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Scurvy: still a threat in the well-fed first world?

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ABSTRACT

We report three cases of scurvy in previously healthy children referred to us for leg pain and refusal to walk. All children had no significant medical history, symptoms had started months before and subtly advanced. Two of them presented with gingival hyperplasia and petechiae, another one reported night sweats and gingival bleeding in the past few weeks. Two had vitamin D deficiency, and all had microcytic anaemia (in one case requiring transfusional support). A nutritional screening revealed low or undetectable levels of ascorbic acid. This, along with the clinical and radiological findings, led to a diagnosis of scurvy. Vitamin C supplementation was started with rapid improvement of the children's clinical condition. Scurvy is a rare disease in the 'first world', but there are anecdotal reports of scurvy in children without any of the known risk factors for this condition. In our cases, a selective diet was the only risk factor.

INTRODUCTION

In developed countries, nutritional problems are mostly due to excessive calorie intake instead of a lack of nutrients. Scurvy is rarely included in the evaluation of a limping child.[1] It is considered a disease confined to certain categories: socially isolated individuals, patients with malabsorption, psychiatric conditions or undergoing extreme diets. We present three cases of children without predisposing conditions that presented with leg pain, limping and/or refusal to walk and had a final diagnosis of scurvy.

CASE 1

A 2.5-year-old Caucasian boy who 6 months earlier had suffered a fracture of the left femur after a fall and from then on, the child never resumed walking. After undergoing various tests including a spine and pelvis MRI (that revealed inflammatory alterations of the soft tissue and cortical bone) and elevated inflammatory markers, he was transferred to our hospital. He weighed 10.9 kg (third to 10th percentile) and was 93.5 cm tall (70th percentile) with a body mass index (BMI) of 12.5 kg/m^2 (<third percentile). He presented with diffused petechiae, gum swelling and bleeding. Blood tests showed a microcytic anaemia (haemoglobin (Hb): 11 g/dL, mean corpuscular volume (MCV): 59.8 fL), while a neurological, rheumatological, immunological, metabolical and haematological (including a bone marrow aspiration) evaluations were all negative. Bone scintigraphy showed an uneven distribution of the radiocompound, with uptake in multiple segments. A whole-body radiograph, performed to exclude alterations in other bones, showed osteopenia and dense iuxtaphyseal bands alternating with radiotransparent ones (figure 1). These finding s suggested the hypothesis of scurvy, confirmed by a vitamin C level of 10 µmol/L (normal range: 26.1–84.6 µmol/L) and vitamin D level of 5.7 ng/mL (normal range: 20–120 ng/mL). When asked about the child's dietary habits, the parents reported that the child refused to eat fruits and vegetables. Given these results, the child was started on an oral supplementation of ascorbic acid and vitamin D. The clinical condition rapidly improved with spontaneous recovery of walking.

CASE 2

A 4.5-year-old Caucasian boy presented to our unit with leg pain and refusal to walk, with legs fixed in flexion at hips and knees (figure 2). The pain had started 7 months before in the left leg and later the child developed pain in both legs until this led to refusal to walk. He presented emaciated (weight: 10.5 kg: <third percentile; stature 108 cm: 90° percentile; BMI: 9 kg/m^2: <third percentile). His legs could not be extended, and he also presented with dental abnormalities and gingival hypertrophy. Medical records showed a weight loss of 25% during the last 10 weeks. Parents reported progressive anorexia, frequent night sweats and gingival bleeding.

Blood tests revealed microcytic anaemia (Hb: 9.4 g/dL, MCV: 70.4 fL). Considering the history of bone pain, night sweats and anorexia with weight loss, to exclude a haematological disorder we performed a peripheral blood immunophenotyping and a head CT to exclude an intracranial mass. Both were negative. Due to the history of selective diet, he also underwent nutritional screening, including vitamins levels, that showed low vitamin C levels below recordable laboratory sensitivity. At this point, a whole-body radiograph was performed that showed a widening of the anterior rib ends at the costochondral junctions and metaphyseal lucent bands in the distal femur, proximal tibia and superior limbs. These findings, along with the extremely low level of vitamin C, led us to the diagnosis of scurvy.

Intravenous ascorbic acid and enteral feeding were started and the symptoms dramatically improved: 4 weeks later the child could stand and walk on his own. The weight at discharge was 13.8 kg (+3.3 kg in 12 days) and vitamin C serum level was 58.7 µmol/L.

CASE 3

A 2-year-old boy of African origin was transferred to our unit from another hospital, where he was

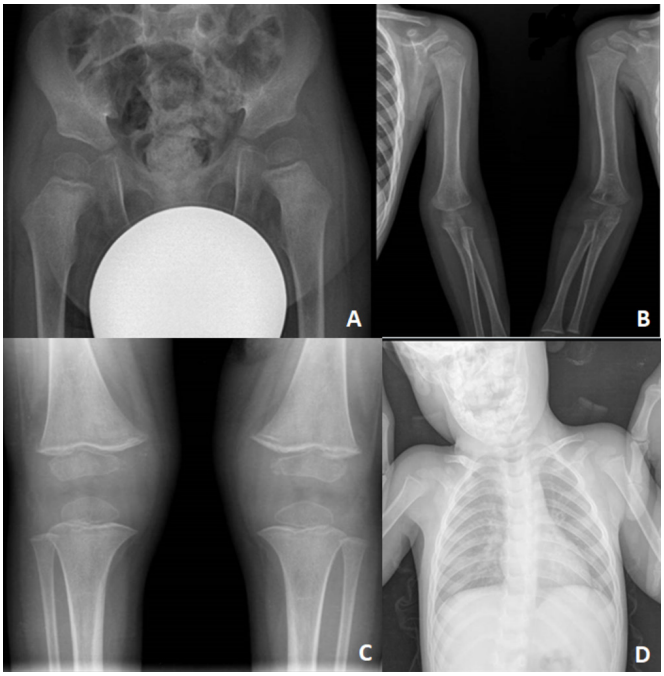

Figure 1 Whole-body radiography of patient 1 shows a reduced calcic tone and radiotransparent bands under the metaphyseal plate of femur necks bilaterally (A) and dense iuxtaphyseal bands alternating with radiotransparent ones in the metaphyseal regions of humerus, radius, ulna (B), femur, tibia and fibula (C). In (D), note the widening of costochondral junction.

admitted for limping and swelling of the right knee. The child was obese (weight: 20 kg ,>97° percentile, height: 100 cm, >97° percentile; BMI: 20 kg/m^2: >97° percentile) with diffused oedema and a swelled, painful right knee. During the previous hospitalisation, immunological and microbiological tests were normal. The child had severe anaemia (Hb: 6.8 g/dL) treated with blood transfusion, and diffused oedema with hypoalbuminaemia (albumin: 2.4 mg/dL) which also required treatment. The parents reported that the child only consumed milk and cookies; a nutritional screening revealed ascorbic acid level of

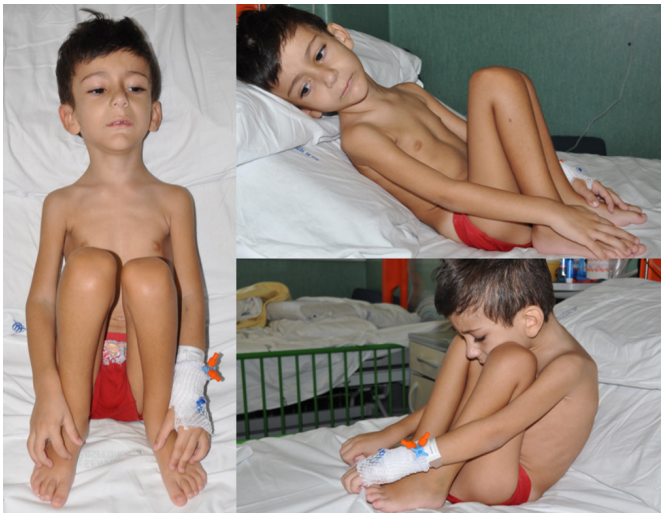

Figure 2 Frog-legged position (patient 2) typical of scurvy: the child lies with both legs bent at the knees and hips. Passive or active motion elicits vivid pain.

Table 1 Main features and differences of three cases

Characteristic	Case 1	Case 2	Case 3
Age (months)	29	53	26
Main symptom	Refusal to walk	Leg pain	Limping
Other symptoms	Petechiae, gum swelling	Dental abnormalities, gum swelling	Swelling of the knee
First clinical suspicion	Fracture of femur	Neoplasm	Osteomyelitis
BMI (kg/m^2)	12.5 (<third percentile)	9 (<third percentile)	20 (>97° percentile)
Instrumental tests	Bone scintigraphy, Whole-body radiograph	Head CT	None
Other tests	Bone marrow aspiration	Peripheral blood immunophenotyping	Immunological and microbiological tests
Vitamin C level (normal: 26.1–84.6 µmol/L)	10 µmol/L	Below sensitivity	6.4 µmol/L
Other deficits	Vitamin D (5.7 ng/mL)	None	Vitamin D (5.7 ng/mL) Folate (0.86 ng/dL)
Haemoglobin level (g/dL)	11	9.4	6.8

BMI, body mass index.

6.4 µmol/L (normal range: 26.1–84.6 µmol/L), vitamin D level of 5.7 ng/mL (normal range: 20–120 ng/mL) and folate level of 0.86 ng/dL (normal range: 3–17 ng/mL) with normal B_{12} levels. Intravenous and subsequently oral vitamin C, D and folate therapy were administered. His clinical condition improved with recovery of walking. One month after discharge, the boy had normal vitamins' levels.

DISCUSSION

Most animals derive ascorbic acid by glucose metabolism. Humans have lost this ability and must acquire it through fruits and vegetables.[2] This need is due to the non-functional mutation of the L-gulonolactone oxidase gene that occurred in our ancestors and led to a 'species enzymopathy'. Vitamin C is a potent antioxidant and a cofactor for numerous enzymes, also involved in the biosynthesis of collagen. Collagen is first synthesised as procollagen and to transform into the mature form it needs the hydroxylation of amino acid residues, requiring vitamin C as a cofactor.[3] The absence of hydroxylated residues makes collagen unable to assemble into rigid triple helixes, resulting in fragility of different tissues. This mechanism is responsible for scurvy's signs like easy bruising, poor wound healing, nail changes, corkscrew hair, gingival and teeth anomalies, bleeding tendency and anaemia.

In all three cases, the main symptom was limping and refusal to walk due to pain in lower limbs (patients' main features and differences are described in table 1).

The concomitant finding of other nutritional deficiencies is common, as we saw in our cases reported. Two out of three patients had concomitant vitamin D deficiency, all had microcytic anaemia and in one case we also found a folate deficiency.

Ratanachu *et al* found that these were the main clinical features of scurvy in childhood.[4] The blood vessels fragility cause subperiosteal haemorrhages, responsible for bone pain. Pseudoparalysis is also often reported with the child assuming a frog-legged position with hips and knees fixed in flexion. Swelling may also be present at costochondral junction configuring the so-called scorbutic rosary. Ascorbic acid is necessary in the bones to deposit a new matrix, the defective matrix is also responsible

for the limb pain and most of the typical radiological findings (eg, Wimberger ring sign, Frankel line).

The symptoms of scurvy dramatically resolve by supplementation and also, the children's appetite usually rapidly improve with the normalisation of vitamin C levels, as happened in our experience.

CONCLUSIONS

Scurvy is rare in developed countries and is mostly found in children with specific risk factors, and its true prevalence is unknown.[5]

In the cases reported, patients' history revealed a selective diet based on carbohydrates, with no vitamins and proteins intake, which led to malnutrition with loss of weight in two cases and obesity in the third one. The last case highlights that nutritional deficiencies are not a prerogative of underweight children but can also present in overweight and obese patients. In our cases, the selective diet was a result of bad food education. A neuropsychological assessment was performed in the three children described and showed normal development, excluding autistic traits. These cases show that when evaluating a limping child or a child who refuses to walk and pain in the lower limbs, scurvy must be considered as one of the possible differential diagnosis not only in children with classic risk factors but also in healthy ones with a selective diet. The underestimation of scurvy in the panel of differential diagnosis often leads to long hospitalisation and excessive tests, often invasive, to rule out other conditions.

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Ethics approval Comitato Etico dell'Opsedale Pediatrico Bambino Gesù (Ethics Committee of the Bambino Gesù Children Hospital).

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