Progressive Motor Regression in a 3-Year-Old: Dietary Trends Revive an Overlooked Diagnosis

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CASE DESCRIPTION

A 3-year-old female presented to the emergency department following a month of progressive lower extremity motor regression, limb pain, and an inability to bear weight. Her upper body strength and mobility remained intact. Her medical history was unremarkable, with the exception of a recent COVID-19 infection and 2 minor falls resulting in hesitancy to walk and a presumed pinched nerve, for which she received physical therapy. She was seen by orthopedics who noted bone demineralization, but presumed this was secondary to inactivity following injury. Her family history was significant for Graves disease and hypothyroidism.

In the emergency department, the patient was irritable and lethargic. Physical examination revealed a low-grade fever, weight loss, a papular rash across the trunk and lower limbs, and movement consistent with ascending paralysis. However, it was difficult to determine whether the patient was unable to walk due to pain, effort, or ability, given her age and disposition. The parents reported that she had experienced recent appetite loss and had become an increasingly selective eater, although she had displayed no gastrointestinal symptoms. An appropriate work-up was performed, including repeat X-rays and magnetic resonance imaging (MRI) of the brain and spinal cord; all returned normal, although once again bone demineralization was noted. Laboratory results at admission (Table 1) demonstrated iron deficiency anemia and anion gap metabolic acidosis, presumably secondary to ketosis in the setting of decreased food intake. Her white blood cell count was decreased and serum C-reactive protein (CRP) concentration was within the reference interval, decreasing the likelihood of concurrent infection. Serum alkaline phosphatase activity was decreased, consistent with lack of weight bearing activities.

The patient was admitted for correction of her acid-base status and anemia, in light of the persistence of her neuromuscular symptoms. Consultations were obtained from neurology, endocrinology, and orthopedics, resulting in further laboratory evaluation (Table 2). To exclude the possibility of heavy metal toxicity, urine lead, mercury, and arsenic analyses were performed; all results returned below the limit of quantitation. Growth hormone deficiency was considered and serum insulin-like growth factor 1 (IGF-1) was measured, with the result within the lower end of the reference interval (Table 2). Given the increased serum thyroid stimulating hormone (TSH) and suppression of T4 and fT4 concentrations, a diagnosis of hypothyroidism was pursued, and thyroid hormones were traced over time. Additionally, the positive tissue transglutaminase result prompted consideration of celiac disease. However, none of these diagnoses were sufficient to explain the neuromuscular symptoms.

As a component of routine inpatient care, the family met with a dietician to develop a nutrition plan, where an evaluation of her growth trajectory was performed. The patient's height to body mass index z score was −1.5 (reference interval −1.0 to +1.0), indicating inadequate weight gain for her height. The low z score combined with iron deficiency fulfilled the criteria for chronic malnutrition, prompting the care team to order a serum vitamin C test that returned below the limit of quantitation at <0.1 mg/dL (<5.7

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µmol/L; reference interval 0.3–2.5 mg/dL, 17–142 µmol/L, Table 2). Concurrently, the family disclosed to the nutritionist that the household adhered to a strict vegan diet. This led to a detailed discussion of nutrient availability as well as the patient's selective eating habits; her diet was rich in carbohydrates and legumes with no mention of citrus or fruit juice intake. This patient's presentation was likely exacerbated by her selectivity and malabsorption secondary to early celiac disease in the context of a restrictive diet.

QUESTIONS TO CONSIDER
1. What are causes of a decreased serum vitamin C concentration?
2. Physiologically, how are vitamin C concentrations regulated?
3. How could celiac disease affect vitamin concentrations?
4. What are risk factors for scurvy in a pediatric population?
5. How does severe illness impact the thyroid and thyroid testing?

Table 1. Serum laboratory results at the time of clinical presentation.

Analyte	Result	Reference interval
White blood cell count	4.61 x10^9/L	6.0–17 x10^9/L
Hemoglobin	11.1 g/dL (6.89 mmol/L)	11.6–13.6 g/dL (7.2–8.4 mmol/L)
Hematocrit	34.8%	34.0–40.0%
Iron	28 µg/dL (5.0 µmol/L)	50–120 µg/dL (9.0–21.5 µmol/L)
Ferritin	17 ng/mL (38 pmol/L)	13–150 ng/mL (29–337 pmol/L)
Transferrin	330 mg/dL (3.3 g/L)	200–400 mg/dL (2.0–4.0 g/L)
Percentage transferrin saturation	7%	20%–55%
TIBC	413 µg/dL (73.9 µmol/L)	250–450 µg/dL (44.8–80.6 µmol/L)
Sodium	135 mmol/L	135–148 mmol/L
Potassium	4.2 mmol/L	3.5–5.1 mmol/L
Chloride	99 mmol/L	99–111 mmol/L
Bicarbonate	15 mmol/L	21–31 mmol/L
Glucose	84 mg/dL (4.66 mmol/L)	71–99 mg/dL (fasting) (3.9–5.5 mmol/L)
Anion gap	21 mmol/L	7–16 mmol/L
Creatinine	0.2 mg/dL (18 µmol/L)	0.5–1.2 mg/dL (44–106 µmol/L)
Calcium	9.8 mg/dL (2.45 mmol/L)	8.4–10.5 mg/dL (2.1–2.6 mmol/L)
Phosphorus	4.5 mg/dL (1.45 mmol/L)	3.2–6.3 mg/dL (1.0–2.0 mmol/L)
Alkaline phosphatase (ALP)	87 U/L	100–320 U/L
Creatine kinase	48 U/L	24–170 U/L
C-reactive protein (CRP)	<0.3 mg/dL (<28.6 nmol/L)	<0.5 mg/dL (<47.6 nmol/L)

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Table 2. Serum laboratory results of follow-up testing.

Analyte	Result	Reference interval
Parathyroid hormone (PTH)	12 pg/mL (1.3 pmol/L)	10–65 pg/mL (1.1–6.9 pmol/L)
Insulin-like growth factor 1 (IGF-1)	56 ng/mL (7.3 nmol/L)	38–214 ng/mL (5.0–28 nmol/L)
Thyroid stimulating hormone (TSH)	5.74 µIU/mL	0.50–4.50 µIU/mL
T4	3.4 µg/dL (43.8 nmol/L)	4.5–11.5 µg/dL (58–148 nmol/L)
Free T4	0.5 ng/dL (6.4 pmol/L)	0.8–1.8 ng/dL (10.3–23.2 pmol/L)
Vitamin C (ascorbic acid)	<0.1 mg/dL (5.7 µmol/L)	0.3–2.5 mg/dL (17–142 µmol/L)
Endomysium IgA	Not detected	Not detected
Gliadin, deamidated, IgG	17.7 AU	<20 AU
Gliadin, deamidated, IgA	<5.2 AU	<20 AU
Tissue transglutaminase, IgA	68.3 AU	<20 AU
IgA, total	34 mg/dL (2.1 µmol/L)	50–255 mg/dL (3.1–15.9 µmol/L)
25-hydroxy vitamin D	31 ng/mL (77.4 nmol/L)	30–100 ng/mL (75–250 nmol/L)
Vitamin B12	1312 pg/mL (968 pmol/L)	232–1245 pg/mL (171–919 pmol/L)
Vitamin B6	8.3 ng/mL (33.6 nmol/L)	3–35 ng/mL (12.1–141.6 nmol/L)
Zinc	58 µg/dL (8.9 µmol/L)	29–115 µg/dL (4.4–17.6 µmol/L)

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the December 2024 issue of *Clinical Chemistry*. To view the case and comments online, go to https://academic.oup.com/clinchem/issue/70/12 and follow the link to the Clinical Case Study and Commentaries.

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