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SKELETAL PAIN IN CHILDREN: DON'T FORGET SCURVY! A PAEDIATRIC CASE SERIES

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ABSTRACT

Appropriate nutritional intake is an important aspect in children's overall health. In developed countries, malnutrition is related to chronic illness or restrictive dietary habits, related to psychiatric or behavioural conditions such as anorexia or neurodevelopmental disabilities. Recent studies consider vitamin C deficiency a re-emerging disease, although it is historically believed a disease of the past. We report 4 cases of scurvy in children which occurred in 2021 in our tertiary hospital in Catania. They were admitted for skeletal pain, refusal and/or inabilities to walk. Primary diagnostic considerations included infectious etiologies, malignant disease or orthopaedic problems. In anamnesis, only one out of four presented a diagnosis of neurodevelopmental disabilities. However, after scurvy was diagnosed, the remaining patients received an adequate neuropsychiatric evaluation reporting eating selective habits in children affected by behavioural disturbances. Recognition of the cutaneous findings, associated with skeletal pain, was vital in two cases for the diagnosis. Bone imaging findings (X-ray and MRI) were considered typical of scurvy after a good response to treatment with vitamin C.

1. Introduction

Appropriate nutritional intake is an important aspect in children's overall health. Although health care workers in developing countries are confronted daily with patients with various forms of nutritional deficiencies, these important health issues can also manifest in affluent countries with abundant food supplies [1]. In developed countries, malnutrition is related to chronic illness or restrictive dietary habits; the latter condition is usually attributable to psychiatric or behavioural conditions such as anorexia, autism spectrum disorder or neurodevelopmental disabilities [2-4]. Recent studies highlight vitamin C (ascorbic acid) deficiency as a re-emerging disease in children with selective eating habits for whatever reason [5]. Vitamin C is not synthesized by humans and therefore must be obtained through the diet in the form of fruits and vegetables. Scurvy has been known since ancient times, described first by Hippocrates [6].

The prevention of scurvy with citrus fruits was discovered by James Lind in 1753, who understood that navigators got sick during long expeditions without fresh citrus fruit. Subsequently, ascorbic acid was first isolated in 1928 [6-7].

Ascorbic acid is involved in the hydroxylation of collagen, L-carnitine and certain neurotransmitters.[8] Vitamin C has a half-life of 10 to 20 days. However, signs of deficiency generally develop after 3 months of inadequate vitamin C intake [4]. Scurvy manifests with symptoms such as gingival haemorrhages, petechial rash and ecchymosis caused by defective collagen synthesis of blood vessel walls [1]. Clinically, the differential diagnosis is with systemic diseases such as rheumatologic, orthopaedic, infectious or hematologic disorders. Because it is presently considered a rare diagnosis, it is not well known by paediatricians and radiologists causing unnecessary delays in diagnosis and treatment [4-5].

We report four cases of unexpected scurvy in children which occurred in 2021 in our tertiary hospital in Catania.

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Two patients were around 3 years old, one was 7 years old and one 12 years old. All patients were admitted for skeletal pain, refusal and/or inabilities to walk. In anamnesis, none conveyed a history of neurodevelopmental disabilities, but all patients had selective eating habits. Recognition of selective habits in anamnesis, associated with skeletal pain, was vital for the diagnosis.

2. Case presentations

Case 1

A 3-year-old boy was admitted to the hospital for sudden refusal to walk and with skeletal pain, referred especially to the spine. There was negative anamnesis for trauma. Two weeks before, the child presented with fever associated with petechial rash which self-resolved, casting doubt of a viral infectious etiology. He was exclusively breastfed for the first 8 months of his life. His psychomotor development was normal. Clinical examination revealed difficulties with walking. There were no cutaneous findings. The hypothesis of osteomyelitis was excluded because the septic workup was negative, including a normal white blood cell count and indices of inflammation. The examination of the osteo-tendinous reflexes and the strength and tone of the lower limbs was normal, discarding the hypothesis of a flaccid paralysis after the viral infection. A bilateral antero-posterior knee X-ray initially was reported uninformative. During the hospitalisation, we noted a selective diet, exclusively composed of bread, pasta and milk without fruits. A nutritional assessment revealed low ferritin level (5 µg/L, N = 15–80) and plasma Vit C content (0.5 µmol/L, normally 40–100 µmol/L).

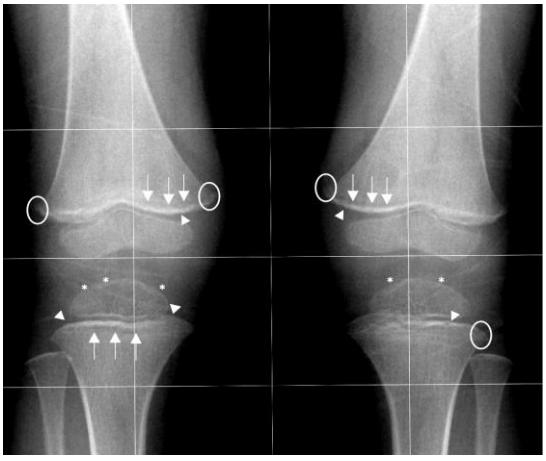

Figure 1. Scurvy in 3-year-old boy with walking disorders. Bilateral Antero-posterior knee X-ray shows the classic radiographic signs for Scurvy: dense zone of provisional calcification at edge of metaphysis (white line of Frankel) (head arrows), transverse radiolucent metaphyseal line (Trümmerfeld zone) (white arrows), radiodense shell surrounding epiphyses (Wimberger sign) (stars) and beaklike metaphyseal excrescences (Pelken spurs, corner or angle sign) (white circles).

On the suspicion of scurvy, a radiological team discussion of the X-ray images revealed the classic radiographic signs (Figure 1): dense zone of provisional calcification at edge of metaphysis (white line of Frankel), transverse radiolucent metaphyseal line (Trümmerfeld zone), radiodense shell surrounding epiphyses (Wimberger ring) and beaklike metaphyseal excrescences (Pelken spurs, corner or angle sign). A nutritional assessment revealed low ferritin level (5 µg/L, N = 15–80) and plasma Vit C content (0.5 µmol/L, normally 40–100 µmol/L). On the suspicion of scurvy, a radiological team discussion of the X-ray images revealed the classic radiographic signs (Figure 1): dense zone of provisional calcification at edge of metaphysis (white line of Frankel), transverse radiolucent metaphyseal line (Trümmerfeld zone), radiodense shell surrounding epiphyses (Wimberger ring) and beaklike metaphyseal excrescences (Pelken spurs, corner or angle sign).

Treatment was started and rapidly effective. This child regained motor function and his general condition greatly improved. A neuropsychiatric evaluation suggested a psycho-educational rehabilitation in child affected by mild behavioural disturbances.

Case 2

A 2.7-month-old boy was admitted to this hospital for disturbances walking and leg pain for 6 months, at the first time attributed to transient synovitis or “growing pains”. His mother conveyed that the child’s appetite was suppressed, probably due to the increased pain with worse general conditions. His diet had become poor, consisting of bread and dairy products. The growth showed an important weight loss, a bone-marrow aspiration was performed in the suspicion of a malignant disease, which was normal. Initial radiograph findings of the knee showed generalized osteopenia. (Figure 2)

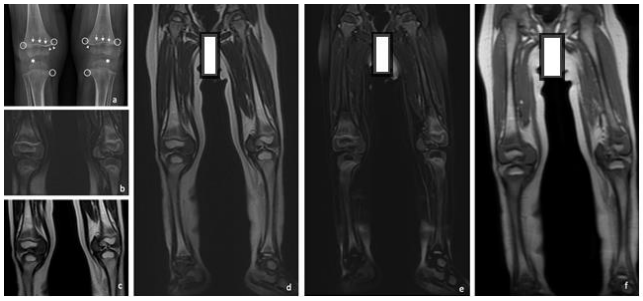

Figure 2. Bilateral Knee radiography (a) and MRI (b-c-d) in 2- and 7-year old boy with Scurvy. Anteroposterior radiograph of the knee (a) shows irregular dense zone of provisional calcification (Frankel line) (head arrows), lucent metaphyseal band underlying Frankel line (white arrows), metaphyseal spurs (white circles) and generalized osteopenia. Coronal T2 weighted MR images with (e) and without (d) fat-suppression and Coronal T1 weighted MR image (f) shows bone marrow edema in the proximal and distal juxta-metaphyseal regions of the femur and tibia bilaterally.

(a). MRI (magnetic resonance imaging) was performed, showing in coronal T2 weighted MR images with (e) and without (d) fat-suppression and in coronal T1 weighted MR image (f) bone marrow edema in the proximal and distal juxta-metaphyseal regions of the femur and tibia bilaterally. Thus, a successive staff meeting discussion revealed in the X-ray the signs of scurvy: irregular dense zone of provisional calcification (Frankel line), lucent metaphyseal band underlying Frankel line, metaphyseal spurs. Nutritional assessment was required, showing plasma Vit C content markedly reduced (1,4 µmol/L, normally 40–100 µmol/L) and confirming scurvy. Vitamin C treatment had a positive effect on pain, and motor function, until a complete resolution of the symptoms. A neuropsychiatric evaluation suggested a psycho-educational rehabilitation.

Case 3

A 7-year-old boy, affected by autism spectrum disorder, was admitted to our hospital for skeletal pain, especially to the legs, and difficulty walking. Parents conveyed that the child demonstrated these symptoms for about four months. The first diagnostic consideration was an orthopedic problem; thus X-ray and ultrasound of the legs and hips were performed, reporting no signs of fracture or other abnormalities. At the clinical examination, we noted hypertrichosis in the lower legs (Fig. 3), previously diagnosed as atopic dermatitis, and gingival hypertrophy. A nutritional assessment revealed low ferritin level (8 µg/L, N = 15–80) and plasma Vit C content (0.2 µmol/L, normally 40–100 µmol/L). On the suspicion of scurvy, substitute treatment was started and rapidly effective.

Figure 3. Follicular hyperkeratosis in a the left leg of a child affected by autism spectrum disorder and scurvy.

Case 4

A 12-year-old girl was admitted to our hospital with worsening musculoskeletal pain and refusal to walk. There was negative anamnesis for trauma. Family and personal histories were unremarkable for diseases. At the clinical examination, the girl had ecchymosis at the knees and signs of gum bleeding (Fig.4). Bleeding disorder work up including prothrombin time, partial thromboplastin time, international normalized ratio, platelet aggregation tests were normal. C-reactive protein, chemistry including calcium, phosphorus and magnesium, autoimmunity screening were also normal.

The first diagnostic suspicion was a rheumatologic problem; thus ultrasound of the knees and X-ray of the legs were performed, reported negative. A nutritional assessment revealed low ferritin level (4 µg/L, N = 15–80) and plasma Vit C content (0.1 µmol/L, normally 40–100 µmol/L). During the stay, we noticed that the alimentary habits of the girl was characterised by very selective diet. The patient's mother conveyed increasingly selective eating habits by the patient over the past six months. The girl had a good response with Vit. C treatment. A neuropsychiatric evaluation suggested a psycho-educational rehabilitation.

Figure 4. Ecchymosis to the knees (a) and gingival hypertrophy with bleeding signs (b) in a girl of 12 years

3. Discussion

These four different cases highlight that scurvy is frequently misdiagnosed, giving the doubt of other various pathologies requiring specialist advice such as orthopaedists, neurologists or haematologists. In fact, in the first case the diagnostic suspect was for an infectious or neurological disease, in the second case for a malignant problem, in the fourth for a rheumatologic disease. The present cases were linked by selective and poor intake diet. In paediatric age, as reported in this case series, it is not easy to understand if the dietary restrictive is cause or consequence of the basal general disorder.

Daily, healthcare providers visit more and more children affected by obesity in affluent countries, thus it's difficult to suspect nutritional deficiencies in a country with usual abundant food supplies. As reported by our experience, unlike severe behavioural disorders, mild disturbances could be misdiagnosed and scurvy could be the first clinical expression of the neuropsychiatric pathology. In literature, most paediatric cases reported scurvy in children with autism spectrum and neurodevelopmental disorders, such as in the third case, but not only [8-11]. More and more children have a selective diet, totally devoid of fresh fruit and vegetables. These children present with an avoidant/restrictive food intake disorder or with very selective eating behaviour [5].

Vitamin C or ascorbic acid is an essential vitamin, absorbed by the ileum and eliminated by renal excretion. Clinical signs of deficiency start to manifest within 3-6 months [11]. Ascorbic acid plays a role in the formation of type II collagen, thus his deficiency contributes to bone lesions [12]. In the present cases, the symptoms leading to hospitalization in all cases were refusal and/or impossibility to walk because of skeletal symptoms. Clinical signs of scurvy include also gingival lesions together with inflammation and hypertrophy, follicular hypertrophy and ecchymosis.[1]

Recognition of skin lesions is vital for the diagnosis, but they could also be missed, such as what happened with the first and second cases reported, making the diagnosis more challenging.

Radiographic findings suggestive of scurvy are located in the metaphysis of all long bones and include a clear metaphyseal band, also named Trummerfeld zone; marked white line corresponding to thickened zone of calcification also named white line of Frankel; irregular metaphyseal margin or metaphyseal fractures known as Pelkan spur and diffuse osteopenia. MRI findings are concordant with radiographic findings: multifocal, symmetric bone-marrow changes in the metaphysis of long bones [13].

In conclusion, the present cases underline the opportunity that paediatricians should suspect scurvy in cases of general skeletal pain. Anamnesis has the most important role to suspect nutritional deficiencies. It's important to require a food diary to investigate the child's alimentation, because nutrition considered correct by parents may not really be. In addition, mild behavioural disturbances could manifest with selective eating behaviour and not yet diagnosed, thus scurvy should be suspected not only in children with noted neurodevelopmental disturbances. For these selective-eating toddlers, in addition to psycho-educational rehabilitation, formula for young children can be continued after 3 years of age and vitamin C must be given as orange juice or vitamin supplements.

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