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Case Report

Pediatric scurvy MRI appearance ☆,☆☆

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ABSTRACT

We present a rare case of pediatric scurvy in a 9-year-old male who presented with nontraumatic knee pain. MRI was obtained due to the puzzling presentation. MRI demonstrated a systemic bone marrow abnormality which led to a conversation with the clinician and further elucidation of an extremely narrow diet lacking sufficient vitamin C (ascorbic acid). Diagnosis was confirmed biochemically with undetectable ascorbic acid level and clinically with compatible exam and history. This case highlights a thought process for unexpected bone marrow abnormality on MRI.

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Introduction

Scurvy is a rare nutritional deficiency in modern society and results from severe dietary hypovitaminosis C (ascorbic acid). This vitamin plays a pivotal role in the production and regulation of collagen critical for skin, blood vessels, and connective tissue [1]. The classical feature of scurvy is hemorrhage. Musculoskeletal manifestations including myalgias and arthralgia in the knees, ankles and wrists are present in 80% of patients with scurvy [2]. MRI may detect bone marrow abnormalities secondary to gelatinous transformation of the bone marrow [3–5]. Scurvy is a consideration when there is abnormal confluent T1 hypointense/T2 hyperintense signal in multiple bones in a patient with select risk factors [3].

Population groups at risk for vitamin C deficiency include alcoholics, people with eating disorders, elderly and children with narrow diets [4]. In developed countries, pediatric presentations of scurvy have been reported in developmentally delayed or autistic children with a very select diet [1].

The differential for knee pain is wide, with additional considerations specific in pediatrics. In the absence of trauma, the differential includes chronic/overuse injuries, cancer/tumors, developmental variants, inflammatory conditions and metabolic/nutritional abnormalities. Radiographs are the initial imaging modality, but are not sensitive for abnormalities of the bone marrow. Computed tomography is superb for evaluating the bone structure in the case of trauma, however provides limited information regarding the characterization of bone lesions and bone marrow. Magnetic Resonance Imaging

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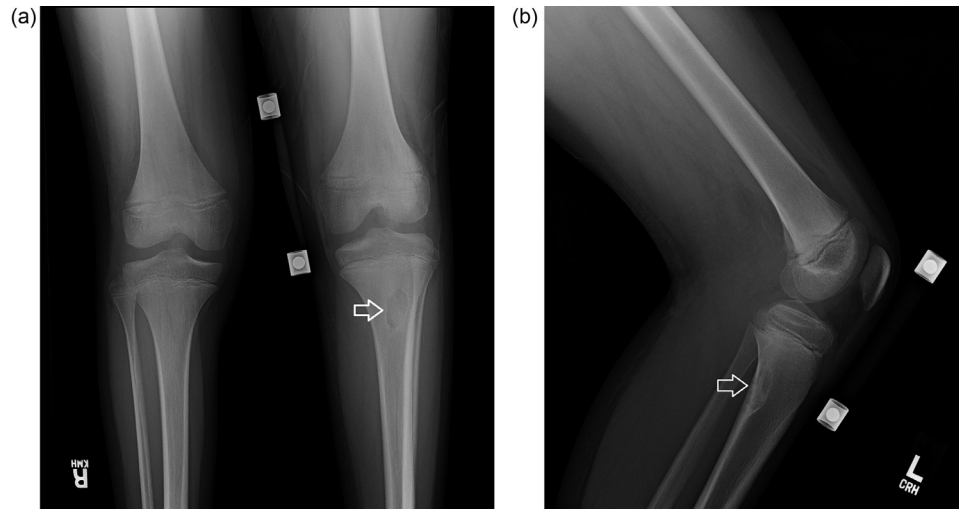


Fig. 1 – Left knee radiographs at the time of presentation. (a) Anterior-posterior projection), (b Lateral) Incidentally noted is a benign non-ossifying fibroma (arrow). No knee joint effusion, malalignment or fracture. The appearance of the bones is normal.

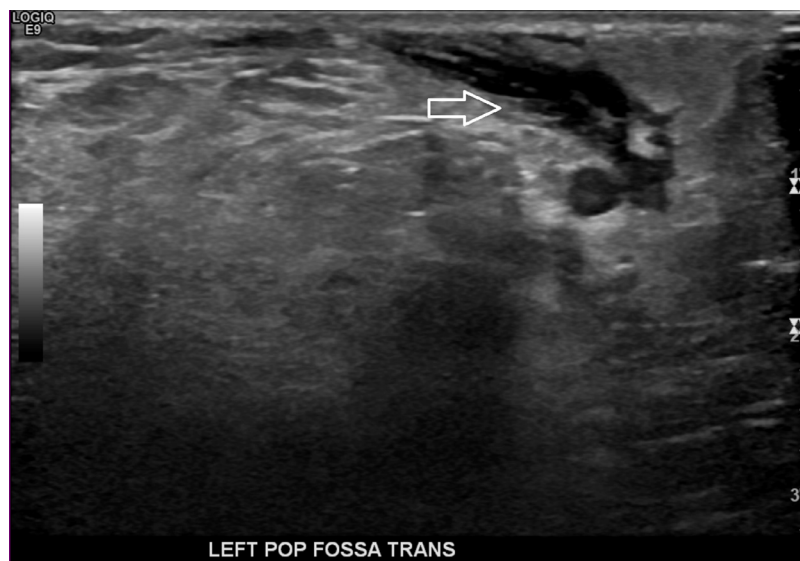


Fig. 2 – Grayscale ultrasound of the popliteal fossa shows subcutaneous edema and thickening, and ill-defined fluid tracking (arrow) in the soft tissues. No knee joint effusion was seen.

(MRI) allows high resolution multiplanar evaluation with excellent spatial resolution and soft tissue evaluation, including the bone marrow [6]. To adequately evaluate the bone marrow in children, knowledge of the normal patterns of bone marrow development throughout childhood is critical [7]. When abnormal bone marrow is noted, pertinent questions include location within the bone (epiphysis, metaphysis, shaft, or diffuse), pattern of involvement including bone involvement (single versus multiple plus laterality), and age of the patient. Systemic stress (severe illness/chemotherapy) and nutritional deficiencies can affect the appearance of bone marrow and tend to be bilateral, symmetric, and multifocal or diffuse [3].

Case report

A 9-year-old male presented to our health system's emergency department with 1 week of nontraumatic, left greater than right leg pain and progressive difficulty ambulating. Initial radiographs demonstrated a benign nonossifying fibroma in the left proximal tibia metadiaphysis, with no additional abnormality (Fig. 1). The primary physician advised rest, ice, and Tylenol. Tylenol twice daily improved the pain temporarily; however the child represented 3 days later unable to walk, with left leg pain greatest behind the knee. Lower extremity ultrasound of the left popliteal fossa

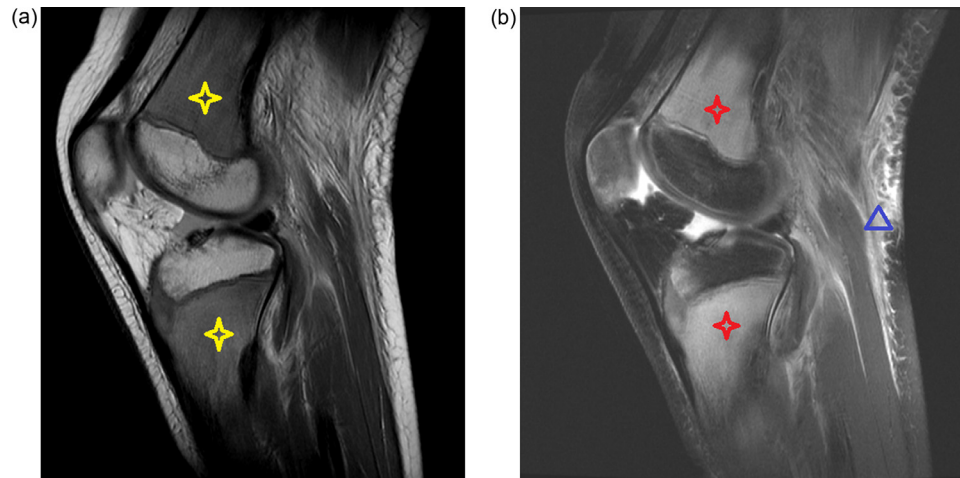


Fig. 3 – Sagittal fast spine echo T1 (a) and T2 with fat saturation sequences (b) show confluent T1 hypointense signal (yellow star) and T2 hyperintense bone marrow signal (red star) in the metaphyses. There is some preservation of fat signal within the bone marrow as seen on the T1 images. The epiphyses are spared and appear normal. Extensive edema-like T2 hyperintense signal (blue triangle) infiltrates through the soft tissues in the popliteal fossa. (Colored version of figure is available online.)

demonstrated an ill-defined fluid collection with overlying soft tissue swelling possibly representing a ruptured popliteal cyst (Fig. 2). Additionally, the child endorsed vague pain in his right leg and chest wall. To facilitate further evaluation, including advanced imaging, the child was transferred to our facility four days after initial presentation. Initial exam noted an afebrile 9-year-old male in no acute distress, with refusal to ambulate and pain directed at the posterior left knee. The child was 140 cm tall (84%) and weighed 40.6 kg (95%). Microcytic anemia was noted (Hemoglobin 10.2g/dL and MCV 72.5 fL), which the mother attributed to the patient's "poor diet." Mild leukocytosis (White Blood Cell count $12.0 \times 10^9/L$ with left shift) and elevated C-Reactive Protein at 16.8 mg/L were also noted. Repeat WBC count normalized at $6.9 \times 10^9/L$. Clinical differential diagnosis considerations at this point included septic joint, osteomyelitis, ruptured Baker's cyst, osteoid osteoma and malignancy. MRI was ordered.

The MRI exam protocol included 3 plane imaging (axial, sagittal, and coronal) T1 and T2 fat saturated sequences to be checked prior to gadolinium administration. Somewhat unexpectedly, there was confluent abnormal T1 hypointense/T2 hyperintense metaphyseal bone marrow signal in the left distal femur and proximal tibial metaphyses. Additionally, there was extensive T2 edema-like signal throughout the popliteal fossa, interdigitating in the calf muscles, greatest about the myotendinous junctions, and in the subcutaneous tissue (Figs. 3 and 4). The field of view was extended to include the contralateral leg as well as the proximal hips (Fig. 5). The abnormal confluent T1 hypointense/T2 hyperintense signal was symmetric in the distal femoral and proximal tibial metaphyses and milder changes were seen in the proximal femurs, suggesting a systemic process. Gadolinium was not administered due to the symmetry of the marrow abnormalities indicating a systemic process rather than a focal lesion (tumor or osteomyelitis).

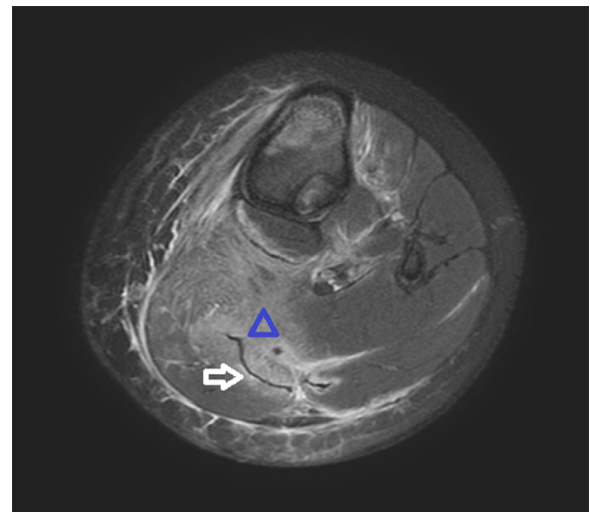


Fig. 4 – Axial fast spin echo T2 fat saturated sequence shows prominent edema-like hyperintense signal (blue triangle) along the myotendinous junction (arrow) of the medial head of the gastrocnemius muscle consistent with tendonitis. No high-grade or complete tear of the tendon was seen. (Colored version of figure is available online.)

A classic appearance for residual appendicular red bone marrow in an adolescent is patchy or flame shaped foci. These foci are typically mildly T1 hypointense/mildly T2 hyperintense in the metaphyses, expected to be greater in the proximal femurs near the hip – which was not the case. The symmetry and abnormal signal could be seen with leukemia or potentially lymphoma, but still atypical to be symmetric in only the metaphyses. Osteomyelitis was deemed extremely unlikely to be symmetric in a child without fever or

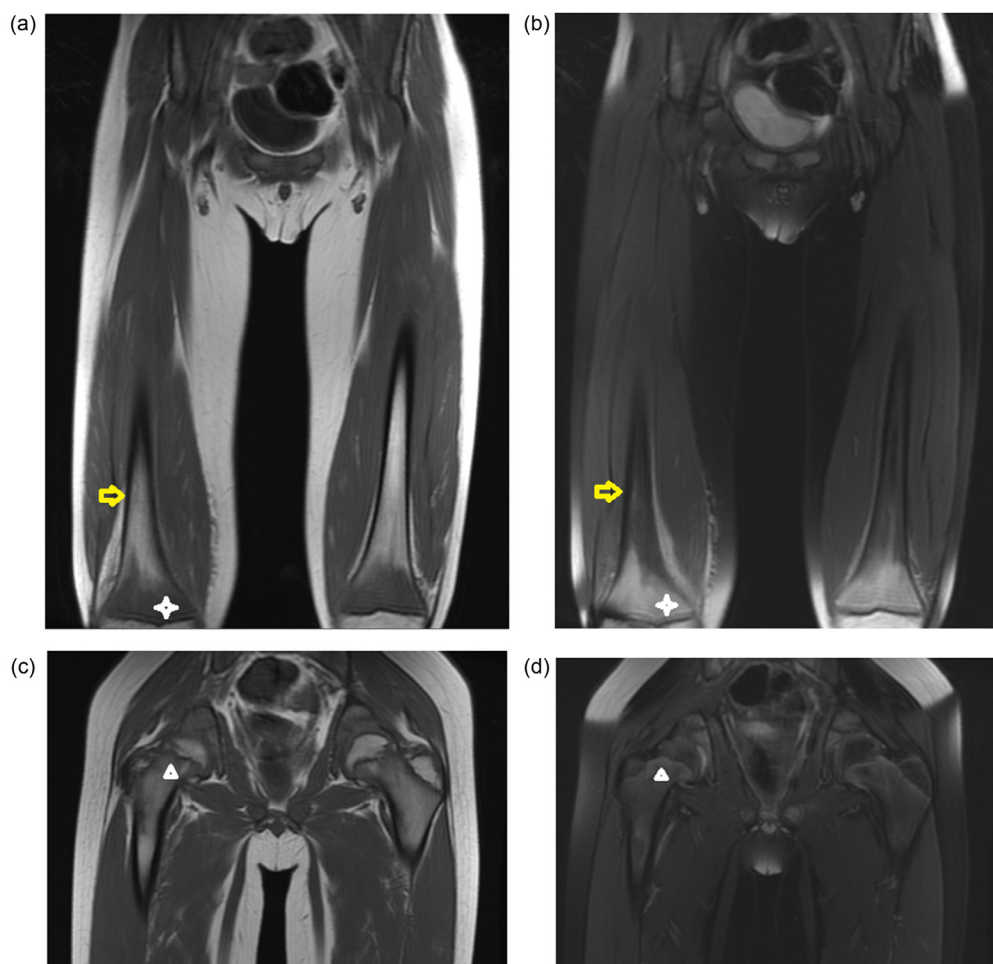


Fig. 5 – Large field of view coronal fast spin echo T1 (a, c) and T2 fat saturated images (b, d) of the femurs. The abnormal signal changes are symmetric and involve both distal femoral metaphyses (star). There are likely early subtle marrow signal changes in both proximal femoral metaphyses (triangle). The diaphyseal bone marrow is spared (arrow). No definite marrow changes were seen in the pelvis.

leukocytosis. An osseous tumor would not be symmetric and involve numerous bones. The possibility of gelatinous transformation of bone marrow in the setting of malnutrition and possible scurvy was discussed with the hospital pediatric clinician.

Further history was elicited from the care provider, including nutritional history. The boy was on the autism spectrum and his diet consisted of milk, yogurt, and pudding from the age of 2-9 years old, and prior interventions aimed at increasing variety of foods had been unsuccessful. According to the US Department of Agriculture FoodData Central online database, milk and most pudding provides no dietary vitamin C, while yogurt can provide 2.1 mg per serving. Of note, MayoClinic.org states the recommended daily amount of vitamin C is 65-90 mg. Thus, the child's dietary intake was far short of needed intake.

A directed physical exam documented ecchymoses overlying the popliteal fossa, keratosis pilaris, dry raised lesions and scattered petechial lesions on the arms and legs. The child was diagnosed with scurvy biochemically on the grounds of an undetectable ascorbic acid level <0.1 mg/dL (reference range

0.4-2.0 mg/dL) and a highly compatible clinical picture. The extensive popliteal fossa and muscular T2 hyperintense signal was compatible with subacute hemorrhage in this clinical context, but edema from muscular/connective tissue strain could have a similar appearance. The child was placed on a daily multivitamin, vitamin C supplement, and PediaSure. By discharge from the hospital, the patient was ambulating using a walker and described decreased tenderness/swelling. One-month laboratory recheck ascorbic acid level normalized at 1.5 mg/dL. At three month follow up clinic visit, the child and mother reported resolution of musculoskeletal pain, normal ambulation and weight gain with dietary supplementation. Currently height of 145 cm (85%) and weight 45.4 kg (95%).

Discussion

Scurvy is a rare disease which can present in select at risk populations. In developed countries, children with developmental delay and select narrow diets could present with

manifestations of scurvy [1,4]. Gelatinous transformation of bone marrow is characterized by replacement of fat and hemopoietic cells with hyaluronic acid [5]. This is a physiologic sign of severe malnutrition, starvation and usually seen in individuals with cachexia or those suffering from anorexia [5]. Since hyaluronic acid is a mucopolysaccharide made of alternating residues of monosaccharides rich in hydroxyl groups, it readily forms hydrogen bonds with water molecules, hence the T2-prolongation on MRI. Normally hyaluronic acid is a filler material in connective tissue (skin and joints) which allows cushion and lubrication [8]. Based on the pathologic autopsy proof of hyaluronic acid in gelatinous transformation of bone marrow and the function of hyaluronic acid in water homeostasis/lubrication, the abnormal bone marrow MRI appearance of scurvy (abnormal low T1 and high T2 signal at the metaphyses) is likely due to normal marrow components being replaced by hyaluronic acid and water [5,8]. Additionally, hemorrhage is the key feature of scurvy [2].

Radiologists should consider expanded field of view imaging when abnormal bone marrow signal is noted around a joint. This allows evaluation for symmetry and multifocal or diffuse nature of the disease (think systemic process). Knowledge of the normal pattern of red marrow regression and resurgence is critical to accurate assessment of the bone marrow. Epiphyses quickly convert from red to yellow marrow within 6 months age [7]. Next marrow conversion starts in the diaphysis and progresses toward the metaphyses, faster distally than proximally. Commonly residual red marrow is found only within the proximal metaphyses of the humeri and femurs until early adulthood [3,7]. Marrow resurgence occurs in reverse order. An astute radiologist may play a

pivotal role in guiding appropriate care for a patient while decreasing additional tests and procedures.

Patient consent statement

All radiologic images were anonymized and no protected health information was used, thus obviating the need for formal consent.

REFERENCES

- [1] Byard RW, Maxwell-Stewart H. Scurvy-characteristic features and forensic issues. *Am J Forensic Med Pathol* 2019;40(1):43–6.
- [2] Fain O. Musculoskeletal manifestations of scurvy. *Joint Bone Spine* 2005;72(2):124–8.
- [3] Chan BY, et al. MR imaging of pediatric bone marrow. *Radiographics* 2016;36(6):1911–30.
- [4] Gulko E, et al. MRI findings in pediatric patients with scurvy. *Skeletal Radiol* 2015;44(2):291–7.
- [5] Böhm J. Gelatinous transformation of the bone marrow: the spectrum of underlying diseases. *Am J Surg Pathol* 2000;24(1):56–65.
- [6] Sanchez R, Strouse PJ. The knee: MR imaging of uniquely pediatric disorders. *Magn Reson Imaging Clin N Am* 2009;17(3):521–37 vii.
- [7] Laor T, Jaramillo D. MR imaging insights into skeletal maturation: what is normal? *Radiology* 2009;250(1):28–38.
- [8] Laurent TC, Laurent UB, Fraser JR. Functions of hyaluronan. *Ann Rheum Dis* 1995;54(5):429–32.