Scurvy in the 21st century?

Vitamin C deficiency presenting to the neurologist

Karl Meisel, MD, MA

Susmitha Daggubati

S. Andrew Josephson, MD

Scurvy is caused by L-ascorbic acid (vitamin C) deficiency and was common in the 15th century.¹ Vitamin C is important to the nervous system during myelination and Schwann cell differentiation, although neurologic manifestations are not commonly reported in the historical description of scurvy.^{1,2}

Case 1

A 3-year-old boy presented with a selective diet lacking fruits and vegetables. He regressed from using utensils and developed right foot weakness that progressed to right hip pain, causing him to crawl rather than walk. He was admitted to the hospital with upper extremity weakness, gingival hyperplasia, halitosis, petechial rash, and allodynia to light touch. On examination, he was anxious and unable to maintain antigravity in his upper extremities, with diffusely decreased spontaneous movements. His tone was diminished in the lower extremities but normal in the upper extremities. The lower extremities appeared pale and edematous. Brisk patellar reflexes were present bilaterally. Dried blood was present on his lips and a large black eschar was observed on the upper gums of his front teeth. An extensive evaluation with MRI of the brain and spine along with lumbar puncture was unrevealing. A peripheral smear demonstrated spherocytes, suggesting hemolysis. He underwent a bone marrow biopsy, which showed erythrodysplasia and small hypolobulated megakaryocytes. The bone marrow biopsy results suggested a nutritional deficiency. A broad nutritional evaluation revealed an undetectable ascorbic acid level of <0.1 mg/dL (0.6–2 mg/dL). Vitamin A was also deficient at 9.2 µg/dL (11.3–64.7). Ferritin, riboflavin, niacin, copper, iron, vitamin D, and reticulocyte count were normal. He was started on vitamin replacement therapy. Gingival hyperplasia, bleeding, and rash rapidly improved, with more gradual improvements in allodynia and ambulation. Within months he fully recovered. He was later diagnosed with autism, which likely contributed to his limited diet.

Case 2

A 19-year-old man from the same low-income housing unit as the prior case presented with a 6-month history of severe upper back pain. He reported progressive symptoms of fatigue, decreased concentration, vertigo, occipital headaches, and transient diffuse weakness. He had lost weight and his meals lacked fruits or vegetables. He was thin and unkempt and had a fine positional hand tremor. He had severe paraspinal tenderness, decreased cervical neck range of motion with lateral flexion, and right scapular winging with atrophy. He had diffuse

Practical Implications

Vitamin C deficiency can lead to nerve dysfunction. Neurologists should be aware of the risk factors and that supplementation may result in dramatic improvement in symptoms.

Department of Neurology (KM, SAJ) and Neurohospitalist Program (SAJ), University of California San Francisco; and Kalamazoo College (SD), Kalamazoo, MI.

Funding information and disclosures are provided at the end of the article. Full disclosure form information provided by the authors is available with the **full text of this article at Neurology.org/cp.**

Correspondence to: karl.meisel@ucsf.edu

Table 1 Clinical manifestations of vitamin C deficiency

Case	Age, y	Sex	Medicaid	Tobacco use	Alcohol abuse	Psychiatric diagnosis	Sensory	Weakness	Bleeding or bruising
1	3	M	Yes	No	No	Yes	Neuralgia	Foot drop	Yes
2	19	M	Yes	Yes	No	Yes	Neuralgia	Scapular winging	No
3	60	F	Yes	Yes	No	No	Neuralgia	Foot drop	Yes
4	30	F	No	No	No	No	Neuralgia	No	Yes
5	55	M	Yes	Yes	No	No	Numbness	No	No
6	43	F	Yes	Yes	Yes	No	Imbalance	No	No
7	53	F	Yes	Yes	No	Yes	Numbness	No	Yes
8	50	M	Yes	Yes	Yes	Yes	Neuralgia	Yes	Yes
9	39	F	Yes	Yes	No	Yes	Neuralgia	Yes	No

hyperreflexia without clonus, and he was unable to tandem walk. Sensory examination testing with pinprick, vibration, and proprioception was normal. Ascorbic acid was deficient at 0.1 mg/dL (0.2–2.0). Serum analysis revealed normal electrolytes, complete blood count with differential, thyroid-stimulating hormone, free T₄, creatine kinase, vitamin B₁₂, copper, ceruloplasmin, and folic acid. MRI of the cervical spine was normal. The patient started vitamin C supplements and the scapular winging, fatigue, and concentration improved.

Seven additional patients with a variety of neurologic symptoms presented to the neurology clinic over 1 year (table 1). All patients reported neuralgia, and 56% demonstrated focal weakness, which led to MRI imaging that did not reveal a CNS lesion to explain the symptoms (table 2). Similarly, about half the patients had minor bruising, typically on the thighs. Many of these patients underwent evaluation for vitamin B₁₂ deficiency, thyroid dysfunction, and autoimmune disease (table 2). Additional common symptoms were fatigue, decreased concentration, anxiety, imbalance, and headaches. All patients are from a rural geographic area in northern Michigan with restricted access to fresh produce. Nearly all of the patients were of low-income status based on Medicaid qualifications. The apparent increased prevalence of scurvy in this population was likely due to poor access to fresh produce and lower socioeconomic status. The common comorbid psychiatric complaints in these patients appeared to precede the discovery of scurvy; however, the causal nature of this relationship is unknown.

DISCUSSION

Reports of scurvy rarely mention neurologic manifestations. A 26-year-old healthy man induced scurvy experimentally by selectively restricting vitamin C in his diet for 91 days.³ After 71 days, he started to complain of numbness and sensitivity to touch and pinprick in bilateral calves. By the 82nd day he lost sensation of pinprick and touch over the entire distribution of the left femoral nerve. On the 89th day a petechial rash and ecchymosis developed on both legs. Within 4 months of vitamin C repletion he fully recovered.³ A Mayo Clinic review from 1976 to 2002 described 11 similar cases. The most common symptoms were bruising, arthralgias, and joint swelling. Typical examination signs included pedal edema, bruising, and mucosal changes; 36% had myalgias and fatigue.⁴

Latent scurvy manifested by fatigue, irritability, aching pain, and weight loss is likely under-recognized.⁵ Plain radiographs can demonstrate thin bone cortex and scurvy lines.⁶ It is unclear why patients have a variety of focal symptoms, but it is speculated that even minor trauma could cause hemorrhage into the nerve sheath, leading to patchy involvement. Other nutritional

Table 2 Laboratory and MRI findings for the case series

Case	Vitamin C, normal values mg/dL	TSH, mIU/L	Vitamin B ₁₂ , pg/mL	ESR, mm/h	MRI
1	0.0 (0.6–2)	NA	NA	23	Negative
2	0.1 (0.2–2)	1.76	418	20	Negative
3	0.2 (0.6–2)	1.25	651	16	NA
4	0.0 (0.2–2)	1.27	380	20	Negative
5	0.1 (0.2–2)	2.8	293	NA	Negative
6	0.2 (0.6–2)	0.47	469	27	Negative
7	0.1 (0.2–2)	1.44	365	11	Negative
8	0.0 (0.2–2)	1.80	250	2	Negative
9	0.0 (0.2–2)	0.74	NA	NA	Negative

Abbreviations: ESR = erythrocyte sedimentation rate; NA = not available; TSH = thyroid-stimulating hormone.

deficiencies more typically associated with neuropathy are summarized in table e-1 at Neurology.org/cp. While some of these patients may indeed have other nutritional deficiencies due to malnutrition, the strikingly low ascorbic acid levels combined with the clinical presentation make vitamin C deficiency the likely culprit, and it should be remembered that supplementation may result in dramatic improvement in symptoms.^{3,6}

REFERENCES

1. Scheicher RL, Carroll MD, Ford ES, Lacher DA. Serum vitamin C and the prevalence of vitamin C deficiency in the United States: 2003–2004 National Health and Nutrition Examination Survey. *Am J Clin Nutr* 2009;90:1252–1263.
2. Lehmann HC, Höke A. Schwann cells as a therapeutic target for peripheral neuropathies. *CNS Neurol Disord Drug Targets* 2010;9:801–806.
3. Hood J. Femoral neuropathy in scurvy. *N Engl J Med* 1969;281:1292–1293.
4. Olmedo JM, Yiannias JA, Windgassen EB, et al. Scurvy: a disease almost forgotten. *Int J Dermatol* 2006;45:909–913.
5. Prinzo ZW. Scurvy and its Prevention and Control in Major Emergencies. Geneva, Switzerland: World Health Organization; 1999. Available at: http://www.who.int/nutrition/publications/en/scurvy_in_emergencies_eng.pdf. Accessed March 12, 2015.
6. Algahtani HA, Abdu AP, Khojah IM, et al. Inability to walk due to scurvy: a forgotten disease. *An Saudi Med* 2010;30:325–328.

AUTHOR CONTRIBUTIONS

Karl Meisel designed, analyzed, wrote, edited, and reviewed the manuscript. Susmitha Daggubati researched, wrote, and reviewed the manuscript. S. Andrew Josephson wrote, edited, and reviewed the manuscript.

STUDY FUNDING

No targeted funding reported.

DISCLOSURES

K. Meisel and S. Daggubati report no disclosures. S. Andrew Josephson serves as Editor-in-Chief of *Journal Watch Neurology* and as an Associate Editor for *The Neurohospitalist* and *Continuum* Online Edition. Full disclosure form information provided by the authors is available with the **full text of this article at Neurology.org/cp**.

Supplemental Data

Neurology.org/cp