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ORIGINAL ARTICLE

Scurvy hidden behind neuropsychiatric symptoms

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Abstract Approaching an uncommon disease may result in diagnostic delay even in patients with typical clinical features. In this respect, diseases related to nutritional deficiencies may represent a diagnostic challenge. We describe a 2.5-year-old child with typical features of scurvy, who was referred for autistic-like behavior and severe muscle weakness and pain in lower limbs. Extensive investigations for non-nutrition-related disorders were first performed, including a muscle biopsy showing a selective type II fibers hypotrophy. Scurvy was eventually considered, after recalling the child's peculiar dietary habits.

Keywords Nutrition-related disorders · Vitamin C · Autistic behavior · Myalgia

Introduction

Scurvy has been known to exist for more than 2 millennia. However, its prevention by citrus fruits and causal relationship to ascorbate (vitamin C) deficiency were not systematically described until the eighteenth century.

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Nowadays in developed countries, technological advances in food processing and better dietary habits make scurvy a rare disease. It is still occasionally encountered in adults with poor and unbalanced diets, i.e. alcoholics, homeless and food faddists. Scurvy is exceptional in children, often making this diagnosis a challenge [1–3].

Case report

A 2.5-year-old boy was referred to our Department for suspected psychogenic-motor disorder after 3 months of reduced gross motor activity, evolved to a complete refuse to walk. The child had progressively reduced his intake and presented frankly irritable.

He is the second child of a middle class couple, the parents lived together sharing the child care. The boy met the normal psychomotor developmental milestones, but was shy, clinging to his mother, had sleep disturbances and was very selective in food intake.

Extensive serological examinations, CSF-analysis, X-ray of lower limbs, brain and spinal MRI studies were unrevealing, thus, given the reported behavioral disturbances, a psychogenic motor disorder was hypothesized and he was referred to us.

On admission, he appeared extremely distressed, withdrawn and oppositional. He spontaneously maintained his lower limbs in semi-flexion, refusing to stand or walk. The skin over his lower limbs was hyperkeratotic, with perifollicular hemorrhages, plantar desquamation and distal edema. His gums were red and hypertrophic and he had multiple skin granulomatous lesions. A diffuse muscle wasting and flabbiness were evident. The clinical observation ruled out the psychogenetic hypothesis. By contrast,

the association of pain and weakness pointed to acute myositis or polyradiculoneuritis.

Blood tests revealed a mild microcytic anemia with moderate increase of circulating markers of inflammation. Electromyography showed polyphasic low-amplitude, short-duration motor unit potentials and both spontaneous and insertion activities. Electroneuronography was normal. Muscle biopsy depicted scarce hypotrophic type II muscle fibers. These findings, although slightly abnormal, were not consistent with a neuromuscular disease.

During the following days, the child lost weight, developed gingival bleeding and anemia worsened; a bone marrow aspiration was performed and ruled out a lymphoproliferative disorder.

We reconsidered the clinical picture, and focusing on the association of lower limb pain with gingival lesions, we hypothesized the diagnosis of scurvy. Further questioned about their child's diet, the parents admitted that he assumed exclusively ultra high temperature (UHT) milk. Re-evaluation of X-rays showed osseous thickened strips in proximal and distal femoral metaphyses (Fig. 1). A diet supplement with vitamin C was started, resulting in a rapid and dramatic clinical improvement: resolution of gingival bleeding, establishment of a positive mood, disappearance of limb pain, and restoration of ambulation.

Discussion

Like primates and guinea pigs, humans lack the ability to convert glucose to ascorbate and, therefore, depend on the diet to provide for the daily metabolic requirements. Ascorbate is a cofactor in collagen biosynthesis, being essential for the hydroxylation of proline in precollagen.

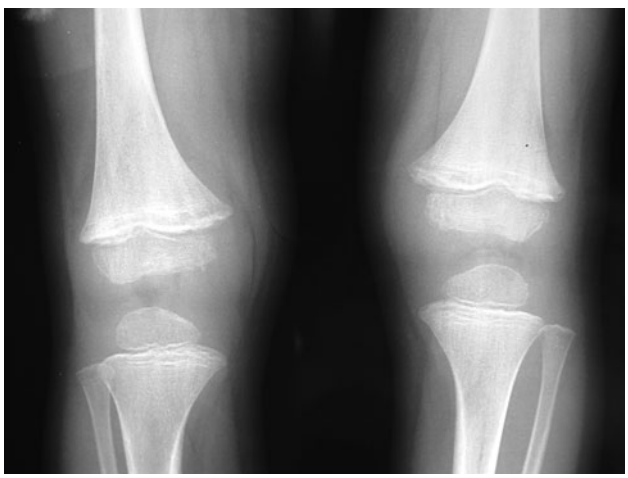

Fig. 1 Anteroposterior radiograph of the knees, showing a dense line at the growing metaphyseal end of the femora involving the provisional zone of calcification

Vitamin C deficiency prevents collagen fibrils to adopt the normal triple helix configuration, inducing the abnormalities underlying most clinical manifestations of scurvy: easy bruising and gingival bleeding due to vessel wall damage, edema, abnormal dentine production and loss of teeth, skin changes related to keratin abnormalities and, in children, bone changes due to the inability of osteoblasts to produce the osteoid seam [4–7].

Scurvy in children is uncommon, but reports still appear describing this disorder in infants fed with UHT milk, in which ascorbate is destroyed by heat, and children with dietary restrictions stemming from developmental or psychiatric disorders, or living in neglectful environments. Vitamin C depletion may be precipitated by the co-occurrence of many factors, such as increased growth-related requirements, and recurrent trivial infections [1]. The opening symptoms of scurvy in childhood include failure to gain weight, loss of appetite and, typically, marked irritability, whereas mucocutaneous and musculoskeletal abnormalities may appear later.

As often reported, the diagnosis may be misled as the presenting symptoms mimic diseases more commonly seen in developed countries [8]. In the present case, other diagnoses were first considered, including a psychiatric disorder, myositis and a blood malignancy. The first two hypotheses deserve a particular comment.

Minor behavioral disturbances, including alimentary and sleep problems together with shyness and withdrawal, were present in this child prior the onset of symptoms. In retrospect, the worsening of these behavioral features following a trivial infection might have been the first symptom of vitamin C deficiency, given that ascorbate acts also as a cofactor in the synthesis of catecholamines and, notably, in the conversion of dopamine to norepinephrine [1]. By contrast, the active refusal of walking, which was first interpreted as a psychogenic symptom, was most probably due to initial bone involvement.

The hypothesis of a muscle inflammatory disease stemmed from the association of severe pain in lower limbs with some degree of muscle weakness. Actually, electromyographic findings were consistent with myositis, although muscle biopsy showed only minimal changes, i.e., a selective type II fibers hypotrophy. In an animal model, scurvy was associated with neurogenic muscle atrophy secondary to motor neuron involvement [9]. This was not the case of our child, which did not display any sign of peripheral nerve involvement. The mild muscle weakness observed clinically, as well as the minimal atrophic changes documented histologically, could rather be related to both the prolonged inactivity and to the general malnourishment with severe weight loss. The possibility of a coexisting reduction of carnitine synthesis, previously hypothesized as a co-cause of muscle weakness in

ascorbate-deficiency [7], is not sustained in this child by both the absence of lipid storage in muscle and the normal carnitine concentrations in plasma and, as later assessed, also in muscle.

In conclusion, our child indeed presented since the onset with symptoms typical of scurvy. However, the diagnosis was initially misled as part of the clinical picture was overlooked and the child was extensively investigated for a 'first-world' disease. We suggest that in any child presenting with neuromuscular symptoms in the context of an apparent multi-system disease, the possibility of a nutritional cause, particularly vitamin C deficiency, should always be considered. Given that scurvy is life-threatening, but also promptly responsive to ascorbate supplementation, an empirical course for both diagnostic and therapeutic purposes should be considered before undertaking extensive investigations.

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References

1. Fain O (2004) Vitamin C deficiency. Rev Med Interne 25:872–880
2. Rajakumar K (2001) Infantile scurvy: a historical perspective. Pediatrics 108(4):e76
3. Shetty AK, Steele RW, Silas V, Dehne R (1998) A boy with a limp. Lancet 351:182
4. Akikusa JD, Garrick D, Nash MC (2003) Scurvy: forgotten but not gone. J Paediatr Child Health 39:75–77
5. Chaudhry SI, Newell EL, Lewis RR, Black MM (2005) Scurvy: a forgotten disease. Clin Exp Dermatol 30:735–736
6. Khonsari H, Grandière-Perez L, Caumes E (2005) Scurvy, a re-emerging disease. Rev Med Interne. 26:885–890
7. Fain O (2005) Musculoskeletal manifestations of scurvy. Jt Bone Spine 72:124–128
8. Pimentel L (2003) Scurvy: historical review and current diagnostic approach. Am J Emerg Med 21:328–332
9. Oria RB, Costa CM, Santos Tde J, Vieira CM (2003) Pharmacological, morphological and behavioral analysis of motor impairment in experimentally vitamin C deficient guinea pigs. Arq Neuropsiquiatr 61:25–33