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David F. Gaieski

Original Article

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David F. Gaieski

Department of Emergency Medicine, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA, USA

Abstract

Introduction: Scurvy, the disease state caused by ascorbic acid deficiency, was once an extremely common disease but is now thought to be a rare disease in postmodern societies. Physicians are not trained to consider scurvy as a possible diagnosis in patients at risk; rather, it is considered a rare diagnosis to add to a differential for completeness's sake. **Methods:** We sought to describe the scorbutic patients seen by one physician during a busy academic emergency medicine career. Case series of patients seen by one physician between 1993 and 2023 at five academic teaching hospitals with Emergency Departments (EDs) in the mid-Eastern United States. Presenting signs and symptoms, known scurvy risk factors, Vitamin C levels, clinical course, and outcome for each patient are described. **Results:** There were 14 presentations by 12 patients diagnosed with scurvy who were initially evaluated in the ED between 1993 and 2023. Each patient had a known risk factor for inadequate Vitamin C intake. All had clinical findings suggestive of scurvy and all but one had a subnormal serum Vitamin C level detected on serum samples sent from the ED. **Conclusion:** The detection of 12 cases of scurvy by one physician over a three-decade period highlights the importance of screening for scurvy in at-risk populations and generates the hypothesis that scurvy is not a rare disease but rather a rare diagnosis. This research hypothesis should be investigated in further studies.

Keywords: Alcohol use disorder, ascorbic acid, collagen disorder, dietary restrictions, emergency department, emergency medicine, fatigue, scurvy

"Though the disease has of late raged with great mortality in different parts of the world…no spot has exhibited more numerous or more different cases of it than Hasler Hospital: I here frequently visited, during 5 years of the late war with France, three or four hundred scorbutic patients in a day; every morning furnishing me with original pictures of the disease, in all its various forms and stages, in patients brought from all quarters of the globe."

--James Lind

"A Treatise on the Scurvy," 3rd Edition, 1772.

Introduction

Scurvy is a disease state caused by a deficiency of Vitamin C, or ascorbic acid.[1] Ascorbic acid deficiency leads to the production of defective collagen, which contributes to the tissue and capillary fragility that characterize scurvy.[2] The clinical symptoms of scurvy emerge as the total body pool of ascorbic acid is depleted.[3] Lind noted that early clinical scurvy was manifested solely as fatigue.[4] Research suggests that fatigue is caused by a deficiency of carnitine production and inadequate fatty acid transport.[5] Lind's experience treating sailors with scurvy resulted in a planned experiment many epidemiologists consider the first randomized control trial (RCT). In this trial, described in "A treatise on the scurvy," Lind started with a hypothesis, that arose from his hearing a story about a sailor with scurvy who was marooned on an isolated island, subsisted on a diet of wild grasses, and who, eating this diet, recovered from scurvy. This generated the hypothesis that a dietary intervention could treat scurvy. Lind then found twelve soldiers and went through meticulous efforts to control for several variables that could influence the trial's outcome: He identified 12 subjects as similar as possible in their scurvy symptoms; they were housed in the same location on the ship; and they were served the same diet. Then, in groups of two, they were subjected to different interventions with the primary outcome being improvement in scurvy signs and symptoms. The interventions included a quart

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Address for correspondence: Dr. David F. Gaieski, Department of Emergency Medicine, Sidney Kimmel Medical College, Thomas Jefferson University, 1025 Walnut Street, Suite 300, Philadelphia, PA 19107, USA.
E-mail: david.gaieski@jefferson.edu

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of cider per day, a dose of elixir vitriol, two spoonfuls of vinegar, nutmeg, seawater, two oranges and a lime. The sailors receiving the two oranges and a lime each day showed the most rapid and complete resolution of their scurvy symptoms.[4,5] Despite this compelling RCT data, Lind's conclusion that citrus fruits should be included in the diet of all sailors was rejected by the English navy for over four decades leading to thousands of avoidable cases of scurvy.[6]

Without Vitamin C repletion, obvious clinical signs of scurvy will emerge. The first objective signs are typically follicular congestion and perifollicular hemorrhages. Ecchymoses, joint effusions, and intramuscular hemorrhages soon follow. In children, classic bone findings of scurvy, including periosteal proliferation and osteolysis, can emerge. With further depletion, patients may develop gingival hyperplasia, bleeding gums, and characteristic corkscrew hairs. When the total body pool reaches zero, more severe symptoms including dyspnea, edema, oliguria, and peripheral neuropathy emerge.[7] Terminally, a sepsis-like syndrome with hypotension and shock leads to death.[8] Scurvy is primarily a clinical diagnosis, supported by laboratory tests (serum ascorbic acid level, normal range, 0.6–2.0 mg/dL or 0.2–1.5 mg/dL depending upon the reference laboratory performing the test).[9] The therapy is simple: Ascorbic acid, 100 mg, by oral or intravenous routes, several times a day.[7] Signs and symptoms usually resolve rapidly with ascorbic acid administration.

Scurvy was a prominent disease in antiquity and during the grand age of maritime exploration.[10] By the 19th century scurvy, in developed countries, had become primarily a disease of the urban poor, which slowly faded from epidemic to sporadic with improvements in transportation, food processing, and electricity.[1,9,11] In modern times, it is commonly believed that scurvy has become an extremely rare disease, limited to (but still unusual in) patients with specific risk factors including schizophrenia,[12] alcohol use disorder,[13] those who pursue fad or extreme diets,[14,15] and elderly bachelors.[16] There is a paucity of high-quality modern epidemiological studies of Vitamin C hypovitaminosis and the true incidence of scurvy in different settings around the world remains elusive. Vitamin C hypovitaminosis is probably common in low- and middle-income countries and present and not uncommon in higher income countries.[17]

In this article, I report a case series including 14 presentations of 12 patients, each of whom initially presented to the Emergency Department (ED) at an academic medical center between 1993 and 2023 and was subsequently diagnosed with scurvy. A summary of the clinical presentation in each case [Tables 1 and 2] is followed by a discussion of scurvy risk factors in 21st century America.

Methods

Case series of patients seen by one physician between 1993 and 2023 at six different academic medical center EDs. Basic clinical information including age, sex, chief complaint, signs and symptoms of scurvy, results of Vitamin C assays, treatment, and outcomes were obtained for each patient. For this project,

Table 1: Scurvy cases over 30 years: Demographics, risk factor(s), Vitamin C level, and presentation

Encounter (patient)	Year	Age (years), sex	Risk factor(s)	Vitamin C level	Clinical presentation
1 (1)*	1993	38, female	Schizophrenia; dietary restrictions	<0.6 mg/dL	Fatigue; corkscrew hairs, perifollicular hemorrhages; ecchymoses; hemarthroses; gingival hypertrophy
2 (1)*	1993	38, female	Schizophrenia; dietary restrictions	<0.6 mg/dL	Corkscrew hairs, perifollicular hemorrhages; ecchymoses; hemarthroses; gingival hypertrophy; hypotension; SIRS; hemothorax
3 (2)	1996	45, male	Severe alcohol use disorder	<0.6 mg/dL	Fatigue; corkscrew hairs, perifollicular hemorrhages; ecchymoses; SIRS; gingival bleeding
4 (3)	1999	62, male	Severe alcohol use disorder	<0.6 mg/dL	Fatigue; perifollicular hemorrhages; ecchymoses; SIRS
5 (4)	2002	37, female	Severe alcohol use disorder	0.5 mg/dL	Profound fatigue; muscle weakness; nausea; SIRS
6 (5)	2003	41, male	Severe alcohol use disorder	0.2 mg/dL	Aura suggesting upcoming seizure; perifollicular hyperkeratosis; subcutaneous nodules
7 (5)	2003	41, male	Severe alcohol use disorder	0.4 mg/dL	Aura suggesting upcoming seizure; perifollicular hyperkeratosis; subcutaneous nodules
8 (6)	2003	41, male	Severe alcohol use disorder; IVDU	<0.12 mg/dL	Fatigue; change in mental status; agitation; hallucinations; gingival hypertrophy and bleeding; corkscrew hairs, perifollicular hemorrhages; ecchymoses
9 (7)	2004	77, female	Severe alcohol use disorder	0.3 mg/dL	Ecchymoses on shins; change in mental status
10 (8)	2004	60, male	Severe alcohol use disorder	0.5 mg/dL	Fatigue
11 (9)	2008	29, female	Severe cognitive disabilities; dietary restrictions	<0.6 mg/dL	Change in mental status; urinary tract infection; septic shock; ecchymoses
12 (10)	2016	23, female	Dietary restrictions	0.2 mg/dL	Fatigue; gingival hypertrophy; hemarthrosis
13 (11)	2022	50, female	Alcohol use disorder; dietary restrictions	<0.12 mg/dL	Fatigue; corkscrew hairs; hypertrophied, bleeding gingiva
14 (12)	2023	76, female	Alcohol use disorder; lives alone; dietary restrictions	0.3 mg/dL	Fatigue; perifollicular hyperkeratosis; ecchymoses

*This patient was previously reported in reference by Mowad *et al*.[21] SIRS: Systemic inflammatory response syndrome, IVDU: Intravenous drug use

the information was completely anonymized, and no code was created so they cannot be linked to the medical record or patient. This research was deemed appropriate to be performed without Institutional Review Board (IRB) approval or exemption by the author's university's IRB (May 05, 2023; #0256_001).

Results

There were 14 presentations of 12 patients diagnosed with scurvy who were initially evaluated in the ED between 1993 and 2023. Each patient had a known risk factor for inadequate ascorbic acid (Vitamin C) intake. All had clinical findings suggestive of scurvy and all, but one had a subnormal serum Vitamin C level detected on serum samples sent from the ED [Table 1 and Figure 1]. All patients, except one who left against medical advice (AMA), were admitted to the hospital and responded to the repletion of Vitamin C with resolution of the clinical symptoms of scurvy. The patient who left AMA was lost to follow-up and no additional information was available about his clinical course [Table 2].

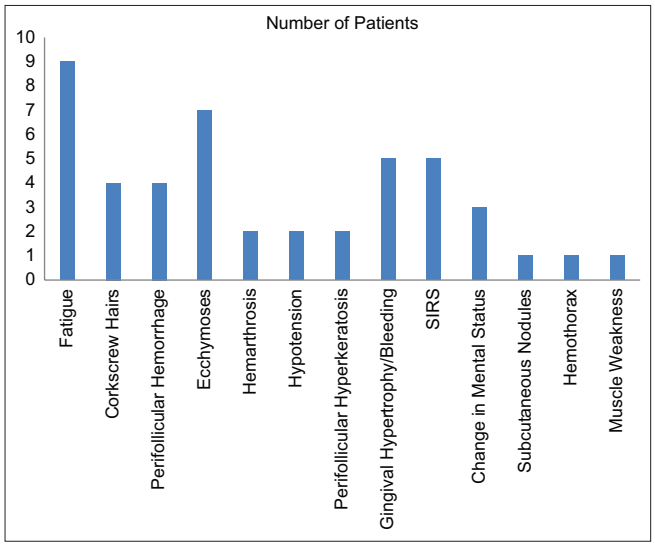

Figure 1: Frequency of scurvy signs and symptoms in the case series. SIRS: Systemic inflammatory response syndrome

Discussion

The twelve patients with fourteen presentations to the ED described in this article spanned the career to date of one academic physician. The cases are unified by the presence of known risk factors for inadequate Vitamin C intake and the development of Vitamin C hypovitaminosis – including schizophrenia, severe dietary restrictions from fad diets or as a component of mental illness, severe alcohol use disorder, and intravenous drug use – and the shared diagnosis of scurvy. The highest ascorbic acid level (0.5 mg/dL [range 0.2–1.5 mg/dL or 0.6–2.0 mg/dL depending on laboratory doing analysis]) was seen in two patients (Presentation 5, Patient 4 and Presentation 10, Patient 8), both of whom had alcohol use disorder and were admitted with severe fatigue and symptoms of alcohol withdrawal. All the other cases had clear external, objective clinical signs of scurvy at the time of ED presentation, abnormally low Vitamin C levels, and, excluding one patient lost to follow-up, responded rapidly to Vitamin C repletion.

Presentations 6–8, for patients 5 and 6, support the observations that classic findings of scurvy often go unrecognized, obvious scurvy is frequently unappreciated by examining clinicians, and scurvy can be misdiagnosed as a variety of problems.[18,19] These misdiagnoses can lead to extensive evaluations for

Table 2: Scurvy cases over 30 years: Clinical outcomes

Encounter (patient)	Clinical outcome
1 (1)	Vitamin C level sent; patient left against medical advice, stating, "I just need to change my diet"
2 (1)	Represented 2 weeks later; resuscitation; tube thoracostomy; IV Vitamin C; resolution of hypotension, hemothorax, and SIRS with Vitamin C therapy
3 (2)	Admitted to in-patient medicine ward; oral Vitamin C; level sent by in-patient team; resolution of all symptoms
4 (3)	Refused admission; prescribed oral Vitamin C; lost to follow-up
5 (4)	Admitted to in-patient medicine ward; IV Vitamin C and treatment for alcoholic ketoacidosis; discharged to home after clinical improvement
6 (5)	Seen by infectious disease consultation; diagnosed with tinea versicolor; discharged; treated at home, without improvement, with topical antifungal cream; no treatment or acknowledgment of Vitamin C level in clinical documentation
7 (5)	Admitted to in-patient medicine ward; IV Vitamin C for scurvy and benzodiazepines for alcohol withdrawal; discharged to home after clinical improvement including rapid resolution of bilateral skin lesions
8 (6)	Admitted to in-patient medicine ward; IV Vitamin C and treatment of delirium tremens; discharged to home after clinical improvement including rapid resolution of gingival bleeding
9 (7)	Intubated for airway protection; admitted to the MICU; treated for sepsis and hypoglycemia and with IV Vitamin C for scurvy
10 (8)	Admitted to in-patient medical ward; treated for alcohol withdrawal, alcoholic ketoacidosis, and with IV Vitamin C for scurvy with rapid improvement
11 (9)	Admitted to MICU; treated with fluids, vasopressors, and IV Vitamin C for *Escherichia coli* sepsis and scurvy; rapid clinical improvement
12 (10)	Rapid improvement of hemarthrosis with PO Vitamin C repletion; debate about whether scurvy was the diagnosis among in-patient team; dietary counseling
13 (11)	Correction with IV Vitamin C complicated by concomitant severe electrolyte and nutritional deficiencies
14 (12)	Rapid improvement with IV Vitamin C repletion

SIRS: Systemic inflammatory response syndrome, MICU: Medical intensive care unit, PO: Per oral

other diseases, unnecessary interventions, such as total dental extraction, and inappropriate therapies, such as topical antifungals applied to perifollicular, hyperkeratotic lesions.

In 1772, in the "Advertisement" to the 3rd Edition of his classic "A Treatise on the Scurvy," James Lind mentioned that he frequently saw up to 400 patients a day with scurvy on the wards of Hasler Hospital in Portsmouth, England.[4] By the 20th century, these statistics had changed dramatically as advances in food distribution, improved food storage techniques, and public health initiatives produced a rapid decline in the prevalence of scurvy.[11] British health statistics also show a rapidly declining mortality rate from scurvy between 1907 and 1967, from 1.5 in 1,000,000 to 0.1 in 1,000,000 annually.[20] However, in the mid-20th century, occasional large case series still appeared in the medical literature, documenting that scurvy continued to cause real morbidity and mortality.[19,21] For example, in 1944, McMillan and Inglis reported a series of 53 adult patients admitted to the medicine wards of an Edinburgh general hospital between 1939 and 1944.[19] Since then, case reports have appeared sporadically in the literature but the true prevalence of scurvy in postmodern society remains unknown and very elusive.[14,18,22,23]

Two basic perspectives on scurvy are suggested by these case reports: scurvy is a rare disease, and the case report is presented to remind clinicians of the typical presentation of an uncommon disease; scurvy is underreported because it is underrecognized, and the case report aims to increase recognition.[18,23] In fact, there is no actual reported prevalence of scurvy in postmodern, industrial society. The haphazard nature of case reports precludes comment on statistical percentages and raises the possibility that the true prevalence of scurvy in our society is hidden in the complex interface between physician and disease, buried within the complexities of ascertainment bias, diagnostic creep, lack of recognition of classic signs and symptoms, and the false, confusing need for a "high index of suspicion" to make the diagnosis. In a case series from a US hospital, published in JAMA in 1985, Reuler *et al*. presented three adult patients with classic signs and symptoms of scurvy and concluded: "With an enlarging at-risk population of elderly individuals with marginal economic resources, clinicians are likely to encounter scurvy more frequently."[18]

I propose that Reuler *et al.*[18] were prescient, and that scurvy is currently not a rare disease but, rather, a rare diagnosis. Epidemiological research over decades supports this hypothesis. Screening studies looking at the prevalence of ascorbic acid deficiency in the general population and populations at risk for the development of scurvy have shown higher-than-expected rates of Vitamin C hypovitaminosis in serum samples. For example, Johnston *et al*.[24] demonstrated that 2% of apparently healthy, nonsmoking college students had Vitamin C deficiency as measured by serum Vitamin C levels. In subsequent work, Johnston and Thompson[25] found that 6% of patients presenting to a health maintenance organization's laboratory for outpatient diagnostics had Vitamin C deficiency. Further, in the United States in the first decade of the 21st century, patients enrolled in the Third National Health and Nutrition Examination Survey III had a prevalence of Vitamin C hypovitaminosis of 8.4%, ranging from 5% to 17% depending on the at-risk category.[26] This was significantly higher than the prevalence found in England in the European-EPIC-Norfolk study, which demonstrated a prevalence of Vitamin C deficiency of 1.4%.[27] Earlier, along similar lines, in populations traditionally considered at risk for scurvy, McClean *et al*.[28] found that 83% of a sample of elderly men living in a home for war veterans had Vitamin C deficiency based on serum Vitamin C levels. They also noted that the average Vitamin C levels of these elderly men eating institutional food were lower than those of elderly men who lived alone and eating noninstitutional food.[29] In addition, in clinical settings of increased stress and critical illness, Schorah *et al*.[30] reported that Vitamin C levels in intensive care unit patients are significantly lower than those of noncritically ill hospitalized patients; and Singh *et al.*[31] found that patients with acute coronary syndromes are, on average, Vitamin C deficient at the time of hospital admission.

Interest continues in scurvy and the question of whether it is a rare diagnosis or a rare disease. For example, in 2021 the New England Journal of Medicine's Clinical Problem-Solving section presented a case of a 71-year-old man with a 6-month history of melena, 3-month history of bleeding gums, and a recent large thigh hematoma, whose serum Vitamin C level was undetectable and whose symptoms resolved rapidly with Vitamin C repletion.[32] This case does not require the illogical high index of clinical suspicion to make the correct diagnosis – It merely requires a knowledge of the natural history of scurvy and a belief that the disease has not been eradicated. None of these facts reveal the actual prevalence of scurvy. The presence of significant Vitamin C depletion and deficiency in at-risk populations, in the critically ill, and prevalence studies of healthy populations is inconsistent with the sporadic nature of case reports of overt clinical scurvy. This raises two possibilities: the prevalence of Vitamin C deficiency far exceeds the progression to overt scurvy, or the prevalence of overt scurvy is underappreciated and thus underreported.

Clinical recommendations

We recommend obtaining Vitamin C levels in patients at risk for scurvy who present with equivocal symptoms including severe fatigue, nonspecific rashes, and joint pain.[33] Further, it is important to perform nutritional and dietary reviews of systems in at-risk patients including bachelors and widowers who live alone,[16] patients with alcohol use disorder,[13] fad or extreme diet adherents,[14,15] patients with gastrointestinal diseases including irritable bowel syndrome[34] and celiac disease,[35] oncology patients,[36] schizophrenia[12] and depression,[37] patients with restricted diets,[38,39] and the homeless.

Research recommendations

We suggest three basic recommendations for further research: (1) screen Vitamin C status of at-risk populations during scheduled primary care visits to assess the prevalence of hypovitaminosis C in asymptomatic patients; (2) screen Vitamin C status of at-risk populations during unscheduled ED visits to assess the prevalence of hypovitaminosis C in symptomatic patients with

signs and symptoms suggestive of scurvy; and (3) screen the Vitamin C status of sepsis and other critically ill patients to further characterize the role of hypovitaminosis C in critical illness.

Conclusion

Given that ED visits in the United States exceed 100 million/year, one physician detecting 14 presentations of scurvy in 12 patients over a 3 decades-long internal and emergency medicine career clearly raises the possibility that scurvy is much more common than currently appreciated. That, perhaps, several thousand cases of scurvy present to EDs in the United States each year and that most clinicians working on the front lines of medical care should expect to see cases of scurvy on an infrequent but regular basis. As a physician, you cannot diagnose something that you are not considering in your differential and of which you do not know the natural history or typical presentation. This is hypothesis generating and produces important research questions that should be studied, as Lind did over 250 years ago, in a systematic, scientific fashion. I propose that if scurvy was entertained as a diagnosis at appropriate times, case reports would gradually be replaced by case series and a more accurate understanding of the prevalence of scurvy in modern societies would emerge.

Research quality and ethics statement

This research was performed in accordance with the Declaration of Helsinki and was deemed appropriate to be performed without Institutional Review Board (IRB) approval by the Thomas Jefferson University IRB.

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Conflicts of interest

There are no conflicts of interest.

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