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CASE REPORT

Scurvy: a rare case in an adult

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Abstract
A 69-year-old man presented with unilateral calf pain, swelling, and erythematous rash. He was initially treated with antibiotics for suspected cellulitis. A venous duplex ultrasound, performed to exclude deep venous thrombosis, revealed multiple heterogeneous hypoechoic foci of unknown etiology throughout the calf musculature. His condition did not improve with antibiotics, instead progressing to a necrotic ulcer along the medial malleolus. Clinical suspicion of vascular insufficiency or vasculitis prompted an extensive imaging work-up. CT and MRI revealed the intramuscular abnormalities observed on previous ultrasound represented foci of intramuscular hemorrhage. Marrow signal abnormality was also noted in the proximal tibia. A punch biopsy of the skin rash ultimately demonstrated distorted hair follicles with perifollicular inflammation and hemorrhage concerning for scurvy. The diagnosis was confirmed by low vitamin C levels and dietary history. A resurgence of scurvy has occurred in the pediatric population in recent years. However, this diagnosis remains uncommon in adults, with limited reports of the potential advanced imaging findings in the current literature.

Keywords Scurvy · Intramuscular hemorrhage · MRI · CT · Ultrasound

Introduction

Scurvy is a disease caused by ascorbic acid (vitamin C) deficiency that is infrequently encountered in developed countries. A wide range of clinical symptoms have been described, including malaise and diarrhea in early stages, to myalgias, cutaneous manifestations, impaired wound healing, and hemorrhage following months of deficiency [1]. The rare nature of the disease and nonspecific clinical picture can result in a delay in diagnosis, often after an extensive diagnostic workup that includes radiological imaging. Recent case reports and case series have been described in the pediatric population, increasing awareness of the condition and its associated findings on imaging [2, 3]. The adult dermatology and rheumatology literature features several case reports on scurvy mimicking other common clinical conditions; however, scurvy remains an uncommon diagnosis in adult patients and consequently little has been described in the literature about its advanced imaging findings.

Case report

A 69-year-old man presented to the clinic with left leg pain, swelling, and erythema for 1 week. The swelling began around the medial side of the left ankle and progressed proximally into the left calf and thigh. He denied fevers, chills, or drainage, although he did report mild fatigue. Aside from smoking every day for most of his life and consuming a six-pack of beer per day, his past medical history included only hypertension. Physical examination revealed erythema on the medial side of the left lower extremity along with mild pitting edema. The patient was started on trimethoprim-sulfamethoxazole for suspected cellulitis. Duplex ultrasound of the calf was negative for deep venous thrombosis, but revealed multiple small nodular heterogeneous hypoechoic foci of unknown etiology within the calf musculature (Fig. 1).

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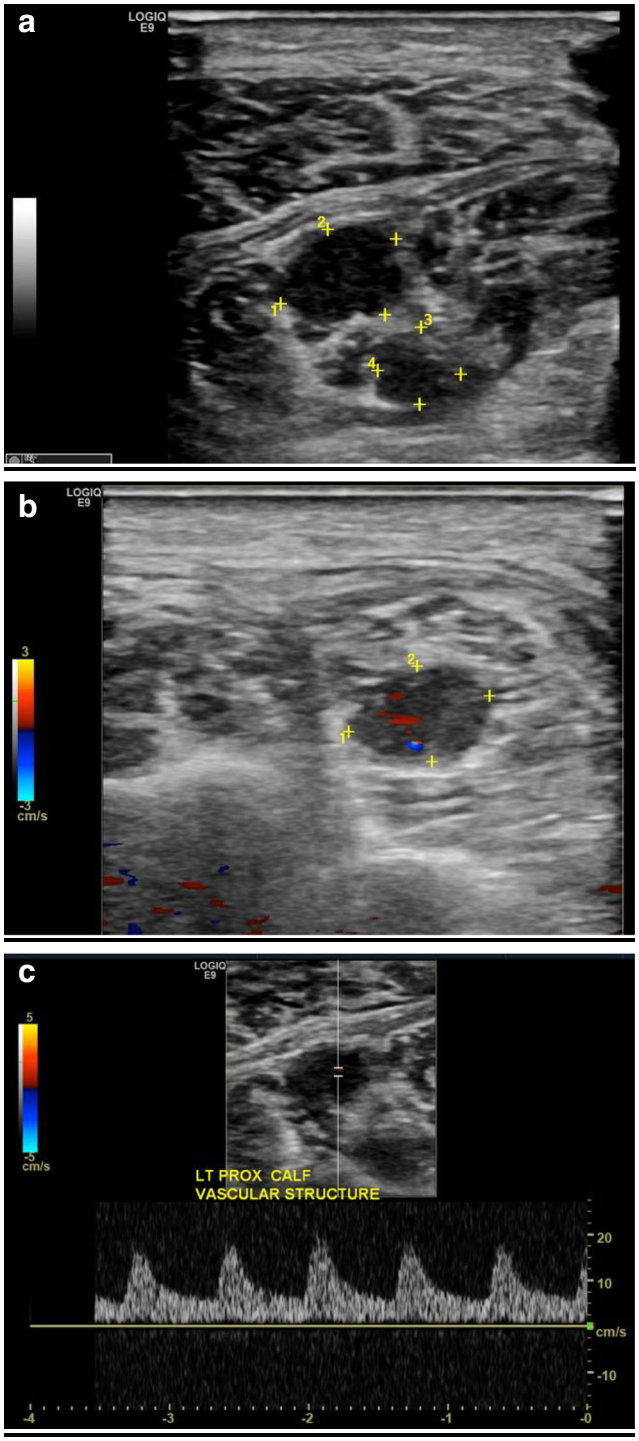

Fig. 1 **a** Grayscale ultrasound image of the proximal calf shows heterogeneous hypoechoic foci within the deep posterior compartment musculature. **b** Power Doppler and **c** spectral Doppler ultrasound images show a vessel within the central portion of the lesion, but absent blood flow at the periphery, suggesting the perivascular nature of the foci

Five days later, the patient presented to the emergency department complaining of increasing lower extremity pain and swelling. Physical examination at this point noted formation of an open necrotic eschar at the medial malleolus along with a purpuric rash extending from the ankle to the proximal calf (Fig. 2). The left dorsalis pedis pulse was nonpalpable. Laboratory findings included moderate anemia (Hb 8.4 g/dL; reference range 13–17 g/dL) and a mildly elevated CRP (CRP 4.9 mg/L; reference range < 0.5 mg/L). Radiographs of the left calf demonstrated mild diffuse soft-tissue swelling without osseous abnormality (Fig. 3). Lower extremity arterial duplex ultrasound revealed atherosclerotic changes throughout the left lower extremity arteries in addition to occlusion of the mid and distal anterior tibial artery. However, the ankle-brachial index was within normal limits, measuring 1.19 mm mercury (Hg) on the right and 0.92 mmHg on the symptomatic left side (reference range 0.9–1.3 mmHg). Given the absence of vascular symptoms (claudication, pain at rest), an essentially normal ankle-brachial index, and intact motor function and sensation, his symptoms were deemed inconsistent with vascular ischemia. The patient was given IV fluids and broad-spectrum antibiotics. A contrast-enhanced CT was ordered to exclude deep abscess and necrotizing fasciitis.

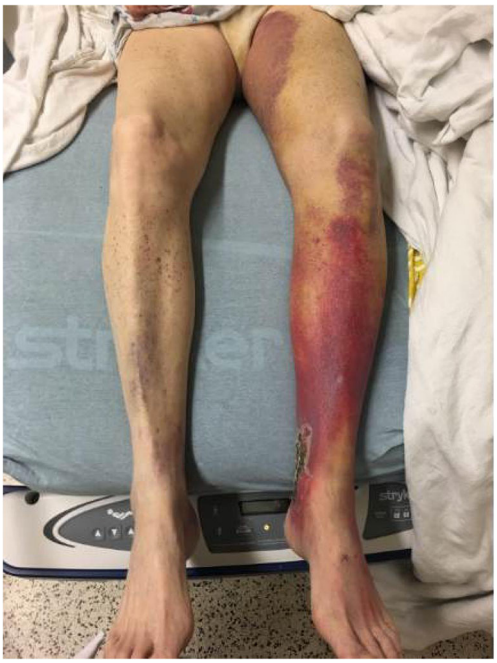

Fig. 2 Open necrotic eschar at the medial malleolus along with a purpuric rash extending from the ankle to the proximal calf. Additional area of ecchymosis on the medial left thigh. Note the perifollicular hemorrhages on the right anterior calf and shin mimicking petechiae

The left lower extremity CT revealed innumerable small hyperdense intramuscular masses in the left calf (Fig. 4 a, b). The differential diagnosis for this finding included hemorrhage, granulomatous disease, hypervascular neoplasm, or vascular etiology. Retrospective review of the original CT data acquisition with open field of view (Fig. 4c) revealed similar, yet less widespread, hyperdense intramuscular masses in the contralateral right calf.

An MRI with contrast enhancement confirmed multiple round T1/T2 hypointense intramuscular masses in the deep

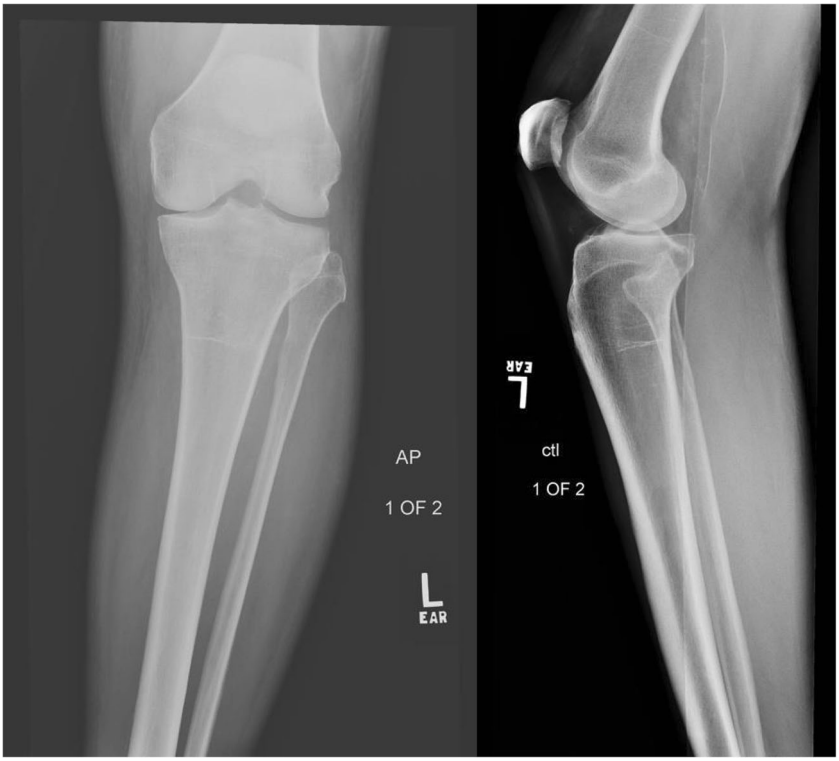

Fig. 3 Anteroposterior and cross-table lateral views of the left tibia and fibula show nonspecific mild diffuse subcutaneous swelling and edema without osseous abnormality

and superficial posterior compartments of both calves that corresponded to the abnormalities seen on CT (Figs. 5, 6). Additional MRI findings included nonspecific increased T2 signal in the proximal left tibial metaphysis (Fig. 6) and diffuse subcutaneous edema.

With no clinical improvement in the left leg, the patient began to experience similar symptoms in his right lower extremity as well. A punch biopsy of the skin erythema was performed to assess for possible vasculitis. Histology showed distorted hair follicles with perifollicular inflammation and hemorrhage (Figs. 7, 8). The pathological differential diagnosis for these findings includes resolving folliculitis or scurvy. Subsequent testing confirmed a plasma vitamin C level of <5 μmol (reference range 23–114 μmol/L). Upon interrogation of his dietary history, the patient admitted to a poor diet limited mainly to fast food such as pizza and hamburgers. Vitamin C supplementation was initiated. The patient was discharged with recommendations for a daily multivitamin and juice to treat his nutritional deficiency. At a follow-up visit 5 months later, his rash had resolved and both his plasma vitamin C level (135 μmol/L) and anemia (Hb 15.4 g/dL) had normalized.

Discussion

Clinical vitamin C deficiency is referred to as "scurvy" and has significant metabolic effects owing to impaired collagen synthesis resulting in disordered connective tissue. Vitamin C (ascorbic acid) plays a critical role in collagen fiber generation, forming supportive sheaths around blood vessels and facilitating rapid growth of osteoid tissue, thus explaining the musculoskeletal manifestations of deficiency [4].

Although scurvy is frequently encountered in developing or third-world countries, it is less common in the USA because of the widespread availability of vitamin C in the western diet. Nevertheless, data from the National Health and Nutrition Exam Survey (NHANES) in 2003–2004 found the overall prevalence of vitamin C deficiency in the USA to be 7.1%, with marginal vitamin C levels in more than 20% of adults [5]. Humans cannot synthesize or store ascorbic acid and thus require 75–90 mg/day from diet or supplementation [6]. Important dietary sources include citrus fruits, potatoes, strawberries, cabbage, spinach, bell peppers, and cauliflower [7]. Scurvy occurs mainly through inadequate dietary intake, often related to severe malnutrition, alcohol abuse, low socioeconomic status, old age, or chronic illness [8]. It has also been described in children with developmental delay or autism spectrum disorder eating highly selective diets and in those with medical conditions leading to iron overload, which may precipitate scurvy owing to an acceleration in ascorbic acid catabolism [9]. Other conditions leading to malabsorption that may also cause scurvy include Crohn's disease, gluten-sensitive enteropathy, and end-stage renal disease. After approximately 40 days of a vitamin-deficient diet, serum vitamin C

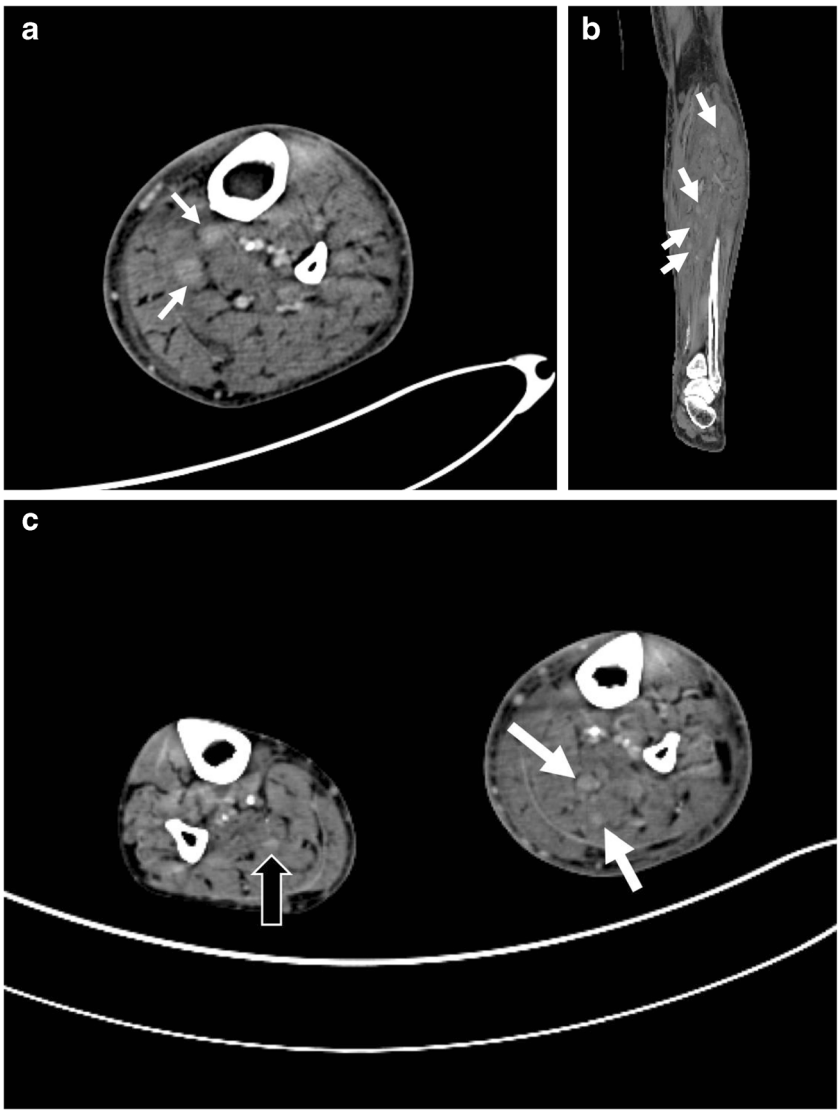

Fig. 4 **a** Axial and **b** coronal images from the left lower extremity CT with contrast enhancement show multiple small hyperdense foci within the posterior calf musculature. **c** CT lower extremity with contrast enhancement after opening the field of view to visualize all acquired data shows the small hyperdense intramuscular foci in the soleus of the symptomatic left calf (*white arrows*) in addition to similar, yet less widespread, foci in the soleus of the asymptomatic right calf (*black thick arrow*)

becomes depleted and clinical symptoms typically manifest by 3 months [10].

Although there are significant variations in the clinical presentation of scurvy, the deficiency is characterized by prominent dermatological manifestations such as perifollicular hemorrhage, superficial ecchymoses, and corkscrew hairs [11]. Impaired wound healing and purpuric skin rash may also occur, mimicking vasculitis [12]. Gingival disease, including bleeding gums, dental caries, and tooth loss is common. In 80% of cases scurvy manifests with musculoskeletal symptoms, including arthralgias, myalgias, hemarthrosis, or muscular hematomas [13].

Laboratory studies commonly reveal anemia resulting in generalized systemic symptoms, such as weakness, fatigue, and malaise. C-reactive protein (CRP) values may also be mildly elevated. Symptoms generally occur when plasma concentrations of ascorbic acid drop to less than 0.2 mg/dL (<5 μmol/L). The diagnosis is typically made with a combination of clinical findings, low serum vitamin C levels, and characteristic punch biopsy findings of skin ecchymoses if necessary.

The prognosis of scurvy is excellent. Treatment involves vitamin C supplementation in addition to treatment of the underlying conditions that led to the deficiency. The response to vitamin C is often dramatic and most symptoms improve rapidly within a few weeks of supplementation [13].

Although rare in the modern world, recent case reports and case series of scurvy have been described with increasing frequency in the pediatric population [14]. Patients often have neurological disorders such as autism or developmental delay with food-avoidant behaviors resulting in restricted diets [14]. Infants fed with evaporated or boiled milk in which ascorbic acid has been destroyed by heat are especially at risk [3]. Scurvy has also been reported in children with underlying medical conditions such as sickle cell anemia or thalassemia that result in iron overload from multiple blood transfusions,

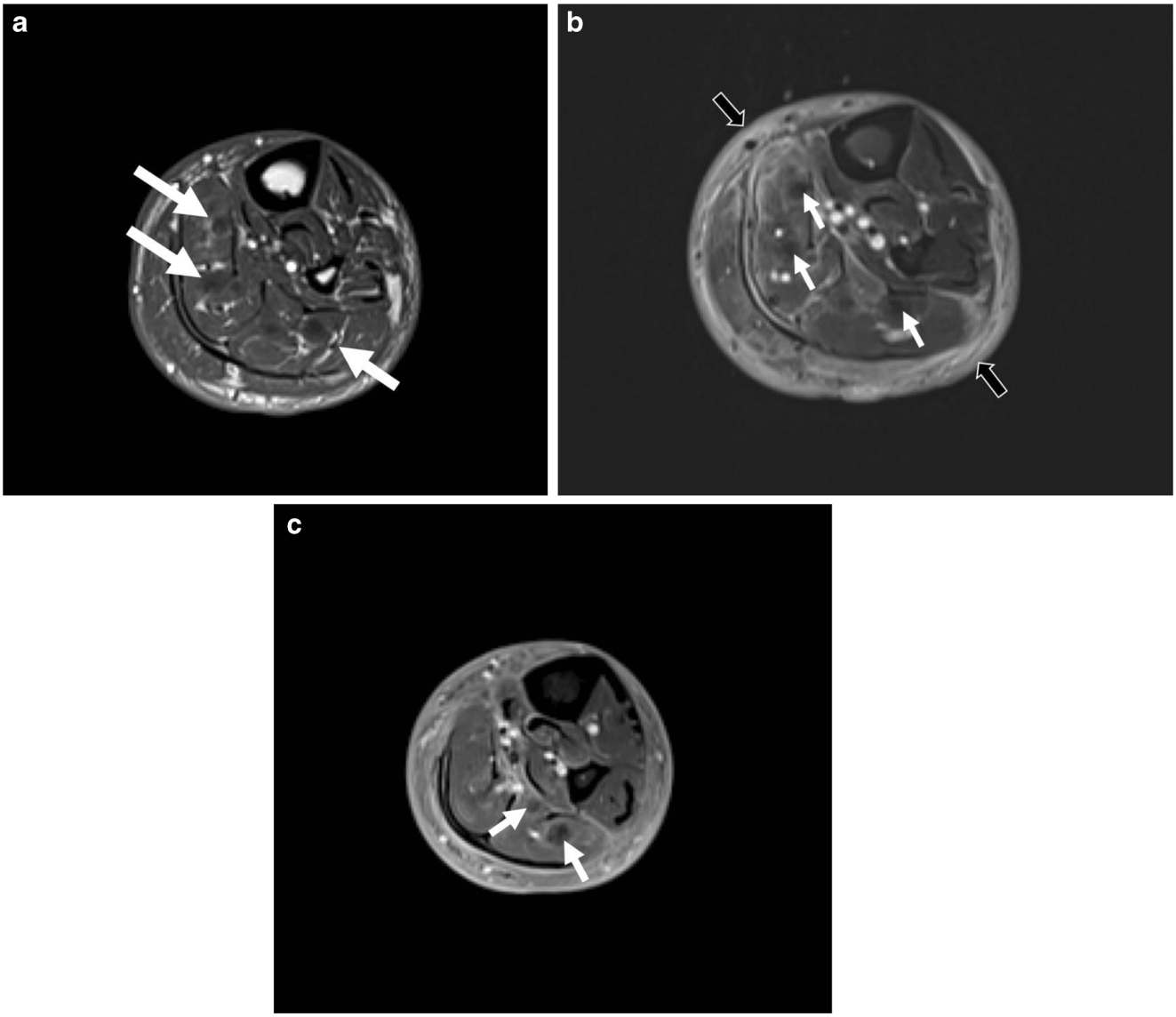

Fig. 5 **a** Axial T1 and **b** axial T2FS and **c** axial T1 fat-suppressed post-contrast enhancement sequences of the left calf show multiple T1/T2 hypointense foci (*white arrows*) within the soleus muscle with subtle surrounding enhancement on the post-contrast sequences probably attributable to vascular fragility from defective collagen synthesis of the vessel wall. Note the diffuse subcutaneous edema on the T2 sequence (*black arrows*)

and in those undergoing bone marrow transplant or chemotherapy [2].

Characteristic imaging findings of scurvy are secondary to abnormal collagen production, leading to vascular fragility and abnormal bone matrix. Radiographic findings are more common in children and are most prominent in areas of rapid skeletal growth such as the distal femur, proximal tibia and fibula, distal radius and ulna, proximal humerus, and distal ribs [15]. Osseous findings in pediatric patients include generalized osteopenia with cortical thinning, especially at the epiphyses, and occasionally pathologic. Subperiosteal hemorrhage often manifests as a periosteal reaction with increased density in the periosteal soft tissues. Metaphyseal findings include irregularity and widening of the growth plate because of disorganized collagen proliferation. Characteristic findings include dense sclerotic bands along the metaphyseal side of the physis in the provisional zone of calcification (Frankel line) with a lucent line called the Trummerfeld zone, or scurvy line, on the diaphyseal side of the Frankel line due to unorganized osteoid [16, 17]. Other findings include beaking of the metaphyseal corners (Pelkan spur) due to healing fractures and a thin, sclerotic cortical rim around osteopenic epiphyseal ossification centers (Wimberger ring sign) [4].

Magnetic resonance imaging findings in pediatric patients include nonspecific patchy widespread foci of marrow edema in the metaphyses, diaphysis or flat bones of the pelvis [14]. But more characteristic findings of symmetrical, band-like metaphyseal marrow edema (low T1/high T2 signal), most

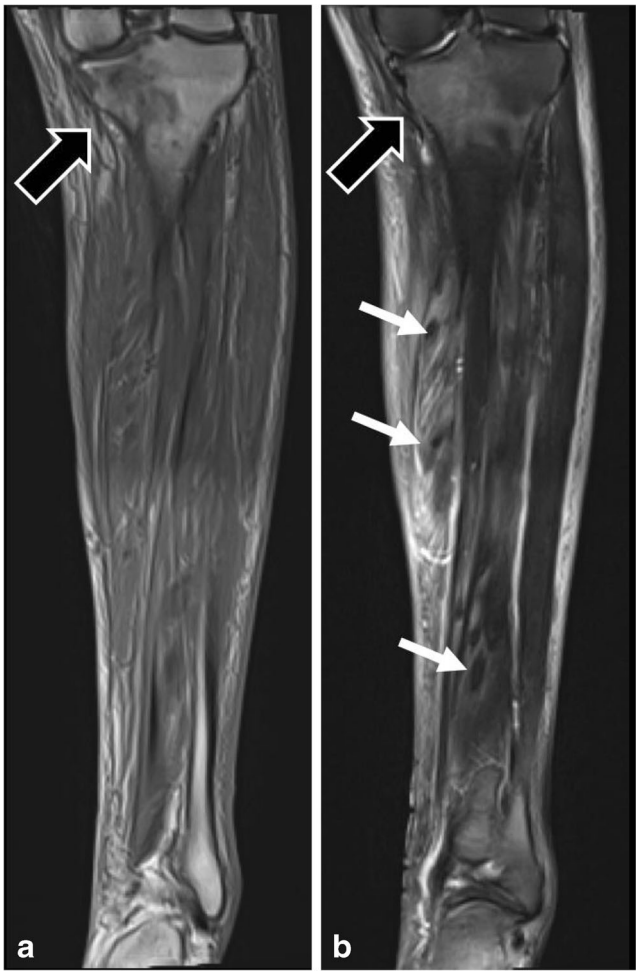

Fig. 6 Coronal **a** T1-weighted and **b** T2-weighted with fat suppression sequences show multiple hypointense intramuscular hemorrhages in the calf musculature (*white arrows*) and ill-defined bone marrow edema in the proximal medial tibial metaphysis (*black arrows*)

conspicuous in bilateral lower-extremity metaphyses about the knees have also been described [4, 18–20]. Additional findings include subperiosteal hemorrhage presenting as periosteal elevation and subperiosteal collections with increased T1 and T2 signal [21, 22]. These features may mimic hematologic malignancy, osteomyelitis, or metastatic disease and prompt unnecessary invasive diagnostic procedures or additional radiological imaging.

In adult patients, scurvy is infrequently encountered, resulting in a paucity of literature on the associated radiological findings. One case report describes multiple small focal areas of bone marrow edema throughout the metadiaphyseal regions of the distal femur and proximal tibia on T1-weighted images in a 56-year-old man with recurrent petechial rash and a history of a diet devoid of fruits and vegetables. Subsequent skin biopsy revealed interstitial hemorrhage consistent with scurvy, which resolved after vitamin C supplementation; a repeat MRI conducted 6 months later showed complete resolution of the bone marrow lesions [23]. Another case report described nonspecific MRI findings of inflammation including dermal thickening, subcutaneous and deep fascial edema, and heterogeneous increased T2-weighted signal bilaterally in the quadriceps and gastrocnemius muscles. Patchy foci of enhancing marrow edema in the distal femur and proximal tibia were nonspecific and thought to represent islands of red marrow [24].

Compared with the literature, this presentation of multiple small bilateral intramuscular hemorrhages, in conjunction with the previously described ill-defined metaphyseal marrow edema on MRI [23–25], appears to be a radiologically unique presentation of scurvy.

Intramuscular hematomas have been described in scurvy cases [10]. In retrospect, the branching pattern of the multifocal

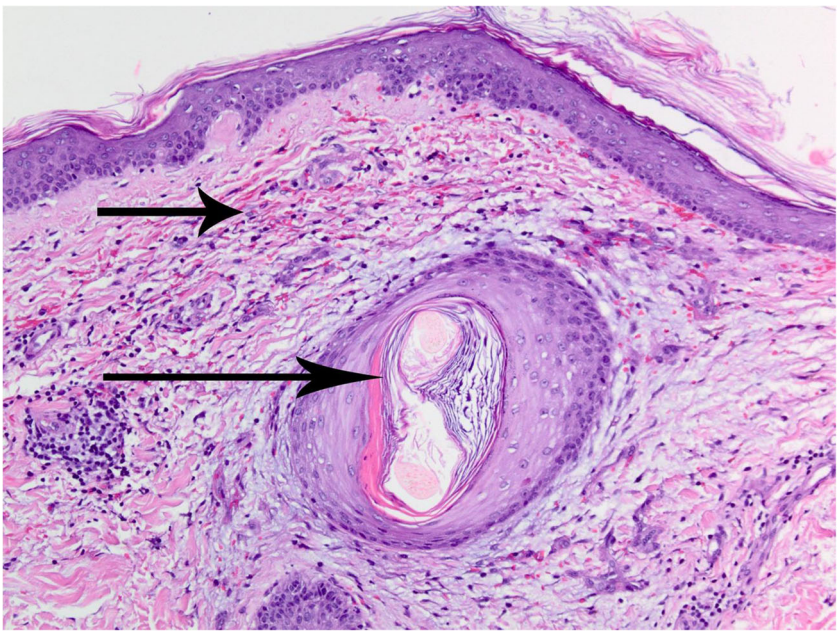

Fig. 7 Pathological demonstration of a distorted hair follicle with perifollicular hemorrhage and minimal inflammation (*long arrow*) and extravasated erythrocytes (*short arrow*)

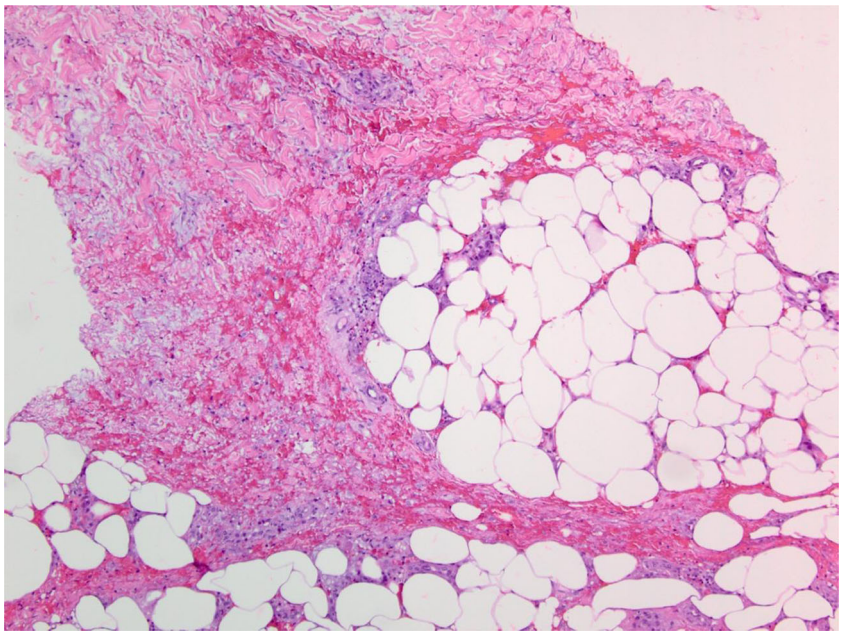

Fig. 8 Pathological demonstration of deep dermal subcutaneous hemorrhage with fat necrosis

hemorrhages in our patient (Fig. 4b) suggests a perivascular distribution. This pattern may be explained by vascular fragility attributable to structural collagen alterations in the vessel wall layers and surrounding connective tissue, allowing red cell extravasation from the capillaries [11, 13]. The lower extremities would be a likely location as the site of highest hydrostatic pressure. Vitamin C also removes oxygen free radicals responsible for increased capillary permeability [26].

In this patient, MRI also revealed ill-defined bone marrow edema in the proximal tibial metaphysis (Fig. 6). In the absence of histological confirmation, a similar etiology may be hypothesized related to defective vascularity and increased capillary permeability, resulting in perivascular edema and hemorrhage. However, biopsy of metaphyseal marrow signal abnormality in pediatric patients with scurvy has revealed gelatinous transformation of the marrow, similar to serous atrophy found in severely malnourished patients [25, 27]. The bilateral presentation of the intramuscular hemorrhages and metaphyseal location of marrow edema are clues to the systemic nature of the disease process and a metabolic work-up may be suggested.

In summary, scurvy should be considered in at-risk patients (restricted or compromised diet, low socioeconomic status, alcoholism, psychological disturbance, or developmental delay) presenting with characteristic dermatological but often nonspecific musculoskeletal symptoms. The diagnosis is frequently overlooked on clinical examination owing to the perceived rare nature of the disease, and the patient may go on to an extensive diagnostic work-up including imaging. Radiological findings are dependent on disease severity and duration, but may include generalized soft-tissue edema and osteopenia, manifestations of bleeding such as subperiosteal hemorrhage, hemarthroses, or intramuscular hemorrhages, and nonspecific patchy or characteristic bandlike bone marrow edema (particularly in the metaphyses) on MRI. Astute recognition of bilateral findings suggests a systemic process that could prompt a metabolic work-up. A thorough dietary history and low serum vitamin C levels confirm the diagnosis, potentially precluding invasive biopsy.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflicts of interest.

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