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Clinical Observations

Highly Selective Eating in Autism Spectrum Disorder Leading to Scurvy: A Series of Three Patients

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ABSTRACT

Background: Some children with autism spectrum disorder (ASD) have highly specific food selectivity and therefore are prone to nutritional deficiencies of different kinds.
Patients: We document three children with ASD who presented with refusal to walk and gingivitis who underwent comprehensive evaluations before establishing the diagnosis of vitamin C deficiency (scurvy). The symptoms resolved after treatment with vitamin C.
Conclusions: Prevention of nutritional deficiencies in children with ASD is essential, and providing multivitamin supplementation whenever high food selectivity is noted may prevent significant morbidity.

Introduction

Autism spectrum disorder (ASD) is a neurobiological disorder characterized by persistent impairment in reciprocal social communication and interaction, and restricted, repetitive patterns of behavior or interests.[1] Its prevalence has increased over the last decade, now approaching one in 68 births in the United States according to the Centers for Disease Control estimate.[2] In Israel, the incidence has also increased and is now reported to be 0.48% to 0.65%.[3]

Among the various symptoms of this complex disorder, a child with ASD might also exhibit food selectivity.[4] This selectivity of food translates into a narrow selection of food items consumed, which may be sufficient to provide adequate calories yet deprive the child from important macronutrients and micronutrients. Several studies have shown altered nutritional intake in children with ASD.[5-7] This restricted eating might give rise to clinically significant nutritional deficiencies and lead to potential comorbidities.[8]

Vitamin C is an essential micronutrient that contributes to collagen formation, serves as an antioxidant and increases iron absorption. Vitamin C deficiency is a rare disease; clinical manifestations develop one to three months after a deficient diet and include irritability, bone tenderness, pseudoparalysis of the legs, subperiosteal hemorrhage, bleeding gums, hyperkeratosis of hair follicles, and mental changes. Anemia might also occur secondary to bleeding, decreased iron absorption, or abnormal folate metabolism. Measurement of serum ascorbic acid can diagnose scurvy if it is low, but can be inaccurate and falsely negative. Diagnosis can also be established by a positive clinical response to an empirical therapeutic trial of vitamin C supplementation.[9]

Scurvy and ASD have been linked in number of studies.[10-12] Nevertheless, given the rarity of this condition among consumers of Western diets, scurvy may be overlooked by pediatricians.[13] We wish to raise awareness of vitamin C deficiency in children with ASD especially when food selectivity is suspected.

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TABLE.
Patients' Clinical, Laboratory and Radiographic Characteristics

Clinical, Laboratory and Radiographic Data	Case 1	Case 2	Case 3
Age (y)	7	7	7
Gender (M/F)	M	M	F
Weight (kg)	26	20	25
Weight for age percentile	75	10	75
Blood tests [normal range]			
WBC [5-14] $\times 10^3/\mu L$	8.7	7.5	12.5
Hb [11-14] (g/dL)	12.6	10.6	9.9
MCV [77-95] (fL)	82	70.6	72
PLT [200-450] $\times 10^6/\mu L$	393	297	490
CRP [0-5] (mg/L)	—*	7.67	4.8
Radiographic tests			
X-ray (pelvis and hip joints)	No fractures	No fractures	No fractures
US (hip joints)	Bilateral mild effusion	Mild effusion on the left	Bilateral mild effusion
Bone scan	Pathologic uptake in the right sacroiliac joint	Pathologic uptake in the right trochanter and left sacroiliac joint	No pathologic uptakes

Abbreviations:
CRP = C-reactive protein
Hb = hemoglobin
MCV = Mean corpuscular volume
PLT = platelets
US = ultrasound
WBC = white blood cells
* Levels were not available for this patient.

Patient Descriptions

Patient 1

This seven-year-old boy with ASD presented with refusal to walk on his right leg. Joint evaluation was unremarkable except for limited internal rotation of the hip. The rest of the examination was normal. He underwent basic laboratory and radiographic tests (Table), and nonsteroidal anti-inflammatory drugs were prescribed.

Three weeks later, because of the progression of the symptoms, now involving both legs and a complete refusal to walk, he underwent a bone scan (Table) followed by a magnetic resonance imaging (MRI) study of the pelvis and spine, which revealed intramedullary infiltration of the vertebrae D1-D2, D8-D9, L3-L5 and of the sacrum, sacroiliac joints, acetabulum, pubis, and the neck of the femur on both sides (Fig 1). On follow-up evaluation two weeks later, severe gingivitis with bleeding was noted.

Patient 2

This seven-year-old boy with ASD presented with limping and refusal to walk, with no history of trauma, fever, or other symptoms. His examination was unremarkable except for mild limitation of movements in both hips. He underwent basic laboratory and radiographic tests (Table). A bone scan revealed hyperemia and a pathologic uptake in the right trochanter and the left sacroiliac joint. MRI of the pelvis revealed a pathologic intramedullary sign on the pubic ramus with a periosteal and muscle reaction of the adductor brevis and obturator extraneous along with intramedullary edema of the anterior aspect of the right femur (Fig 2). Three weeks later, signs of purpura on the lower limbs and severe gingivitis appeared.

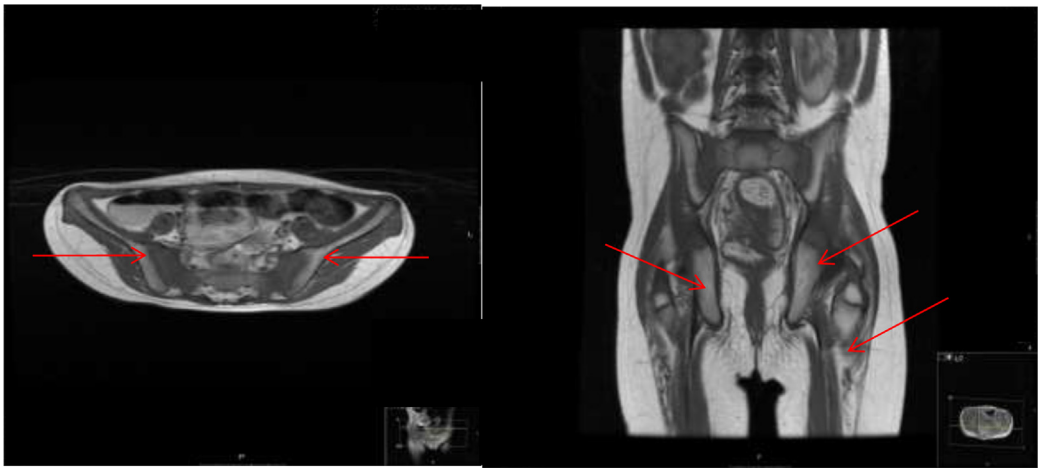

FIGURE 1. Magnetic resonance imaging of the pelvic bones after gadolinium injection—demonstrating areas and foci of intramedullary infiltration in several pelvic bones, proximal femur, and distal lumbar spine (arrows). Note that these findings are not specific for scurvy. The color version of this figure is available in the online edition.

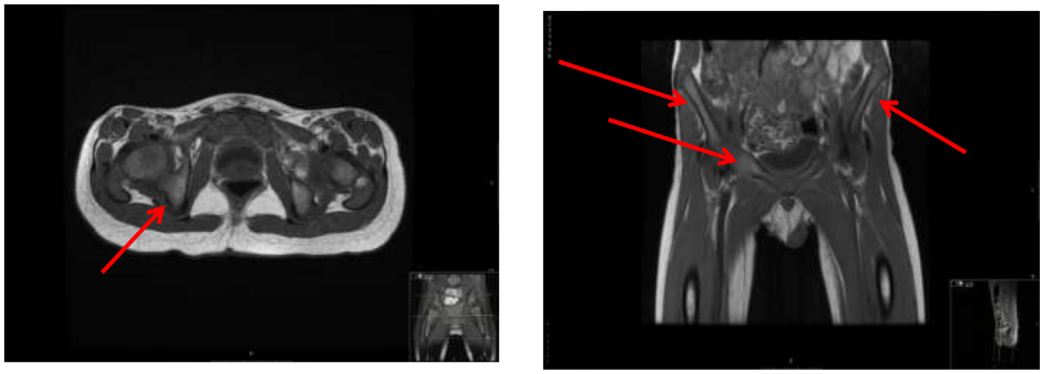

FIGURE 2. Magnetic resonance imaging of the pelvic bones after gadolinium injection—demonstrating an intramedullary pathologic signal in the upper and lower ramus bones around the symphysis pubis, bilateral, accompanied by a periosteal response around the lower ramus bone bilateral, slightly more pronounced on the right side (arrows). Edema can be seen in adjacent muscles. Note that these findings are not specific for scurvy. The color version of this figure is available in the online edition.

Patient 3

This seven-year-old girl with ASD presented with refusal to walk. She had no history of trauma, fever, and other symptoms. Her examination demonstrated refusal to stand on legs, the knee joints were held in flexion position with significantly limited range of movement. Neurological examination was unremarkable. She underwent basic laboratory and radiographic tests (Table), and nonsteroidal anti-inflammatory drugs were prescribed. Two weeks later, she returned because of persistence of her symptoms and the appearance of leg hematomas and gum bleeding.

All three patients eventually developed the classical mucosal and dermal signs of scurvy. A repeat history in each child revealed a very restricted diet that did not include meat, fruits, or vegetables. Selective dietary habits, refusal to walk, skin hematomas, and gingivitis led to the diagnosis of scurvy, and the patients were started on intravenous followed by oral ascorbic acid (300 to 500 mg daily for two weeks). All three improved remarkably within days.

In summary, three children with ASD presented with limping or refusal to walk and were eventually diagnosed with scurvy (vitamin C deficiency). These symptoms preceded the classic signs of gingival bleeding and skin hematomas. All three underwent extensive imaging and were later found to consume a very narrow and restricted diet (without any deliberate restrictions because of other health reasons). All three children responded well to vitamin C administration.

Discussion

Vitamin C deficiency (scurvy) seems to be a disease of the past that is rarely encountered in developed countries and thus rarely diagnosed by young pediatricians. Because most processed food items contain ascorbic acid as a preservative or are fortified with it, having clinically significant vitamin C deficiency is extremely rare in Western populations. Vitamin C is an obligate cofactor in the synthesis of collagen. The capillary fragility that causes the appearance of the mucosal manifestations of vitamin C deficiency is probably because of deficient collagen within the capillary wall. Signs of scurvy tend to develop after about three months of reduced vitamin C intake, depending on pre-existing stores of the vitamin.[14] In adults, early manifestations are typically mucosal manifesting as gingival bleeding and skin petechiae. In children, on the other hand, skeletal manifestations are typically the presenting features. The pathophysiology of skeletal manifestations of vitamin C deficiency is related to the defect in osteoid matrix formation that causes pathologic bone structure, increasing the risk for the development of fractures surrounding the growth plates. Bone pain may be caused by subperiosteal hemorrhage.

Children with ASD may have highly selective and narrow food preferences, translating to the persistent consumption of less than a handful of food items. Although these children receive adequate calories and do not seem clinically undernourished (our patients had normal anthropometric measurements), yet they may still have significant nutrient deficiencies. Because some of these children communicate poorly and are uncooperative during the examination, a high index of suspicion for dietary deficiencies is justified, specifically for vitamin C deficiency. In these three children, a costly extensive evaluation of a limp or refusal to bear weight failed to establish a diagnosis before the classic skin and gingival hallmarks of scurvy developed. A thorough dietary history should be documented for children with ASD as part of their routine care. Moreover, multivitamin supplementation should be recommended for children with ASD or other disorders characterized by highly selective narrow food preferences.

References

1. Brentani H, de Paula CS, Bordini D, et al. Autism spectrum disorders: an overview on diagnosis and treatment. Rev Bras Psiquiatr. 2013;35:62–72.
2. Christensen DL, Baio J, Braun KVN, et al. Prevalence and characteristics of autism spectrum disorder among children aged 8 years—autism and developmental disabilities monitoring network, 11 sites, United States, 2012. MMWR Surveill Summ. 2016;65:1–23.
3. Davidovitch M, Hemo B, Manning-Courtney P, Fombonne E. Prevalence and incidence of autism spectrum disorder in an Israeli population. J Autism Dev Disord. 2013;43:785–793.
4. Marí-Bauset S, Zazpe I, Mari-Sanchis A, Llopis-González A, Morales-Suárez-Varela M. Food selectivity in autism spectrum disorders. J Child Neurol. 2014;29:1554–1561.
5. Malhi P, Venkatesh L, Bharti B, Singhi P. Feeding problems and nutrient intake in children with and without autism: a comparative study. Indian J Pediatr. 2017;84:283–288.
6. Herndon AC, DiGuiseppi C, Johnson SL, Leiferman J, Reynolds A. Does nutritional intake differ between children with autism spectrum disorders and children with typical development? J Autism Dev Disord. 2009;39:212–222.
7. Sharp WG, Berry RC, McCracken C, et al. Feeding problems and nutrient intake in children with autism spectrum disorders: a meta-analysis and comprehensive review of the literature. J Autism Dev Disord. 2013;43:2159–2173.
8. Xia W, Zhou Y, Sun C, Wang J, Wu L. A preliminary study on nutritional status and intake in Chinese children with autism. Eur J Pediatr. 2010;169:1201–1206.
9. Jen M, Yan AC. Syndromes associated with nutritional deficiency and excess. Clin Dermatol. 2010;28:669–685.
10. Ma NS, Thompson C, Weston S. Brief report: scurvy as a manifestation of food selectivity in children with autism. J Autism Dev Disord. 2016;46:1464–1470.
11. Kitcharoensakkul M, Schulz CG, Kassel R, et al. Scurvy revealed by difficulty walking: three cases in young children. J Clin Rheumatol. 2014;20:224–228.
12. Planerova A, Philip S, Elad S. Gingival bleeding in a patient with autism spectrum disorder: a key finding leading to a diagnosis of scurvy. Quintessence Int. 2017;48:407–411.
13. Estienne M, Bugiani M, Bizzi A, Granata T. Scurvy hidden behind neuropsychiatric symptoms. Neurol Sci. 2011;32:1091–1093.
14. Hodges RE, Baker EM, Hood J, Sauberlich HE, March SC. Experimental scurvy in man. Am J Clin Nutr. 1969;22:535–548.