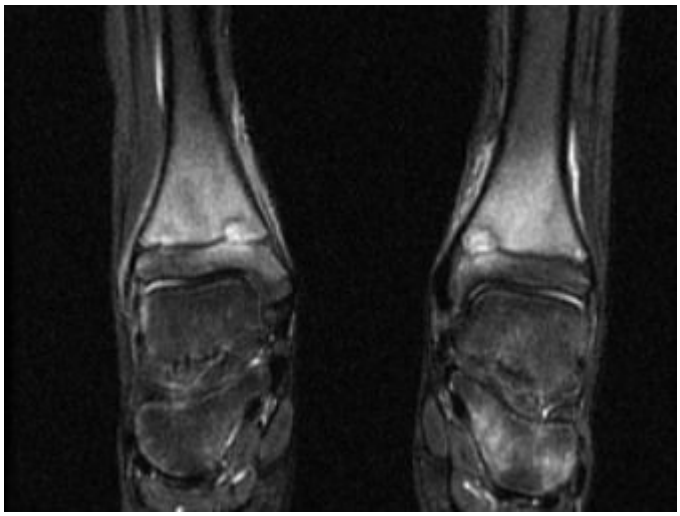

Figure 5. MRI showing diffuse bilaterally STIR hyperintense marrow edema in distal metaphysis of both tibia

Discussion

Autoinflammatory bone disorders are a recently described entity due to unprovoked activation of the innate immune system resulting in an osseous inflammatory process. Culture and histopathology of the lesions do not reveal any organism [1]. The common autoinflammatory bone diseases seen in children are Chronic Recurrent Multifocal Osteomyelitis (CRMO); Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis (SAPHO) syndrome; Majeed syndrome; Deficiency of Interleukin-1 Receptor Antagonist (DIRA); and cherubism [2].

CRMO was described first by Giedion et al in 1972 as "an unusual form of multifocal bone lesions with subacute and chronic symmetrical osteomyelitis" [3]. CRMO may be either sporadic or a part of an autoinflammatory disorder such as Majeed syndrome [4].

The exact etiology of CRMO continues to be elusive. It is thought to be a non-infectious inflammatory disorder but both environmental factors and genetic factors may play significant roles. There may be an overlap in the clinical manifestations of CRMO with some monogenic autoinflammatory conditions. However, no single gene defects contributing to the pathogenesis of CRMO could be identified in various studies [5].

Bjorksten and Boquist in 1980 noted its association with pustulosis palmoplantaris and coined the term "chronic recurrent multifocal osteomyelitis" [6]. CRMO is a very rare disease occurring primarily in children and adolescents with only about 500 cases being reported so far worldwide. This may be because of a lack of awareness of CRMO amongst pediatricians and the lack of good diagnostic criteria [7].

Even though CRMO generally has an unpredictable long-term course lasting from 7 to 25 years, many cases are self-limited resolving without serious sequelae. However, premature closure of epiphyses, kyphosis and bony deformity may be rarely seen [8].

The most common site of pathology is the metaphysis of tubular bones such as the distal femur, proximal tibia, distal tibia and distal fibula, followed by clavicles, mandibles and spines. Occasionally, the ribs may also be affected. It may recur at previously affected sites or may affect new areas along with flare-ups, associated with malaise and low-grade fever. Based on the number of areas affected, it may be unifocal or multifocal [9] Skull bones are usually spared in CRMO. Hence, excluding more serious conditions such as Langerhans cell histiocytosis (LCH) is important if skull bones are affected [10].

CRMO is more common in female children (up to 85%), with the median age of onset being 10 years. The insidious onset of bone pain and recurrent or persistent warmth and swelling are the significant manifestations of CRMO. The diagnosis of CRMO is possible only after ruling out other conditions with a similar picture, based on the following criteria: atypical location of lesions compared to infectious osteomyelitis, frequent involvement of clavicle, absence of fistula, abscess or sequestrum, characteristic prolonged, fluctuating course with recurrent episodic pain lasting several years; and accompanying pustulosis palmoplantaris or acne.

Imaging, laboratory findings and histopathologic features are usually suggestive of subacute or chronic osteomyelitis. The absence of periosteal elevation or sequestra formation helps to exclude pyogenic osteomyelitis, which is the most important differential diagnosis.

Some conditions associated with CRMO include palmoplantar pustulosis (PPP), psoriasis, inflammatory bowel disease, Sweet syndrome, pyoderma gangrenosum, and Takayasu pulseless disease [11]. PPP is the most common associated skin condition and it usually worsens with flares.

As infectious osteomyelitis is the most important differential diagnosis, CBC, CRP, and ESR should be done in all children with suspected CRMO. These will be usually minimally elevated in most patients with CRMO [12]. However, moderate elevation of ESR and CRP may be seen in some patients, as was seen in our patient. Even if musculoskeletal symptoms are not present, patients with FUO (fever of unknown origin) may still be suspected of having CRMO and should undergo an MRI for diagnosis [13].

Even though CRMO is a very rare disease, as pediatricians become more aware of it, more cases may be diagnosed and treated promptly in future which will improve its ultimate prognosis.

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