Scurvy Presenting as Blood Loss Anemia in the United States

Samantha Rivera, MD; Adam Clements, DO; Joshua Hess, MD; Nicolai Gerhartz, PA-C; Aleksander Downs, MD; Linnea Kruit, MD

ABSTRACT

Introduction: Scurvy is a deadly disease caused by a lack of vitamin C in the diet. Although frequently considered a disease from the past, it still occurs in modern-day society, including in developed countries.

Case Presentation: We report a case of an 18-year-old male who was admitted with bleeding into his legs, prolonged prothrombin time and partial thromboplastin time, and anemia requiring a blood transfusion. His history included congenital deafness and a restrictive eating pattern primarily consisting of fast food. He was deficient in folic acid, vitamin K, and vitamin C. Scurvy best explained the bleeding, and he improved with vitamin supplementation.

Discussion: Scurvy is a collagen production disorder that can cause bleeding on the skin and mucous membranes. Although rare in industrialized nations, scurvy is typically the result of a restrictive diet or malnutrition. Those who are at a particularly high risk are the elderly, alcohol abusers, and those with eating disorders.

Conclusions: Scurvy is easily treatable but can be missed; therefore, a high level of suspicion should be present in patients at risk for malnutrition. Those diagnosed with scurvy should be screened for concomitant nutritional deficiencies.

INTRODUCTION

Scurvy is caused by a lack of vitamin C (ascorbic acid) in the diet. The earliest known mention of scurvy occurs in the Ebers Papyrus, a 20-meter-long collection of magico-medical prescriptions that dates to 1550 BC.[1] Scurvy has caused the death and suffering of European sailors, Irish potato farmers, American Civil War soldiers, and Arctic adventurers.[2] Despite significant morbidity and mortality from scurvy, there was little written about it until James Lind's Treatise of the Scurvy was published in 1753. Lind, a British Naval surgeon, conducted trials for a potential scurvy treatment. During those trials, seamen who received supplementary oranges and lemons quickly recovered. However, this seemingly monumental discovery was not implemented for another 42 years because Lind himself believed scurvy was a disease of faulty digestion and excretion and not a direct consequence of dietary insufficiency.[3]

In 1928, a Hungarian biochemist Albert Szent-Gyorgyi isolated an organic acid from adrenal glands, which he called "hexuronic acid." The structure of this acid was identified and chemically synthesized by 1933 and was renamed L-ascorbic acid for its antiscorbutic (ie, against scurvy) properties.[4,5]

Vitamin fortification and the widespread availability of fresh produce in developed countries have made scurvy primarily a disease of the past. However, rare cases still occur in people with severe malnutrition or restrictive eating habits. Such patients often suffer from substance use disorders or psychiatric diseases. Although the incidence of true scurvy is low, it is estimated that up to 7.1% of the US population has some degree of vitamin C deficiency.[6]

CASE PRESENTATION

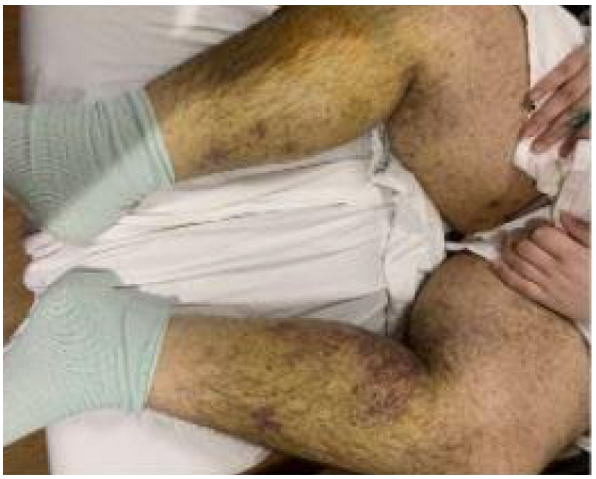
An 18-year-old White male, whose only known past medical history was congenital deafness, presented with bilateral lower leg swelling and pain. He communicated through writing and was accompanied by his mother, who provided supplemental infor-

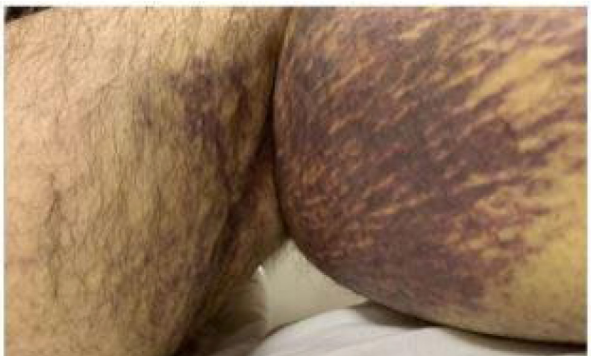
• • •

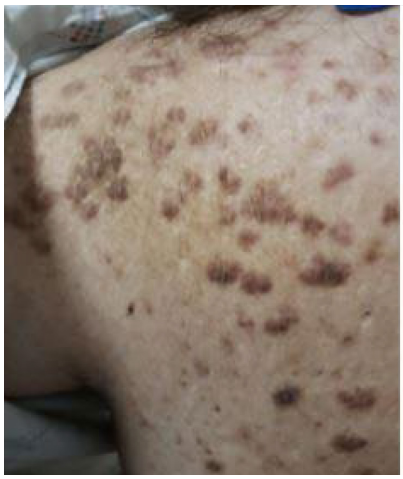
Author Affiliations: Aspirus Wausau Family Medicine, Wausau, Wisconsin (Rivera, Hess); Aspirus Wausau Hospital, Wausau, Wis (Clements, Gerhartz); ProHealth Waukesha Memorial Hospital, Waukesha, Wis (Downs); Western Wisconsin Family Medicine, New Richmond, Wis (Kruit).

Corresponding Author: Samantha Rivera, MD, PGY-3 Family Medicine Resident, Aspirus Wausau Family Medicine, 333 Pine Ridge Blvd, Wausau, WI 54401; phone 720.272.6531; email samarivera0508@gmail.com.

Figure 1. Physical Exam Findings







mation to his history. He had a two-and-a-half-week history of increasing lower leg swelling with pain that gradually worsened to the point that he was unable to walk the day before admission. There was also diffuse ecchymosis to his bilateral lower extremities (Figure 1), specifically near the popliteal fossa and over the gastrocnemius, that was worsening before admission. He also had shortness of breath increasing over the 2 weeks prior to admission. He was not short of breath at rest. He denied any recent trauma to his legs and had no personal or family history of bleeding or clotting disorders. He had no abdominal pain, chest pain, or palpitations and no recent illnesses, ill contacts, or fevers. There was no recent weight gain or loss, no nausea, vomiting, changes in urinary or bowel habits, and no headaches or changes in vision.

The cause of the patient's deafness is unknown, according to his mother. He takes no daily medications, vitamins, or supplements and reported no illicit drug, alcohol, or tobacco use.

She said he was a "picky eater" and "had difficulty with textures." For years, his diet had been limited to plain hamburgers, hotdogs, grilled cheese, and chicken tenders. He also led a sedentary lifestyle and spent most of his days sitting in his room playing video games.

Physical Exam

Exam showed an unkempt, morbidly obese deaf male who was alert and oriented and communicated with writing. He did not have any bruising or bleeding in his mouth, but his gums appeared mildly swollen. Skin exam was significant for follicular hyperkeratosis and perifollicular hemorrhage with petechiae and coiled hairs. He also had extensive bruising noted in his bilateral lower extremities. Heart, lung, and abdominal exams were unremarkable.

Labs

The patient's lab workup demonstrated microcytic anemia with a hemoglobin of 7.1. He was also notably low on folic acid. The coagulation panel revealed an international normalized ratio (INR) of 1.2, partial thromboplastin time (PTT) elevated at 42 seconds (reference 23-36 sec), normal fibrinogen, and normal inflammatory markers. Reticulocyte count was appropriately elevated at 5.5% (0.5%-1.5%). Hemolytic anemia was ruled out with negative direct Coombs, normal lactate dehydrogenase, and elevated haptoglobin 300 mg/dL (30-200). The peripheral blood smear was consistent with a reactive process given neutrophilia, hypochromic-normocytic anemia, and thrombocytosis.

After obtaining the additional history from his mother regarding his restrictive diet, we were concerned about 1 or more nutritional deficiencies. Copper, lead, and zinc were within normal limits. Vitamin K levels were falsely elevated due to supplemental administration before obtaining a sample for testing. His vitamin D level was decreased at 23 (reference 30-80). Ascorbic acid levels resulted on day 4 of hospitalization at <5 umol/L (reference 23-114 umol/L).

Hospital Course

Our patient had bilateral calf pain and was unable to walk. He was admitted to the hospital for acute blood loss anemia. The source of the bleeding appeared to be his bilateral calves, with 1.5 cm hematomas superficial and deep to the gastrocnemius on computed tomography (CT) bilaterally. He was tachycardic, and his blood pressure was normal. He presented with microcytic hypochromic anemia with reactive thrombocytosis. He required a total of 3 units of packed red blood cells during the hospitalization.

Due to his spontaneous bleeding, coagulopathy secondary to factor deficiencies or factor inhibitors were high on the differential. He had normal iron studies. His prothrombin time (PT) and PTT were mildly elevated with thrombin time at the upper limit of normal. This is unexpected in a patient with coagulopathy due to factor deficiency or factor inhibitor. Hematology was consulted, and an extensive workup was started. The patient's mixing studies corrected, again indicating a possible factor deficiency, but his factor activity levels were normal and there was no indication for a factor inhibitor either.

On admission, his history of poor diet combined with his severe anemia prompted a nutritional workup, including vitamins C, D, and B12 and folate levels. His vitamin C, vitamin D, and folate levels were low. Based on his elevated PT, PTT, high/normal thrombin time, low folate, and undetectable levels of vitamin C, we diagnosed him with scurvy. We also suspected vitamin K deficiency leading to an acquired clotting factor deficiency was contributing to his bleeding. Unfortunately, the vitamin K level was drawn after he was supplemented with intravenous (IV) vitamin K. His physical exam was consistent with vitamin C deficiency (scurvy). He had follicular hyperkeratosis, perifollicular hemorrhage with petechiae, and coiled hairs, in addition to his bilateral lower extremity extensive bruising. His gums seemed mildly swollen, but there was no hemorrhage noted. He was supplemented with IV vitamin K for 3 days and oral vitamin C, in addition to a multivitamin. He was educated on the cause of his bleeding and referred to an outpatient dietitian.

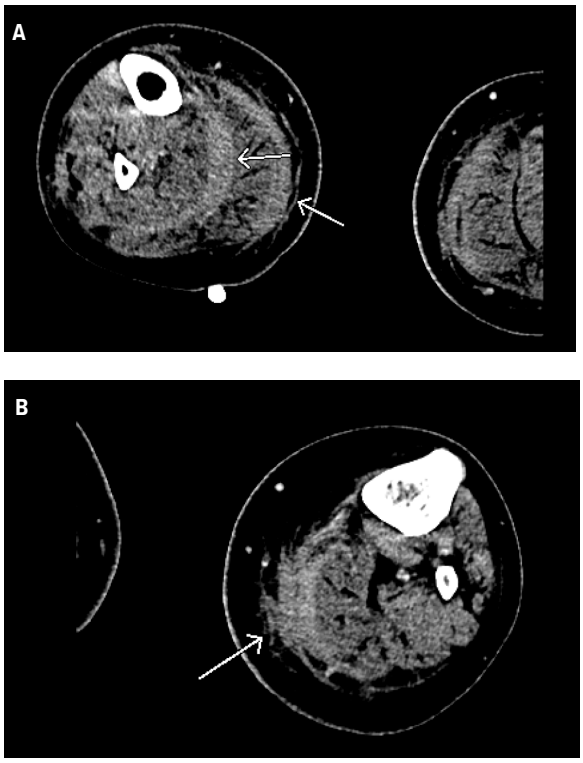
Follow-Up

Approximately 1 month after the patient's hospitalization and adhering to oral vitamin supplementation, his anemia completely resolved, with a hemoglobin at 14.4 g/dL. Chart review showed his bilateral lower leg bruising had resolved after about 4 to 6 weeks. He continues to have a poor diet and has elected to take the necessary supplementation orally.

DISCUSSION

Scurvy is a disease that is more common in history textbooks than in the modern medical literature in developed countries. The illness was prevalent in the 1700s and was a frequent ailment to explorers and sailors who were at sea for long periods without access to adequate nutrition. Humans lack gluconolactone oxidase, an enzyme necessary for the synthesis of ascorbic acid, making dietary intake the only source of this essential nutrient.[7] Vitamin C is generally considered an antioxidant and a reducing agent that is required for many cellular processes, particularly for the hydroxylation of proline. This is necessary for the cross-linking and stabilization of collagen, which provides the structural integrity of many tissues in the body. This protein composes about 30% of cellular protein mass and is frail in the absence of ascorbic acid due to lack of stabilization.

Figure 2. Computed Tomography Scan Images



A. Hematoma of the right lower leg with components that are both deep and superficial to the gastrocnemius muscle.

B. Hematoma of the left lower leg superficial to the left gastrocnemius muscle measuring up to 1.5 cm in thickness with adjacent fat stranding.

Table. Initial Lab Results

Lab Name	Value	Reference Value
Hemoglobin	7.1 g/dL	13.4 - 17.6 g/dL
Mean corpuscular volume	81.7 fL	82 - 96 fL
Platelet count	569 K/uL	140 - 390 K/uL
D-dimer	2.72 ug/mL FEU	0.0 - 0.50 ug/mL FEU
Prothrombin time	14.7 sec	2.0 - 14.6 sec
Partial thromboplastin time	42 sec	23 - 36 sec
Reticulocyte	5.5 %	0.5 - 1.5 %
Folate	2.6 ng/mL	>4.8 ng/mL
Vitamin C, ascorbic acid	< 5 umol/L	23 - 114 umol/L
Vitamin K1	8.17 nmol/L	0.22 - 4.88 nmol/L
Vitamin D 25 hydroxy	23 ng/mL	30-80 ng/mL

Vitamin C deficiency can begin to manifest when plasma levels fall below 0.2 mg/dL,[8] or within 1 to 3 months without dietary consumption. Common symptoms include weakness, malaise, arthralgias, and anorexia. Unstable collagen will result in structurally weak capillary walls that cause bleeding. Patients commonly have purpura in the lower limbs, petechiae, gingival bleeding, and epistaxis. Perifollicular hemorrhages occur in the lower extremities, first due to capillary fragility unable to withstand hydrostatic

pressure.[9] Other common findings include perifollicular hemorrhage, irregularly shaped hair follicles with hyperkeratosis, and corkscrew hair.[8] Ascorbic acid also plays a role in iron absorption,[8] with 54% of adults with scurvy also having iron deficiency anemia.[9] The diagnosis of scurvy is generally considered clinical, established most significantly on the clinical history and physical exam findings. Perifollicular purpura is thought to be specific to this disease.[8]

Though different treatment regimens have been proposed, there are currently no established, evidence-based guidelines for the workup, management, or treatment of scurvy.[9] Both oral and parenteral ascorbic acid supplementation can be given, though it is unclear which, if either, is superior.[9] Generally, adults require 60 mg/day of ascorbic acid to cure or to prevent scurvy.[10] However, other literature describes that as little as 10 mg/day of vitamin C can prevent it.[9] Adequate supplementation can begin to yield symptomatic improvement within 3 to 5 days, while physical exam findings may resolve over a few weeks.[10] Additional laboratory evaluations confirmed low serum folate and vitamin D, though it was assumed that our patient likely had numerous other nutritional deficiencies. In the end, he received dietary counseling from physicians and dietitians and was supplemented with vitamin C, vitamin D, vitamin K, folate, iron, and a multivitamin.

It is important to note that there has been an increase in case reports of scurvy, indicating that this disease is not just a disease of the past but one that occurs today, including in developed countries. The prevalence of vitamin C deficiency varies across the world, being as high as 73.9% in northern India and 7.1% in the United States. It is found more commonly in areas of low socioeconomic status in developed countries. Those who are at a particularly high risk are the elderly, alcohol abusers, and those with eating disorders.[11] It is a disease that can be missed but is easily treated. Therefore, a high level of suspicion should be present in those at risk for malnutrition.

Financial Disclosures: None declared.

Funding/Support: None declared.

REFERENCES

1. Pimentel L. Scurvy: historical review and current diagnostic approach. *Am J Emerg Med*. 2003;21(4):328-332. doi:10.1016/s0735-6757(03)00083-4

2. Carpenter KJ. *The History of Scurvy and Vitamin C*. Cambridge University Press; 1986.

3. Bartholomew M. James Lind's Treatise of the Scurvy (1753). *Postgrad Med J.* 2002;78(925):695-696. doi:10.1136/pmj.78.925.695

4. Szent- Györgyi A, Haworth WN. 'Hexuronic acid' (ascorbic acid) as the antiscorbutic factor. *Nature*. 1933;131(3297):24-24. doi:10.1038/131024b0

5. Svirbely JL, Szent-Györgyi A. The chemical nature of vitamin C. *Biochem J.* 1932;26(3):865-870. doi:10.1042/bj0260865

6. Schleicher 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 (NHANES). *Am J Clin Nutr.* 2009;90(5):1252-1263. doi:10.3945/ajcn.2008.27016

7. Mandl J, Szarka A, Bánhegyi G. Vitamin C: update on physiology and pharmacology. *Br J Pharmacol*. 2009;157(7):1097-1110. doi:10.1111/j.1476-5381.2009.00282.x

8. Souza PRM, Dupont L, Rodrigues FE. Scurvy: hard to remember, easy to diagnose and treat. *An Bras Dermatol.* 2021;96(2):257-258. doi:10.1016/j.abd.2020.03.024

9. Khalife R, Grieco A, Khamisa K, Tinmouh A, McCudden C, Saidenberg E. Scurvy, an old story in a new time: the hematologist's experience. *Blood Cells Mol Dis.* 2019;76:40-44. doi:10.1016/j.bcmd.2019.01.004

10. Pimentel L. Scurvy: historical review and current diagnostic approach. *Am J Emerg Med.* 2003;21(4):328-332. doi:10.1016/s0735-6757(03)00083-4

11. Callus CA, Vella S, Ferry P. Scurvy is back. *Nutr Metab Insights.* 2018;11:1178638818809097. doi:10.1177/1178638818809097

advancing the art & science of medicine in the midwest

WMJ

WMJ (ISSN 1098-1861) is published through a collaboration between The Medical College of Wisconsin and The University of Wisconsin School of Medicine and Public Health. The mission of *WMJ* is to provide an opportunity to publish original research, case reports, review articles, and essays about current medical and public health issues.

Visit www.wmjonline.org to learn more.