

## Multicentric Carpotarsal Osteolysis Mimicking Juvenile Idiopathic Arthritis

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### Abstract

#### Background

Multicentric carpotarsal osteolysis (MCTO), a skeletal dysplasia presents in early childhood mimicking juvenile idiopathic arthritis (JIA). Recognition of this syndrome is essential to avoid unnecessary treatment with immunosuppressive agents because of different course and treatment.

#### Case Report

A 3-year-old boy presented with swelling and restriction of right wrist joint and left ankle joint. Possibility of Oligoarticular (or pauciarticular) JIA was considered. On evaluation his inflammatory parameters were normal. There was poor response to oral steroids and methotrexate. He was lost to follow up and presented at 9 years of age with varus deformities of hand and feet. Radiographs revealed absent carpal and tarsal bones. Based on clinical and radiological examination- MCTO was diagnosed. Oral alendronate was started and clinical improvement was noted.

#### Conclusion

Mimickers of JIA like MCTO, Farber's disease should be actively looked when inflammatory parameters are normal or response to therapy is not appropriate.

**Key Words:** Alendronate, Juvenile idiopathic arthritis, Multicentric carpotarsal osteolysis.

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## 1- INTRODUCTION

Inherited multicentric carpal-tarsal osteolysis (MCTO) is a rare skeletal dysplasia characterized by aggressive osteolysis, particularly affecting the carpal and tarsal bones. MCTO, an autosomal dominant disorder is classified under Group 28 by the Nosology Group of the International Skeletal Dysplasia Society (2010) (1). It clinically presents in early childhood with painful swelling of wrist and ankle joints, mimicking chronic rheumatic disorders like juvenile idiopathic arthritis (JIA). Recognition of this syndrome and differentiation is essential for a clinician to avoid unnecessary treatment with immunosuppressive agents because of a different course and treatment. Progressive renal failure is also a well-recognised complication (2-3). We report a 3-year-old male child, initially presented clinically similar to JIA, later proved to have MCTO with renal disease.

## 2- CASE REPORTS

A 3-year boy presented with complaints of swelling and restriction of right wrist joint and left ankle joint for about 10 months' duration. A possibility of oligo-articular JIA was considered. On evaluation his inflammatory parameters- Total Leucocyte Count-5600 cells/mm<sup>3</sup>, ESR- 5mm/hour; C-reactive protein, Antistreptolysin O titer (AS(L)O titer or AS(L)OT), Antinuclear antibody and rheumatoid factor were all negative. Oral Naproxen (10 mg/kg/day) was initiated. Since articular symptoms persisted, bridging oral corticosteroids was added for

3 months followed by methotrexate for next 2 years. However, he developed subtle deformities of hand and feet at the age of 6 years. Inflammatory parameters were repeated and were found to be normal, but there was poor response to methotrexate, which prompted us to consider an alternative diagnosis. There was discontinuation of therapy and child was lost to follow up for 3 years. He presented again at an age of 9 years with deformities at hand and feet (**Figure.1**), difficulty in getting up from squatting posture and hyper-extensibility at fingers and wrist. Musculoskeletal examination revealed dislocation at bilateral wrist joint, Varus deformities of hand and foot (**Figure.1**). Hematological and biochemical parameters were within normal limits; Rheumatoid factor was again negative. Radiographs of upper limb showed osteopenia, dysplastic base of metacarpals, absent carpal bones and dysplastic distal ends of radius and ulna. Lower limb radiographs revealed absent navicular, medial and lateral cuneiform of left foot with right foot showing dysplastic navicular and absent medial cuneiform (**Figure.2**). Based on the clinical and radiological evidence Multicentric carpotarsal osteolysis (MCTO) was diagnosed. His urine examination showed protein of 25 mg/m<sup>2</sup>/hr, and had normal serum creatinine. Oral Alendronate (5 mg/day) was started along with calcium supplements. Child is currently doing well and is being monitored for renal dysfunction. His 3 generation pedigree charting did not reveal any similar complaints or deformity.



**Fig.1:** Talipes equinovarus and pes cavus deformity.



**Fig.2:** X-ray left foot (a) showing absent navicular, medial and lateral cuneiform; right foot (b) showing dysplastic navicular and absent medial cuneiform. X ray left (a) and right (b) hand showing dysplastic base of metacarpals, absent carpal bones, dysplastic distal radius and ulna.

### 3- DISCUSSION

Inherited MCTO is a rare skeletal dysplasia characterised by bone resorption predominantly involving carpal and tarsal bones. First case of 'disappearing bone

disease' was described by Jackson in 1838 (2). Mutations in MAFB gene has been implicated in pathogenesis (3). Initially MCTO, Torg Winchester syndrome, Gorham's disease were used synonymously. These rare syndromes,

although share many phenotypic characteristics, can differ from each other in modes of transmission, clinical features like presence or absence of mental retardation, nephropathy and extent and anatomic distribution of osteolysis. The International Skeletal Dysplasia Society recently revised their nosology and classification guidelines and differentiated above mentioned diseases into distinct entities (1). Osteolysis is grouped into 28, MCTO (MIM 166300) being part of it. MCTO presents in early childhood (2-3yr of age) with painful swelling of hand and feet which is progressive and deforming and thus mimics JIA (4). These patients can have subtle dysmorphic features (Triangular facies), slender nose, maxillary hypoplasia, micrognathia and exophthalmos (5).

However, no such dysmorphism was present in our index case. Diagnosis is by characteristic osteolytic changes on radiographs. Deformities usually are encountered on follow up as seen in our index case. Lack of inflammatory markers, poor response to Non-steroidal anti-inflammatory drugs should have prompted to alternative diagnosis. Complications like crippling deformities of limbs, contractures and nephropathy can occur leading to increased morbidity and mortality. Index child had proteinuria with normal creatinine. Zankl et al. (3) and Mehawej et al. (6) have shown missense mutations in MAFB gene in patients with MCTO. MAFB gene is mainly involved in regulation of osteoclast differentiation and renal development, which explains the phenotypic features of MCTO. Multicentric osteolysis, nodulosis and arthropathy (MONA) is a close differential of MCTO has osteolysis similar to latter, however has osteoporosis involving entire skeleton and additional manifestations like corneal opacity, heart abnormalities and fibrocollagenous nodules (7). Index child had carpotarsal osteolysis syndrome and

renal involvement suggesting MCTO as likely diagnosis and is planned for genetic workup in follow up. Treatment by medical or surgical means to date is inconclusive. Bisphosphonates have been tried in MCTO (8). Bisphosphonates retard formation and dissolution of hydroxyapatite crystals in the bone. They mainly cause increase in bone mineral density (9). Aminobisphosphonates (aminoBPs) such as alendronate have been found to block farnesyl pyrophosphate synthase, an enzyme in the mevalonate pathway that appears to be critical for osteoclast survival in such conditions. In Index case after starting oral alendronate after a month, child's gait improved and his hand mobility improved.

#### 4- CONCLUSION

Juvenile idiopathic arthritis is a chronic rheumatic disease. When inflammatory parameters or response to therapy is not appropriate, mimickers of JIA should be actively looked like- Farber's, MCTO. MCTO though a rare entity, can be diagnosed with simple radiographs, siblings have to be examined and a trial of bisphosphonates can be given for reducing skeletal complications and should be monitored for development of renal dysfunction.

#### 5- ABBREVIATIONS

MCTO: multicentric carpotarsal osteolysis,

JIA: juvenile idiopathic arthritis

ESR: erythrocyte sedimentation rate.

#### 6- CONTRIBUTORS' STATEMENT

Abhishek Somasekhara Aradhya: diagnosis, review of literature and draft of manuscript,

Deepti Suri: Diagnosis, review of literature and approval of final manuscript,

Arjun Prakash: radiological diagnosis and approval of final manuscript.

**7- CONFLICT OF INTEREST:** None.

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