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Medical Imagery

Scurvy as a mimicker of osteomyelitis in a child with autism spectrum disorder

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ABSTRACT

A case of scurvy in a 10-year-old boy with autism spectrum disorder is described. His clinical presentation was initially thought to be due to osteomyelitis, for which empirical antimicrobial therapy was initiated. Further invasive and ultimately unnecessary investigations were avoided when scurvy was considered in the context of a restricted diet and classic signs of vitamin C deficiency. Infectious diseases specialists should be aware of scurvy as an important mimicker of osteoarticular infections when involved in the care of patients at risk of nutritional deficiencies.

Introduction

Humans cannot convert glucose to vitamin C via gulonolactone oxidase, therefore vitamin C is an essential nutrient obtained solely from the diet. Deficiency results in the depletion of pericapillary collagen, as vitamin C is a necessary cofactor in collagen biosynthesis (Weinstein et al., 2001). Classically described clinical manifestations of very low levels of vitamin C are dermatological (petechiae, ecchymosis, hyperkeratosis, and corkscrew hairs), gingival (bleeding, swelling, and loosened teeth), haematological (anaemia), and musculoskeletal (subperiosteal haemorrhages, bone pain, osteopenia, skeletal muscle degeneration, and arthritis). Early manifestations can include lethargy, weakness, arthralgia, and myalgia (World Health Organization, 1999).

Despite often being thought of as a disease of the past, scurvy (the disease associated with severe vitamin C deficiency) has been described recently in an infant fed exclusively almond beverage (Vitoria et al., 2016), in a child receiving peritoneal dialysis (Kittisakmontri et al., 2016), and in children with neurodevelopmental disability (Weinstein et al., 2001; Erdle et al., 2017; Harknett et al., 2014). Children with autism spectrum disorder (ASD) may be at higher risk of scurvy, as well as other micronutrient deficiencies, because of restricted diet and limited food repertoire; however, there are no published studies on the frequency at of vitamin C deficiency in the paediatric ASD population. Data from the 2003–2004 National Health and Nutrition Examination Survey (NHANES) indicate that less than 2% of the population of the USA aged 6 to 11 years is vitamin C-deficient, while less than 4% of American adolescents are vitamin C-deficient (Schleicher et al., 2009).

The case of a 10-year-old boy with a limp and difficulty weight-bearing in the context of a significantly restricted diet and ASD is reported here. Antimicrobial therapy was initiated for presumed osteomyelitis before a diagnosis of scurvy was considered.

Case report

A 10-year-old boy presented to the emergency department of a paediatric hospital with a limp of 2 to 3 weeks' duration and right ankle swelling (with bruising along the calf and ankle) for 1 week. Six weeks prior, he had suffered a minor knee-twisting injury. There was no fever, night sweats, weight loss, fatigue, or respiratory or gastrointestinal symptoms. There were no symptoms suggestive of a rheumatologic condition. The patient had no history of recent travel and no risk factors for tuberculosis or brucellosis. The family had a cat at home.

The patient was born at term in Canada. His medical history was significant for ASD. He was non-verbal with grossly normal motor skills. There was no history of fracture, osteomyelitis, or invasive infection. The patient was not on any regular medications or supplements. He was fully immunized but had not received a vaccine recently.

On physical examination, weight was below the third percentile. Vital signs, including temperature, were normal. The patient was unable to bear weight on the right leg. The right knee and ankle were swollen and warm with no overlying erythema. The knee was held in a flexed position and seemed painful to palpation, although more precise localization was difficult given the patient's resistance to examination and inability to communicate verbally. Range of motion was limited in the right lower extremity, except for full range of motion at the hip. There were no joint effusions.

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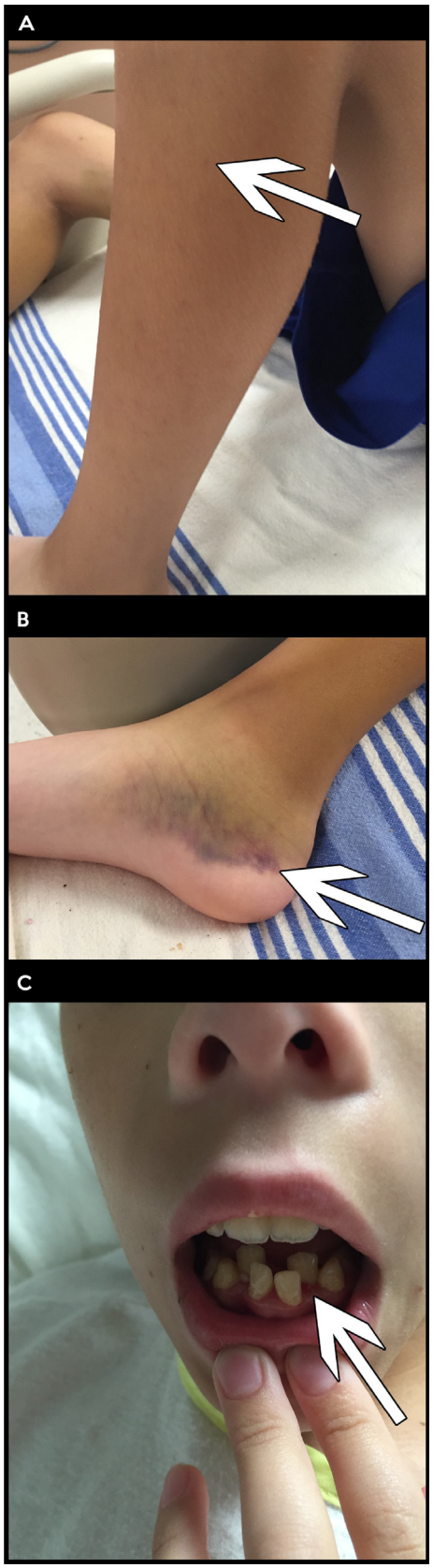

Figure 1. Pre-treatment images of the patient, with (A) parafollicular hyperkeratosis and parafollicular purpura, (B) ecchymosis over the medial aspect of the right ankle, and (C) subtle gingival changes. The white arrows indicate the relevant clinical findings.

Parafollicular hyperkeratosis, parafollicular purpura, ecchymosis and subtle gingival changes were identified (Figure 1). No hepatosplenomegaly or lymphadenopathy was identified.

Blood work showed a mild normocytic anaemia (haemoglobin 110 g/l and mean corpuscular volume 80.8 fl). White blood cell and platelet counts were within normal limits. On blood smear, red cell morphology showed non-specific changes. The erythrocyte sedimentation rate was normal, while C-reactive protein was mildly elevated (10.9 mg/l; normal $\leq$1.0 mg/l). The international normalized ratio and partial thromboplastin time were both normal. Blood culture was negative. X-rays of the right lower extremity showed soft tissue oedema within the popliteal region extending into the upper calf, without fracture. The distal right femur and proximal tibia appeared mildly osteopenic. The ankle mortise appeared congruent with no effusion. The distal tibial and fibular physes were unremarkable.

Following admission under the orthopaedics service, parenteral cloxacillin was started empirically for presumed osteomyelitis. Magnetic resonance imaging (MRI) was obtained (Figure 2), showing multiple areas of focal bone marrow abnormality, without periosteal reaction, throughout both lower extremities. Extensive myositis/cellulitis/fasciitis was seen around the right knee. There was no synovitis or effusion at the hip, knee, or ankle. The possibility of multifocal osteomyelitis was raised. Given the unusual multifocal presentation, a bone biopsy was planned for microbiological and histopathological confirmation of osteomyelitis. The need for bone marrow aspirate to rule out malignancy was also discussed.

The general paediatrics, infectious diseases, and rheumatology services were consulted. Due to the atypical clinical and radiological findings, cloxacillin was discontinued after seven doses. On further questioning, the patient's nutritional history revealed a longstanding, significantly restricted diet comprising exclusively bread, hazelnut cocoa spread, cookies, popcorn, potato chips, chicken nuggets, and croissants.

In the context of restricted diet and classic signs of vitamin C deficiency, a diagnosis of scurvy was strongly suspected. Empirical treatment was initiated with oral ascorbic acid 500 mg daily, along with thiamine, zinc, and multivitamin supplements. As suspected, his ascorbic acid level was ultimately abnormally low ($<$5 μmol/l; normal $>$24 μmol/l). Vitamin A, vitamin D, and zinc were also low (0.1 μmol/l, 61 nmol/l, and 9.1 μmol/l, respectively). Serum folate, transferrin, and ferritin were all within normal limits.

With treatment, the patient experienced rapid improvement and was able to ambulate almost independently within days. Given his favourable clinical evolution, the bone biopsy was cancelled and bone marrow aspirate was deemed unnecessary. Physiotherapy was arranged for ongoing rehabilitation. Vitamin supplementation was continued post-discharge and referral was made to a specialized nutrition clinic.

Discussion

As in the case reported here, the bony and soft tissue manifestations of scurvy can mimic osteoarticular infections, including osteomyelitis (Weinstein et al., 2001; Harknett et al., 2014; Popovich et al., 2009; Gulko et al., 2015). Overlapping clinical manifestations include limping or inability to walk, localized swelling, and tenderness to palpation. Imaging findings in scurvy could be suggestive of osteomyelitis to radiologists who may not have clinical details and who may not be familiar with scurvy, given its relative rarity. On X-ray, the most common finding in scurvy is osteopenia; however, Frankel sign (a white line at the ends of the metaphyses), Pelkan spurs (healing fractures at the periphery of the zone of calcification), and Wimberger ring (increased density outlining the epiphyses) are all well-described

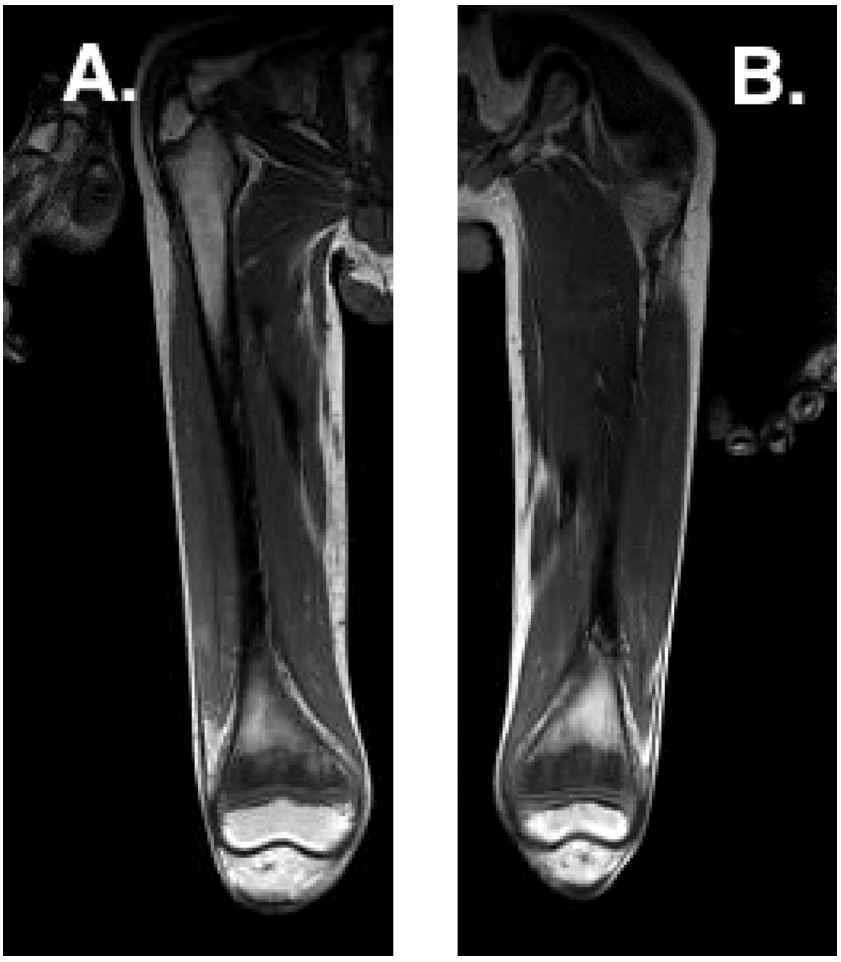

Figure 2. T1-weighted magnetic resonance images of the patient's right (A) and left (B) femur. Multiple areas of focal bone marrow abnormality were seen throughout both lower extremities, with extensive myositis/cellulitis/fasciitis around the right knee.

radiological signs of scurvy (Weinstein et al., 2001; Harknett et al., 2014; Gulko et al., 2015). Subperiosteal bleeding could be mistaken for periosteal reactions found in osteomyelitis (Weinstein et al., 2001; Gulko et al., 2015). On MRI, focal bone marrow signal abnormalities can be seen both in scurvy and in osteomyelitis. Specific findings in scurvy include multifocal, decreased bone marrow signal on T1-weighted images, contrasted with increased signal intensity on T2-weighted images. Enhancement of the soft tissues may represent subperiosteal haemorrhage and periosseous oedema (Gulko et al., 2015; Dubois et al., 2017).

In contrast to scurvy, acute haematogenous osteomyelitis (AHO) tends to involve a single bone, and is multifocal in less than 10% of cases (Peltola and Pääkkönen, 2014). Multifocal involvement, particularly if other aspects of the clinical presentation are atypical, should prompt thought of diagnoses other than AHO. In retrospect, numerous factors made the diagnosis of osteomyelitis less likely in the patient described in this case report: extensive soft tissue involvement, absence of fever, inflammatory markers that were not significantly elevated, and absence of periosteal reaction after several weeks of symptoms (Peltola and Pääkkönen, 2014).

Because an infectious diseases consultation is often sought in cases of presumed osteoarticular infection, infectious diseases physicians should recognize the broad differential diagnosis for a child presenting with a limp and abnormal bone imaging. It includes not only typical and atypical infectious entities (mycobacterial, *Brucella spp*, *Bartonella spp*), but also non-infectious conditions, such as traumatic, neoplastic, rheumatologic, metabolic, and nutritional causes. A thorough review of the history may provide diagnostic clues useful in arriving at the correct diagnosis. In the context of a restricted diet, incongruent clinical features should raise the possibility of scurvy in a child with difficulty ambulating and abnormal bone imaging. Recognition of scurvy as a diagnostic consideration ensures appropriate treatment (i.e., avoids unnecessary, prolonged antibiotic courses) and may avoid unnecessary investigations (e.g., bone biopsy, which is often used for diagnosis after clinical assessment, laboratory work-up, and imaging).

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References

Dubois M, Cousin E, Chouklati K, Bruneau B, Proisy M. Scurvy in a 3-year-old autistic girl: whole-body magnetic resonance imaging findings. Diagn Interv Imaging 2017;99(1):49–50.
Erdle S, Conway M, Weinstein M. A six-year-old boy with autism and left hip pain. CMAJ 2017;189(7):E275–8.
Gulko E, Collins LK, Murphy RC, Thornhill BA, Taragin BH. MRI findings in pediatric patients with scurvy. Skeletal Radiol 2015;44(2):291–7.
Harknett KM, Hussain SK, Rogers MK, Patel NC. Scurvy mimicking osteomyelitis: case report and review of the literature. Clin Pediatr (Phila) 2014;53(10):995–9.
Kittisakmontri K, Swangtrakul N, Padungmaneesub W, Charoenkwan P. Gingival bleeding and bloody dialysate: a case report of scurvy in a child with end-stage renal disease receiving peritoneal dialysis. J Ren Nutr 2016;26(6):407–11.
Peltola H, Pääkkönen M. Acute osteomyelitis in children. N Engl J Med 2014;370(4):352–60.
Popovich D, McAlhany A, Adewumi AO, Barnes MM. Scurvy: forgotten but definitely not gone. J Pediatr Health Care 2009;23(6):405–15.
Schleicher RL, Carroll MD, Ford ES, Lacher DA. Serum vitamin C and the prevalence of vitamin C deficiency in the United States: 2003-2004 National Health and Nutrition Examination Survey (NHANES). Am J Clin Nutr 2009;90(5):1252–63.
Vitoria I, López B, Gómez J, et al. Improper use of a plant-based vitamin c-deficient beverage causes scurvy in an infant. Pediatrics 2016;137(2)e20152781.
Weinstein M, Babyn P, Zlotkin S. An orange a day keeps the doctor away: scurvy in the year 2000. Pediatrics 2001;108(3):E55.
World Health Organization, Office of the United Nations High Commissioner for Refugees. Scurvy and its prevention and control in major emergencies. Geneva: World Health Organization: Office of the United Nations High Commissioner for Refugees; 1999.

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