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【 CASE REPORT 】

Adult Scurvy Presenting with Painful Purpura on the Legs

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Abstract:
Prolonged vitamin C deficiency can result in numerous metabolic abnormalities like impaired tissue repair and defective collagen synthesis. This case report describes a middle-age Japanese man presenting painful purpura on his lower limbs, severe anemia, and altered consciousness. The patient had been eating a selective diet lacking in vegetables and fruits since childhood. A serum analysis demonstrated a low level of vitamin C. The patient was treated with vitamin supplementation and psychological intervention. Scurvy is an under-considered illness with a favorable prognosis if diagnosed early while it is still sporadically encountered in some patients with malabsorption or malnutrition even in modern times.

Key words: vitamin C, malnutrition, malabsorption, peliosis, anemia

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Introduction

Scurvy, caused by a prolonged inadequate intake of vitamin C, is a potentially lethal condition. The disease may also occur in developed countries, typically among poor elderly patients and refugees (1). It is also recognized as an occupational disease among workers such as whalers or among armies with inadequate access to fresh fruits and vegetables (2, 3). The prevalence of scurvy has decreased markedly over the years as the availability of multiple enriched and fortified food products became widespread. However, scurvy still occurs in both children and adults with abnormal dietary habits, mental illness, alcoholism, concomitant gastrointestinal disease, or physical disabilities (4-7).

We herein report an adult patient with scurvy presenting with painful purpura on his legs and gluteal region and muscle weakness. Based on detailed inquiries regarding his eating habits and serum measurement of vitamins, the patient was diagnosed early and successfully treated with vitamins and a balanced diet. The signs of scurvy greatly vary and include systemic, skin, bone, and dental manifestations. In addition, the low frequency of this disease may result in difficulty accurately diagnosing and treating the condition. Our case may highlight the importance of recognizing scurvy as a differential diagnosis when there are atypical presentations of purpura that cannot be explained by another disease such as vasculitis or trauma. Sharing our experience as well as including a review of the pertinent literature may help emergency physicians expedite the treatment process and improve patient prognosis.

Case Report

A 48-year-old male was admitted to the hospital with complaints of impaired consciousness, general fatigue, and leg pain. He had no noteworthy past medical history and had been living a life of seclusion. The patient had cramps in his left dorsal foot and gingival bleeding two weeks before presentation. He denied any physical trauma, insect bites, or general diseases and reported a history of eating a selective diet lacking in vegetables or fruits since childhood. His daily diet had consisted of rice with soy sauce and mayonnaise for the past month and before that, he ate exclusively instant noodles. The patient experienced occasional nasal and gingival bleeding.

His vital signs and physical examination results at presentation were as follows: body temperature of 36.7°C, height

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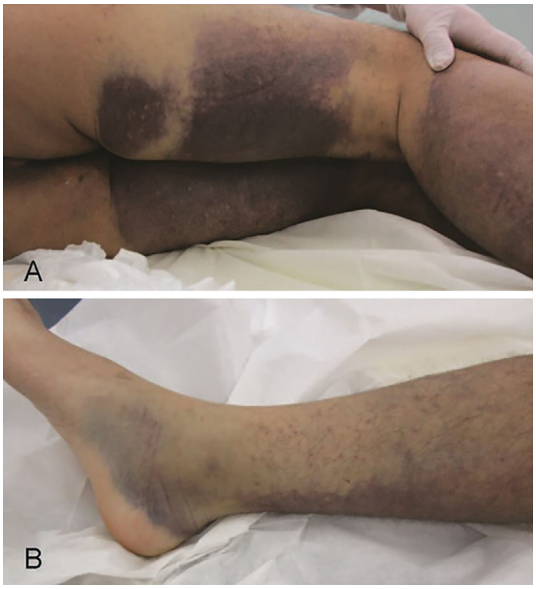

Figure. Purpuric petechiae with edema and tenderness in the gluteal region and posterior thigh were noted (A). Image of right lower extremity (B) shows flat, non-blanchable purpura/ecchymoses ranging from purple to yellow around the calf and ankle.

of 175 cm, body weight of 56.3 kg, body mass index of 23.3 kg/m^2, heart rate of 103 beats/min, blood pressure of 103/70 mmHg, and respiratory rate of 28 breaths/min. His Glasgow Coma Scale score was 15 (E4V5M6). Prior to arrival at the hospital, he had also experienced urinary incontinence. An examination of the skin showed symmetrically distributed purpuric petechiae with edema and tenderness in the gluteal region and posterior thigh (Figure A). There were also numerous dark blue or brown ecchymotic patches with diameters ranging from 3 mm and 5 mm on the lower legs (Figure B). Chest X-rays revealed clear lung fields without pleural effusion or pneumonia. His electrocardiogram was normal and there was no organomegaly. Computed tomography of the brain, chest, and abdomen did not show any abnormal findings. Increased subcutaneous adipose tissue concentration indicating local inflammation was noted in the lower legs.

His laboratory results were as follows: white blood cell count of 4,800/μL, red blood cell count of 1.33×10^6/μL, hemoglobin level of 5.0 g/dL, hematocrit level of 13.7%, mean corpuscular volume of 103.0 fL, mean corpuscular hemoglobin level of 37.6 pg, mean corpuscular concentration level of 36.5 g/dL, reticulocytes level of 5.3%, platelet count of 18.6×10^4/μL, serum albumin level of 2.8 g/dL, aspartate transaminase level of 14 IU/L, alanine aminotransferase level of 5 IU/L, total-bilirubin level of 1.8 mg/dL; creatinine level of 1.01 mg/dL, urea nitrogen level of 20.2 mg/dL, sodium level of 134 mmol/L, potassium level of 3.3 mmol/L; chlorine level of 104 mmol/L; and iron level of 141 μg/dL (normal range; 54-181 μg/dL), ferritin level of 67.0 ng/mL, prothrombin time of 14.2 s, activated partial thromboplastin time of 29.2 s, international normalized ratio of prothrombin time of 1.18, fibrinogen level of 233 mg/dL, D-dimer level of 3.3 μg/mL, Fibrin/fibrinogen degradation products level of 12.8 μg/mL, antithrombin III level of 69%, protein induced by vitamin K absence or antagonist-II level of 36 UA/mL, C-reactive protein level of 1.61 mg/dL. An arterial blood gas analysis on ambient air showed a pH of 7.4, PaO_2 of 118.3 mmHg, $PaCO_2$ of 22.6 mmHg, HCO_3^- of 16.8 mmol/L, base excess of -6.0 mmol/L, and lactate of 6.6 mmol/L. Thyroid function tests revealed a free T3 level of 1.56 pg/mL (normal range; 2.1-3.1 pg/mL), free T4 level of 1.28 ng/mL (normal range; 0.75-1.42 ng/mL), and Thyrotropin level of 0.969 μLU/mL (normal range; 0.45-3.72 μLU/mL). An additional serum analysis showed the following levels of other trace elements: vitamin C <0.2 μg/mL (normal range 5.5-16.8 μg/mL), vitamin B12 80 pg/mL (normal range 180-914 pg/mL), and folic acid 1.9 ng/mL (normal range ≥4.0). His urinalysis test results were as follows: pH level of 5.5, glucose (+-), protein (+), blood (+), ketone bodies (+), bilirubin (-), urobilinogen (3+), nitrite (-), leucocyte (-). We also investigated the possibility of collagen diseases in the differential diagnosis however, all such tests were negative (antinuclear antibody, CH50, IgG, IgA, IgM, C3 and C4).

Scurvy was diagnosed based on the radiological appearance, clinical manifestations, and low blood vitamin C level. Macrocytic anemia seen in this patient was thought to be due to a vitamin B12 deficiency. We thought he was getting very little vitamin C in his diet. We admitted the patient to the emergency intensive care unit for maintenance of nutrition with involvement of the nutritional and psychiatric teams and careful monitoring.

Supplementation of vitamin B1 (100 mg/day) 3 days after initial treatment, and vitamin C (500 mg/day), vitamin B6 (100 mg/day), and vitamin B12 (1 mg/day) was initiated for two days. Thereafter, we started him on 1,500 mg/day of vitamin C in three divided doses and 500 μg of mecobalamin every two days for two weeks. At the same time as antimicrobial agents (ceftriaxone 2 g/day) for urinary tract infection were started on day 10, vitamin K (10 mg/day) was also administered starting on day 11 and 1 week after, we increased the amount of vitamin K to 20 mg/day and administered for a week. All administrations were all done intravenously. On day 2, we started the oral administration of folic acid (15 mg/day) in three divided dose for three weeks. He resumed his meal (1,500 kcal) on the day after initial treatment which contained protein (60 g), lipid (40 g), carbohydrate (225 g), salt (7.5 g), calcium (600 mg), sodium (2,530 mg), potassium (2,279.7 mg), phosphorus (900 mg), iron (7 mg), vitamin A (650 μg), vitamin B1 (1 mg), vitamin B2 (1 mg) and vitamin C (100 mg). The patient's clinical course was uneventful and his general condition rapidly improved. His mobility dramatically improved within 10 days and he regained his ability to walk without support. On day 11, follow-up tests showed that his vitamin C level was back to normal. The patient and his parents were issued proper nutritional guidance and discharged from the hospital on day

Table. Laboratory Date on Admission and Two Months Later.

	On admission	Two months later
White blood cells (/μL)	4,800	5,400
Red blood cells ($\times10^6$/μL)	1.33	4.30
Hemoglobin (g/dL)	5.0	13.8
Hematocrit (%)	13.7	38.5
MCV (fL)	103.0	89.5
MCH (pg)	37.6	32.1
MCHC (g/dL)	36.5	35.8
Reticulocytes (%)	5.3	1.0
Platelet cells ($\times10^4$/μL)	18.6	11.4
Albumin (g/dL)	2.8	3.9
AST (IU/L)	14	13
ALT (IU/L)	5	13
Total-bilirubin (mg/dL)	1.8	0.6
Creatinine (mg/dL)	1.01	0.73
Urea nitrogen (mg/dL)	20.2	11.1
Sodium (mmol/L)	134	142
Potassium (mmol/L)	3.3	3.5
Chloride (mmol/L)	104	106
Iron (μg/dL)	141	105
Ferritin (ng/mL)	67	285
C-reactive protein (mg/dL)	1.61	0.11
PT (s)	14.2	11.5
APTT (s)	29.3	33.6
PT-INR	1.2	1.0
Vitamin C (μg/mL)	<0.2	8.8
Vitamin B12 (pg/mL)	80	404
Folic acid (ng/mL)	1.9	11.9

MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, AST: aspartate transaminase, ALT: alanine aminotransferase, PT: prothrombin time, APTT: activated partial thromboplastin time, PT-INR: international normalized ratio of prothrombin time

25. During the two-month close follow-up period, the patient remained clinically stable without any laboratory abnormalities (Table).

Discussion

Vitamin C is absorbed from the gastrointestinal tract via active transport and passive diffusion. The total pool of vitamin C in the body, mainly found in the liver and muscles, is 1,500-2,000 mg. The daily turnover of vitamin C is 45-60 mg, with a half-life of 10-20 days (4). Ignorance about proper nutrition, malabsorption syndromes, psychiatric disorders, alcoholism, drug abuse, pregnancy/breast feeding, and social isolation are all causes that can lead to the development of scurvy. Symptoms and signs typically develop after three months of insufficient vitamin consumption. Vitamin C, a strong reducing agent and enzyme cofactor, is essential in various biochemical pathways like antioxidant reactions and collagen synthesis. Abnormalities in collagen synthesis cause many of the symptoms of scurvy, including collagen fragility, which in turn makes blood vessels fragile and leads to poor wound healing (7, 8).

Vitamin C also promotes carnitine biosynthesis, which is necessary for biosynthesis of adenosine triphosphate in the muscle mitochondria. Therefore, vitamin C deficiency can cause muscular weakness. In addition, vitamin C deficiency results in behavioral alterations, mental disorders, and neuropathological disruption, which may be associated with altered noradrenergic and dopaminergic signaling (9). Thus, scurvy's early clinical signs such as low grade fever, loss of appetite, and irritability, and dermatological symptoms such as ecchymoses, petechiae, corkscrew hairs, and hyperkeratosis, are not specific (4). Skin purpura without a history of trauma is a distinguishing feature of scurvy (10). Patients with scurvy are often underdiagnosed and they can also develop potentially fatal diseases including cerebral hemorrhaging, severe hemodynamic compromise, and systemic inflammatory response.

Scurvy's differential diagnoses vary widely and include systemic conditions like hematological and rheumatological diseases and localized disorders like periodontal disease. In addition to physical and laboratory examinations, detailed information regarding the patient's lifestyle, occupation, eating habits, food preferences, mental status, and bowel movements help in making an accurate diagnosis of scurvy. Of note, other diseases presenting similar manifestations must be ruled out. Our patient reported that he was a picky eater and a recluse, and lived in a self-imposed isolated room in his house. Under such circumstances, the patient's daily diet may be unbalanced without essential nutrients. As with our patient, scurvy should be suspected in those with behavioral and psychiatric disorders (11). Children with physical disabilities, mental illness, or abnormal dietary habits are prone to developing this condition.

As vitamin C replacement is the only effective therapy for scurvy, early diagnosis and treatment is critical. Even patients with advanced disease usually favorably respond to administration of vitamin C. The coexistence of other biochemical complementary deficiencies of other vitamins and zinc should be considered and are required to be supplemented. Moreover, conditions that can affect compliance with treatment like gastritis, gastro-esophageal reflux, and bowel disease causing malabsorption should also be considered.

The standard treatment for scurvy is a daily oral dose of 1,000 mg of vitamin C for two weeks (12). When administered orally, vitamin C is absorbed well at low doses, but absorption decreases with increasing doses. The median bioavailability after oral administration is 87% at 30 mg, 80% at 100 mg, 72% at 200 mg, and 63% at 500 mg. At 1,250 mg, less than 50% of the dose absorbed and the remainder is excreted in the urine (8). Therefore, the doses should be divided and given throughout the day to obtain adequate absorption (4, 12, 13). Issuing nutritional guidance to the patient is necessary to prevent scurvy from reappearing after discharge from the hospital. Foods rich in vitamin C are often also rich in folic acid. Our patient required both

nutritional guidance and psychological treatment.

Conclusion

Vitamin C deficiency, which is often under-suspected, should therefore be considered in the differential diagnosis when examining patients with skin purpura without a history of trauma.

The authors state that they have no Conflict of Interest (COI).

References

1. Ververs M, Muriithi JW, Burton A, Burton JW, Lawi AO. Scurvy outbreak among south sudanese adolescents and young men - Kakuma refugee camp, Kenya, 2017-2018. MMWR Morb Mortal Wkly Rep **68**: 72-75, 2019.
2. McCord CP. Scurvy as an occupational disease. VI. Scurvy among the whalers. J Occup Med **13**: 543-548, 1971.
3. McCord CP. Scurvy as an occupational disease. VII. Scurvy in the world's armies. J Occup Med **13**: 586-592, 1971.
4. Agarwal A, Shaharyar A, Kumar A, Bhat MS, Mishra M. Scurvy in pediatric age group - a disease often forgotten? J Clin Orthop Trauma **6**: 101-107, 2015.
5. Olmedo JM, Yiannias JA, Windgassen EB, Gornet MK. Scurvy: a disease almost forgotten. Int J Dermatol **45**: 909-913, 2006.
6. Antonelli M, Burzo ML, Pecorini G, Massi G, Landolfi R, Flex A. Scurvy as cause of purpura in the XXI century: a review on this "ancient" disease. Eur Rev Med Pharmacol Sci **22**: 4355-4358, 2018.
7. Lipner S. A classic case of scurvy. Lancet **392**: 431, 2018.
8. Padayatty SJ, Levine M. New insights into the physiology and pharmacology of vitamin C. CMAJ **164**: 353-355, 2001.
9. Ward MS, Lamb J, May JM, Harrison FE. Behavioral and monoamine changes following severe vitamin C deficiency. J Neurochem **124**: 363-375, 2013.
10. Halligan TJ, Russell NG, Dunn WJ, Caldroney SJ, Skelton TB. Identification and treatment of scurvy: a case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod **100**: 688-692, 2005.
11. Adelman HM, Wallach PM, Gutierrez F, et al. Scurvy resembling cutaneous vasculitis. Cutis **54**: 111-114, 1994.
12. Fain O. Musculoskeletal manifestations of scurvy. Joint Bone Spine **72**: 124-128, 2005.
13. Zhang M, Robitaille L, Eintracht S, Hoffer LJ. Vitamin C provision improves mood in acutely hospitalized patients. Nutrition **27**: 530-533, 2011.