Case Report

Chronic Recurrent Multifocal Osteomyelitis: An Unusual Cause of "Aches and Pains"

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Abstract

Children are often brought to the paediatric out-patient department with non specific aches and pains. Though the majority of them have only a benign diagnosis, some may harbour rare conditions like chronic recurrent multifocal osteomyelitis (CRMO). Case: We describe a 11 year old girl who presented with migratory pain across various parts of hip and lower limbs without any significant signs. After six months of OPD visits, she was diagnosed to have CRMO following an incidental X-ray which led to a musculoskeletal MRI. Conclusion: CRMO is a rare auto-inflammatory disorder which must be kept in mind when encountering a relatively healthy child with poorly defined limb pains along with paucity of signs.

Key words: Aches and pains; auto-inflammatory; chronic recurrent multifocal osteomyelitis (CRMO)

Introduction

Musculoskeletal 'aches and pains' in children, without any systemic involvement constitute an important fraction of the paediatric out-patient workload. It becomes more worrisome when children are in early adolescence during which several psychological issues may add to interplay of factors. Growing pains are considered to be a common cause responsible for lower limb pains.[1] Amidst apparently benign causes, one may rarely encounter a condition like chronic non bacterial osteitis (CNO) or chronic recurrent multifocal osteomyelitis (CRMO). CRMO is a rare auto-inflammatory bone disorder which has been increasingly recognized since last few decades.[2] We report a child with non specific lower limb pain who was diagnosed to have CRMO six months after onset, during which she visited multiple specialties.

Case Report

A 11 years old girl child, developmentally normal with no significant past history, reported to us with a six months history of multifocal lower limb pains. The pain started in the right ankle and gradually remitted in three months with no local signs. Her ankle X-ray was normal. She was diagnosed as tendonitis and put on NSAIDs by the orthopaedician. Following this, the pain migrated over outer aspect of right mid thigh, left mid thigh, left knee and left ankle without signs of inflammation. There was no restriction of joint movements. Her repeat

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X-ray of the right ankle had a suspicious finding [Figure 1a]. Clinical evaluation revealed a healthy looking child with normal anthropometry. She only had pain in the left thigh and both ankles (left > right) without any redness, swelling or joint limitation. She had no other relevant history such as fever, rash or constitutional symptoms.

Her haemogram, peripheral blood smear, routine biochemistry including CPK and ionised calcium, serology and autoimmune profile (ASO, RF, Anti-CCP, ANA, ANCA) were all normal. Two ESR values over a fortnight were 22 mm and 50 mm (Westergren). CRP was initially negative followed by a value of 10 mg/L. HLA-B27 was negative, Mantoux-negative, chest x-ray, USG-abdomen and echocardiography – normal. 25-OH Vit D levels were however low (9.8 ng/ml). The x-ray and MRI of ankles, knees, hip and pelvis were done. The radiological survey revealed focal lytic lesion distal metaphysis of right tibia, widening of physis of greater trochanter with marrow edema of left femur, lytic lesion with marrow edema of ischio-pubic synchondrosis (Right) (Figure 1 a, b, c and 2 a, b, c, d). A screening MRI of clavicles and spine thereafter did not reveal any abnormality. This showed a mismatch between sites of pain and radiological findings.

A diagnosis of CRMO was considered based on the overall profile, radiological findings and accepted scoring systems. She was given a course of vitamin D and calcium for the associated Vitamin D deficiency and then started on prednisolone 2 mg/kg/day for a week followed by a taper over next one week along with naproxen 15 mg/kg in two divided doses. However, she developed a rash and hence was switched to indomethacin 25 mg TDS. Over the next eight months, she showed steady improvement. The clinical areas of involvement dropped to zero from four, radiological areas of involvement (repeat MRI was done) dropped to one from three, and there was a significant improvement. Both ESR and CRP levels were normal on follow up. An 18 FDG PET bone scan done at this point did not reveal any abnormal uptake. The child is presently asymptomatic, off medications (since 12 months) and on close follow up.

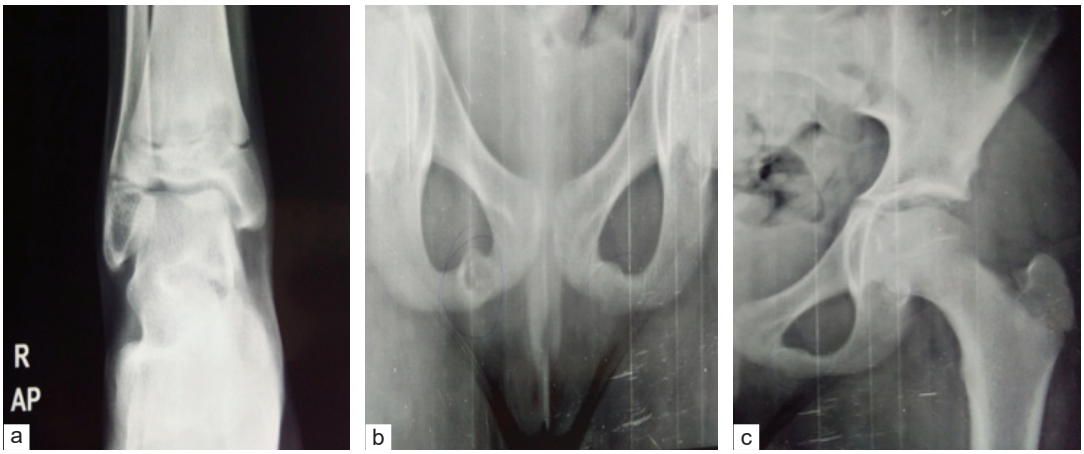

Fig. 1: X-rays depicting the lytic bone lesions
(a) Lytic lesion distal end of tibia (R) (b) Lytic lesion ischio-pubic ramus (R)
(c) Lytic lesion greater trochanter (L)

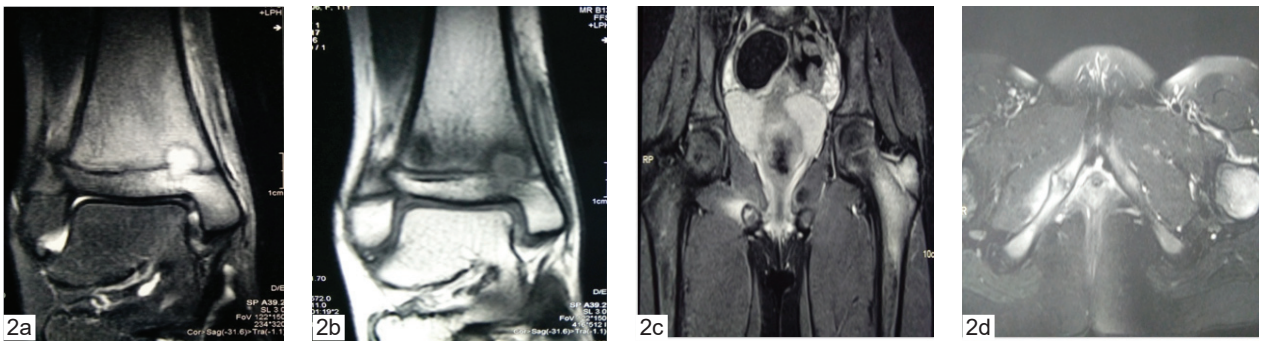

Figure 2. MRI showing involvement of the bones.
2a - STIR hyperintensity of distal metaphysis of Tibia (R)
2b - Lesion over distal tibial (R) metaphysis hypointense on T1
2c - STIR hyperintensity of greater trochanter, proximal neck and diaphysis (L) with widening
2d - STIR edema right ischio-pubic ramus (R) with soft tissue edema

Discussion

CRMO is a rare inflammatory bone disease which was first described in 1972 as an unusual form of multifocal bone lesions with subacute and chronic symmetrical osteomyelitis.3 It belongs to the group of auto-inflammatory disorders which is characterised by an abnormal activation of innate immune system and an absence of antigen specific T cells and auto-antibodies. It is presumed that an underlying genetic abnormality predisposes to activation of the pattern recognition receptors on monocytes/macrophages by danger associated molecular patterns, resulting in activation of the inflammasome and massive cytokine release giving rise to the sterile inflammation and disease manifestations.[2] These include many periodic fever syndromes and non-periodic fever syndromes. Some of the non-periodic fever group of disorders like Majeed syndrome, SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis), DIRA (Deficiency of IL-1 Receptor Antagonist) and CRMO have osseous involvement.4 CRMO affects females more than males at a ratio of 2:1-5:1.2,5 Patients are typically children or adolescents, presenting with bone pain, which may occur with tenderness, swelling, and other inflammatory signs. Symptoms are typically intermittent, lasting weeks to months, after which they may remit and relapse. The mean duration of active disease is between two and five years.[6] In more than 70% cases, the bones of lower limbs, pelvis and clavicle are involved. Up to 25% of cases of CRMO may have manifestations involving skin and gastrointestinal system. The diagnosis revolves around clinical and radiological criteria which may help obviate a bone biopsy.[7] Bone scans are also considered useful though found to be inferior to MRI.[8] Treatment ranges from trial of NSAIDs, steroids, sulphasalazine, methotrexate, bisphosphonates and TNF-blockers in an algorithmic fashion depending on the response.[2] In our child, the diagnosis was corroborated with both the Bristol and Jansson criteria[9,10] (Jansson score-45) and bone biopsy was not performed. The odd features were the complete lack of signs and a mismatch between sites of MRI findings and pain, with some radiological lesions not manifesting with any pain.

Conclusion

Though the last few decades have witnessed an increased awareness of auto-inflammatory bone disorders, they continue to be under diagnosed or diagnosed late.[9] This report aims to highlight this enigmatic condition and increase the awareness amongst general practitioners and paediatricians so that they consider CRMO in the differential diagnosis of non specific aches and pains in children.

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