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Case Report

Juvenile transient bone marrow oedema of the foot associated with Vitamin D deficiency: A case study and an overview of pathogenesis and treatment

Angelos Kaspiris[a,*], Olga D. Savvidou[b], Efstathios Chrronopoulos[c], Elias Vasiliadis[d]

[a] Laboratory of Molecular Pharmacology/Division for Bone Research, School of Health Sciences, University of Patras, Patras 26504, Greece
[b] 1st Department of Orthopaedic Surgery, National and Kapodistrian University of Athens, Medical School, "ATTIKON" University Hospital, Athens, Greece
[c] 2nd Department of Orthopaedic Surgery, National and Kapodistrian University of Athens, Medical School, Konstantopoulio General Hospital, Athens 14233, Greece
[d] 3nd Department of Orthopaedic Surgery, National and Kapodistrian University of Athens, Medical School, KAT General Hospital, Athens 14561, Greece

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ABSTRACT

Bone Marrow Oedema Syndrome during childhood is a rare benign transient condition without clear pathophysiology. It usually resolves after conservative treatment, but resolution may exceed up to 8 months. A 12-year-old child with bone marrow oedema of the left foot which was diagnosed by magnetic resonance imaging (MRI) is reported. She presented with a six week subacute pain and mild swelling on the dorsal surface of the foot. Routine plain radiographs, blood tests, biochemical and serological tests were normal with the exception of serum Vitamin D levels that were reduced. The management of the child included partial weight-bearing, administration of anti-inflammatory drugs and supplementation of Vitamin D due to insufficient Vitamin D intake. After six months the child did not have any clinical symptoms and MRI showed complete resolution of the oedema. This is the first report of a juvenile bone marrow oedema correlated with hypovitaminosis D that was successfully treated with Vitamin D administration.

1. Introduction

Bone Marrow Oedema Syndrome (BMOS) represents a transient clinical-radiological entity, which is associated with non-specific acute or sub-acute pain during activity and diffuse pattern of abnormal bone marrow intensity in magnetic resonance imaging (MRI) scan [1,2]. The clinical manifestations of the disorder include the transient and regional migratory osteoporosis which are primarily presented by a bone marrow oedema pattern. Additionally, the non-specific term of BMOS is also used in patients that do not develop radiographic signs of osteopenia or osteoporosis [3]. As long as bone marrow oedema is a MRI finding in many physiological or pathological conditions, BMOS diagnosis is usually made by the patient's medical history and the exclusion of others pathological disorders like osteonecrosis, trauma, ischemia, infection, inflammatory, rheumatic (especially monoarticular) or neurological diseases, iatrogenic events, tumors or cancers and endocrine or degenerative diseases [4–7]. However, the aetiology of primary bone marrow oedema remains unknown.

Reports regarding the incidence of bone marrow oedema and its manifestations as transient osteoporosis or regional migratory osteoporosis, in children are extremely sparse [8–14]. Despite the fact, that the association between Vitamin D deficiency and BMOS has been observed in small adult patient's series [3], this is the first report that describes a link between juvenile transient bone marrow oedema and insufficient Vitamin D intake.

The aim of this paper is to highlight the differential diagnostic approach of bone marrow oedema in young patients, emphasizing to the possible involvement of Vitamin D on its pathophysiology and to review the aetiology or management of all the literature reported cases during childhood (Fig. 1).

2. Case report

A 12-year-old Caucasian girl presented with a six-week history of subacute pain localized in the left foot accompanied by mild swelling on the dorsal surface of the foot. The initial plain radiograph did not reveal any signs of fracture or other pathology. A non-contrast MRI scan of the feet was performed demonstrating characteristic low intensity signal in T1-weighted and increased signal in T2-weighted sequences in the left talus, calcaneus, navicular and cuboid bones as well as in the cuneiform bones and on the base of first, fourth and fifth metatarsal bones and distal part of tibia. The joint spaces and bony contour were normal, while small subcutaneous effusion areas were observed. It was not demonstrated any abnormal findings of the knees or the right foot.

* Corresponding author.
E-mail address: angkaspiris@hotmail.com (A. Kaspiris).

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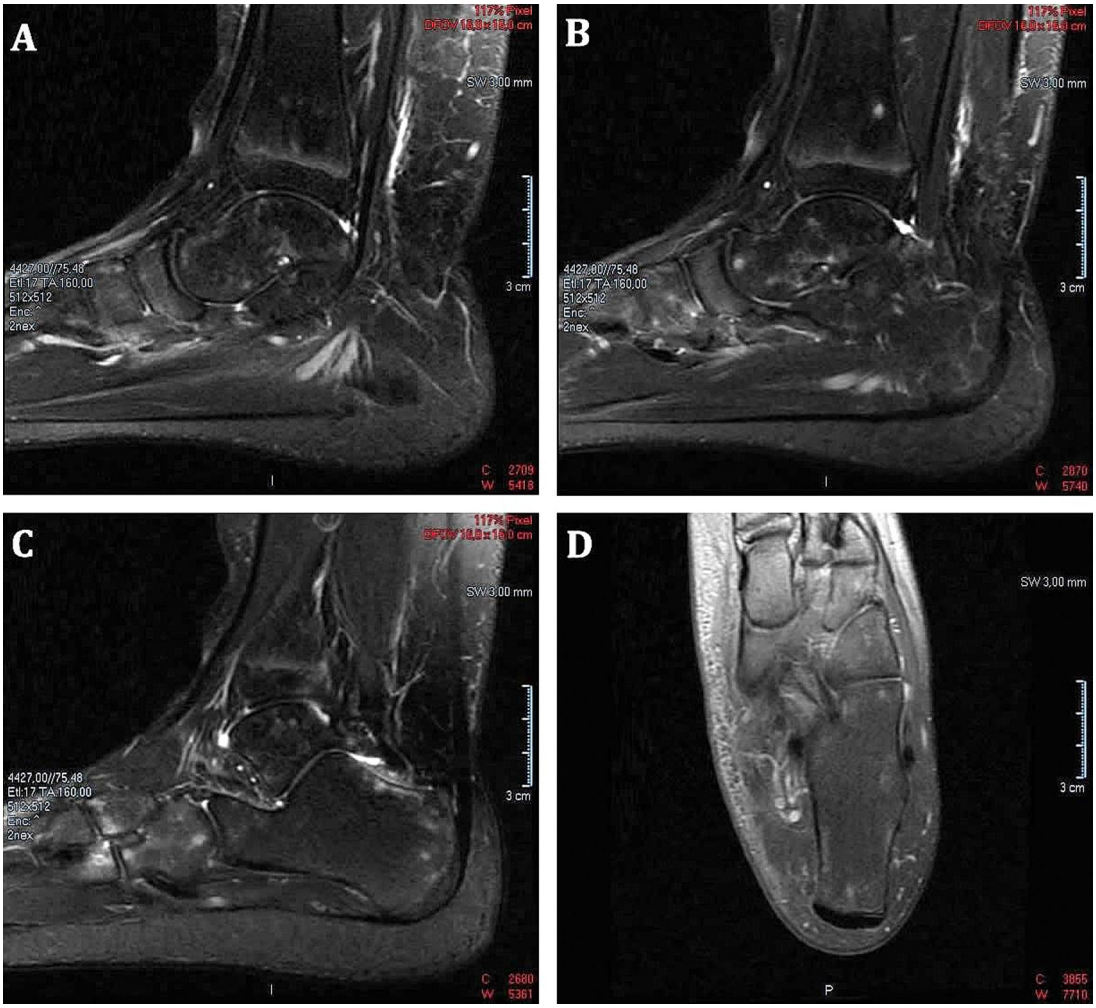

Fig. 1. MRI scan (A–D) of the foot demonstrates diffuse hyperintensity in the tarsal bones and in the lower part of the tibia which is a sign of bone marrow oedema in T2 weight images.

Despite the fact that the patient was active in sports (skateboarding), she denied any incident of recent trauma or injury and she has no history of bleeding or bruising. She did not complain of any knee, hip or joint pain. Palpation of the foot did not cause extra pain and the range of joint motion was within normal limits. The patient's gait was normal. Abdominal, renal and pelvic and leg Doppler ultrasound examinations as well as skeletal scintigraphy bone scan were normal. Axial bone mineral density was calculated by using dual X-ray absorptiometry appeared within physiological limits. Laboratory findings, including ECR, C-RP, serum calcium, potassium, sodium, phosphate, parathyroid hormone (PTH), thyroid-stimulating hormone (TSH), thyroxine (T4), triiodothyronine (T3) and biochemical liver and kidney indices, were also within normal limits. Furthermore, serological results, including ASTO, C3, C4, antinuclear antibodies/ANA, anti-DNA, anti-Ro and La, anti-Sm and anti-RNP, anti-Scl-70, anti-histones, anti-Jo-1 and CENP-B, anti-mitochondrial antibodies (AMA), anti-smooth muscle antibody (ASMA) as well as cytoplasmic and perinuclear anti-neutrophil cytoplasmic antibodies (C- and P-ANCA, respectively) or Serum IgA-tissue transglutaminase antibodies, did not show any pathology. However, the serum levels of Vitamin D3 25-hydroxyvitamin D were low at 09 ng/mL (sufficiency: 20–100 ng/mL, insufficiency: 15–20 ng/mL, deficiency < 15 ng/mL) [15], while serum bone markers levels like osteocalcin were slightly elevated at 54.3 ng/mL, indicating increased rate of bone remodeling.

The patient was administered of nonsteroidal anti-inflammatory or other analgesic agents and was advised to limit her activity, to avoid weight bearing and to correct the Vitamin D deficiency by using Vitamin D supplementation. NSAIDs were administrated for 5 days after the onset of clinical symptoms. Follow-up MRI of the left foot six months after the initial management showed complete resolution of the bone marrow abnormality and restoration of the serum levels of Vitamin D3 25-hydroxyvitamin D within normal limits. Additionally, the patient did not appear any clinical symptoms.

3. Discussion

Transient BMOS is an uncommon condition with unknown aetiology primary affecting the lower limb. Generally, it is a self-limiting disease, occurring three times more often to male subjects, which is usually resolved spontaneously within 6–24 months after conservative management [8–13]. The incidence rate of BMOS in adults is around 0.44%, but its prevalence in children seems to be extremely lower [16,17]. To date, only six reports [8–14] have been published and fourteen children have been diagnosed with BMOS (Table 1). To the best of our knowledge this is the first report that referred, not only in the implication of Vitamin D deficiency on transient juvenile BMOS development, but also in BMOS treatment with supplementary Vitamin D administration.

Although proximal femur was the most common site that was affected during adulthood [8], bony anatomic locations that were commonly affected during childhood included acetabulum [10], foot bones [8,13], distal tibia and fibula [8], femoral head [9,11], knees [12,14], femur [14] and hand bones [8] (Table 1). In our case talus, calcaneus,

Table 1
Literature review on Bone Marrow Oedema Syndromes cases and treatment in children.

References	N	Age (in years)	Sex	Anatomic location	BMOS manifestation form	Treatment
Joshi et al., USA [12]	01	15	Boy	Lateral & medial tibia epiphysis	Regional migratory osteoporosis	Activity limitation
Kröger et al., Finland [8]	01	8	Boy	Foot, tibia, fibula, hand	Regional migratory osteoporosis	Anti-inflammatory drugs, partial weight bearing
Aigner et al., Austria [10]	01	15	Girl	Acetabulum	Non-specific	Rest/iloprost (platelet aggregation inhibitor) infusions
Pay et al., USA [11]	03	3.5–10	Boys, girls	Femoral head	Non-specific	Conservative treatment, bracing/traction in moderate abduction
Santori et al., Italy [14]	02	12	Girls	Knee–hip	Regional migratory & regional idiopathic osteoporosis	Conservative treatment rest/physiotherapy/anti-inflammatory drugs/avoidance of weight bearing
Nicol et al., USA [9]	06	6–12	Girls boys	Femoral head	Transient osteopenia	Conservative treatment rest/salicylates/skin traction/hip spica

navicular, cuneiform and cuboid bones, along with the base of first, fourth and fifth metatarsal bones and distal part of tibia were primarily influenced.

The pathophysiological basis of BMOS in children is uncertain, but its appearance was usually implicated by local vascular disturbances or ischemia, micro-traumas, altered biomechanics and bony contusion or osteoporosis. Based on the reduced extracellular water found at children's MRI compared to adults, there is an assumption that juvenile BMOS represents a different form of the disorder [11]. Indeed, our results showed decreased joint effusion on MRI supporting the above notion. Transient osteoporotic findings were revealed in the case study of Kröger et al. [8], while in the case of Aigner et al. [10] the patient responded to the ilioprost, which was a prostacyclin analogue that induced vasodilation and inhibits platelet aggregation, indicating possible vascular abnormality. Sprinchorn et al. described series of nine patients identifying strong positive correlation between foot and ankle BMOS and transient osteoporosis/osteopenia accompanied by reduced bone mineral density [16]. BMOS development might be a tissue reaction to repeating stress and micro-traumas during overuse injuries applied to osteopenic or osteoporotic weight-bearing foot bones [16]. However the small number of patients, the absence of controls and the limited number of studies supporting the association between transient osteoporosis and BMOS, do not allow to draw final conclusions [2]. Contrariwise, histological sections of hip, knee, ankle bone marrow have detected thinning of the trabecular bone without osteoblastic activity or fat necrosis of the woven bone and without any signs of osteoporosis [16,17]. In our study clinical or laboratory signs of osteoporotic or vascular abnormalities were not observed. However, children's involvement in intense sport activity combined with vitamin D deficiency could be possible leading causes.

In previous reports of children with BMOS, serum levels of Vitamin D metabolites have not been examined [9–14]. Only Kröger et al. [8] referred that in an 8-years-old boy with BMOS serum levels of Vitamin D were normal. However, our findings showed strong association with Vitamin D deficiency due to insufficient Vitamin D intake, which is consistent to the results of Horas et al. [4] and Sprinchorn et al. [16] in adult populations. In specific, in series of 31 and 9 middle aged patients that developed bone marrow oedema respectively, hypovitaminosis D was identified in a percentage of 90%. As long as Vitamin D plays a critical role on the function of bone microenvironment, on bone metabolism, on bone remodeling [18] and on muscle activity, we can speculate that patients with Vitamin D deficiency may be prone to BMOS development associated with musculoskeletal pain especially after bone stressful conditions [4,19].

Treatment of BMOS is focusing mostly on symptomatic measures such as avoidance of weight bearing, core decompression, protective boot or cast application, activity modification, physical therapy and administration of anti-inflammatory and analgesic drugs [13], providing pain relief and averting cracking of the articular surface. However, several clinical and basic science studies have demonstrated that the administration of anti-inflammatory drugs is negatively correlated with bone healing and their use must be limited only during 5–7 days after BMOS clinical onset [20]. Vasodilator treatment was also used in children [10], but the consequenced side effects, like headaches, nausea or flushes and the contraindications in pregnancy, in anticoagulation treatment, in peptic ulcer or in cardiac disorders, made this choice less popular [10]. As hypovitaminosis D is a potential risk factor, administration of Vitamin D should be also considered. In our patient the combination of weight bearing reduction, anti-inflammatory drugs and Vitamin D administration, resulted in a rapid clinical and radiological improvement.

4. Conclusion

BMOS during childhood remains a very rare condition. Our study reports a child, in which BMOS appearance in foot was associated with

deficiency of Vitamin D and was successfully treated with Vitamin D administration, leading us to conclude that hypovitaminosis D could be a significant co-factor in the development of the disease. Vitamin D supplementation might be considered as a potential preventive or therapeutic target in the BMOS management. Nonetheless, future prospective studies are needed to confirm our results and open up new preventive pathways.

Conflict of interest

There are no conflicts of interest.

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