International Journal of Hematology
https://doi.org/10.1007/s12185-018-02575-w

CASE REPORT

Vitamin C deficiency: rare cause of severe anemia with hemolysis

Hira Shaikh[1] · **Muhammad Salman Faisal**[1] · **Prerna Mewawalla**[2]

Received: 2 July 2018 / Revised: 11 December 2018 / Accepted: 25 December 2018

Abstract
Historically known to be a disease of sailors and soldiers in the seventeenth and eighteenth century, scurvy is a rare nutritional deficiency in the developed world, but it can still be seen among the alcoholics and the malnourished. We present a case of a 39-year-old alcoholic male who presented with progressive fatigue and diffuse purpuric rash with scattered ecchymosis for 2 months. Blood work was remarkable for hemoglobin of 9.1 g/dl, which further dropped to 7 g/dl over the next few days. He was then found to have hemolysis on lab work. After an extensive workup, the common causes of hemolytic anemia were ruled out, vitamin C level was checked, which interestingly resulted as 0 mg/dl. Supplementation with oral vitamin C resulted in the gradual resolution of hemolytic anemia and rash. Hemoglobin improved to 15 g/dl in 4 weeks, with normalization of vitamin C level. The clinical features of scurvy can easily be confused with conditions such as vasculitis, deep venous thrombosis, and systemic bleeding disorders. Therefore, comprehensive workup up is required prior to the diagnosis. Although rare, being a reversible condition, early diagnosis and treatment of scurvy in high-risk populations cannot be stressed enough.

Keywords Scurvy · Hemolytic anemia · Vitamin C deficiency · Rash · Petechia

Abbreviations
aPTT Activated partial thromboplastin time
RBC Red blood cell

Introduction

Scurvy is a historical disease that surfaced after afflicting sailors. Caused by vitamin C deficient diet, its prevalence has decreased in the modern world and is currently limited to underdeveloped countries, frequently among the refugees, undernourished, alcoholics, elderly, and homeless [1–3]. Vitamin C cannot be synthesized in human body; therefore, an exogenous source is necessary [4].

The clinical features specifically the rash of scurvy are often difficult to distinguish from other diseases such as vasculitis, venous thrombosis, and systemic bleeding disorders, which warrant an extensive work up in those suspected to have scurvy [5]. We present a case of a 39-year-old alcoholic male with rash and hemolytic anemia that responded rapidly with Vitamin C supplementation.

Case presentation

A 39-year-old male with past medical history of plaque psoriasis, hypertension and alcohol abuse presented to the hospital with progressive diffuse purpuric rash for 2 months along with fatigue. Rash was initially scaly and itchy, located on the face, anterior surface of lower legs and trunk. The rash was initially thought to be from his psoriasis; therefore, he was started on prednisone. However, the rash continued to worsen, now appearing as 2–4 mm purple macules on face, and petechiae and purpura on neck, shoulders, chest, trunk, and lower extremities, as shown in Fig. 1. There were large ecchymoses on left thigh and leg, and well demarcated, erythematous, scaling papules, and plaques on forearms and legs. There was no evidence of mucosal abnormalities or splenomegaly. No clinical findings concerning for gastrointestinal or internal bleeding were appreciated, Corkscrew hairs were visualized, as shown in Fig. 2. The differential diagnosis included bleeding disorder, thrombocytopenia, lymphoma, leukemia cutis, vasculitis, amyloidosis, Kaposi's sarcoma, and scurvy.

✉ Hira Shaikh
Hira_ghazal@hotmail.com; hira.shaikh@ahn.org

[1] Department of Internal Medicine, Allegheny Health Network, 320 N East Avenue, 7th Floor, South Tower, Pittsburgh, PA 15212, USA

[2] Department of Hematology-Oncology, Allegheny Health Network, Pittsburgh, PA, USA

Published online: 22 January 2019

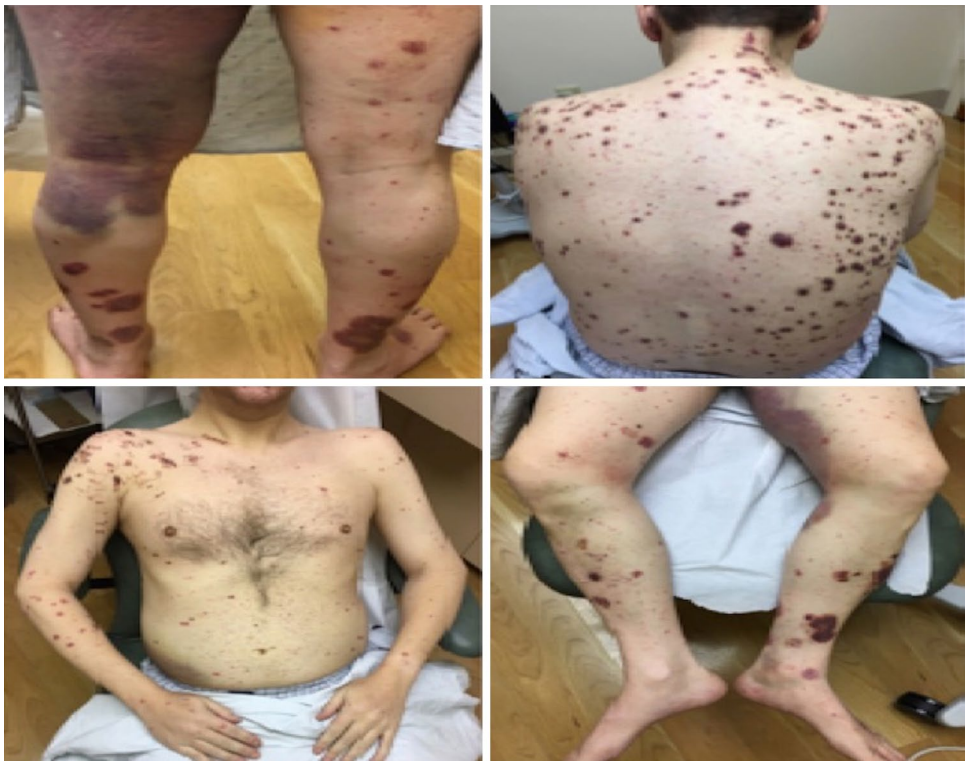

Fig. 1 Rash with petechiae, purpura, and ecchymoses on neck, shoulders, chest, trunk and lower extremities on arrival

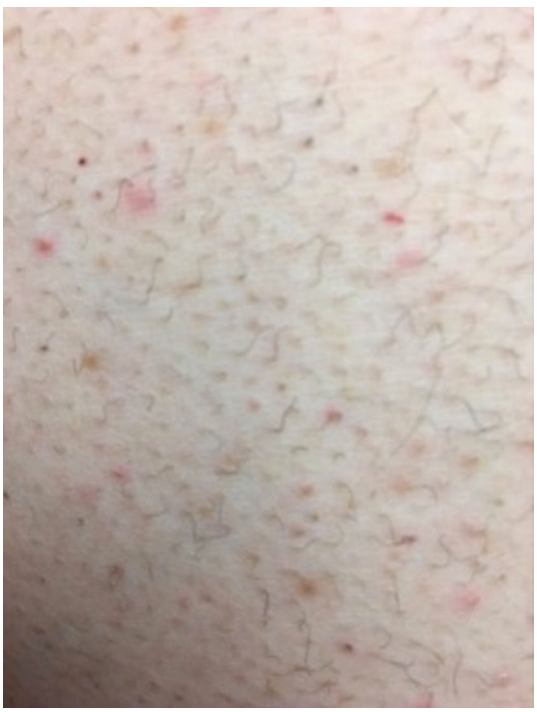

Fig. 2 Corkscrew hair visible on skin

Workup

Blood work was remarkable for hemoglobin of 9.1 g/dl, red blood cell count 2.44×10^9/µl, MCV 105 fL, MHC 37 pg. White cell count was 5.42×109/µl and platelets 147×109/µl. Peripheral blood smear showed anisocytosis and schistocytosis (3 per field). Protime was 17 s, INR being 1.4 and aPTT 32 s. Urea, electrolytes, creatinine, and liver function tests were unremarkable, except for Na of 124 mEq, aspartate transaminase 65 U/l, and total bilirubin elevated to 2.5 mg/dl with normal direct bilirubin of 0.7 mg/dl. The hyponatremia was linked with his history of alcohol use, at least 3–4 beers a day. Further evaluation of anemia revealed normal iron panel except for elevated ferritin to 854 ng/ml. Hemolysis workup revealed elevated lactate dehydrogenase (LDH) to 540 U/l and reticulocyte count to 0.17 m/mcl, and haptoglobin < 10 mg/dl. There was no evidence of hemoglobinuria or hemoglobinemia. Vitamin B12, RBC folate and copper levels were within normal ranges.

Cryoglobulin, Coomb's and cold agglutinin tests were negative. HHV-6, HIV, Hepatitis B and C, parvovirus, malaria, mycoplasma pneumoniae, Epstein–Barr virus and cytomegalovirus testing were negative. Autoimmune workup including antinuclear antibody (ANA), rheumatoid factor (RF), and cyclic-citrullinated peptide (CCP) resulted negative. The skin biopsy showed granulomatous eruptions with intradermal hemorrhages. Tissue stains for bacteria, AFB

(acid fast bacilli), fungi and spirochete infection were negative. Immunoreactivity was negative for immunoglobulins and complement but there was interstitial fibrin deposition.

Hemoglobin continued to drop, to 7 g/dl over the next few days. Given the skin biopsy results in combination with the hemolytic anemia, his vitamin C level was checked which resulted as 0 mg/dl. Thereafter, he was started on 500 mg vitamin C twice daily. Hemoglobin improved to 13 g/dl within 2 weeks and to 15 g/dl at 4 weeks. Rapid improvement of labs including LDH, indirect bilirubin, absence of urobilinogen, and normalization of reticulocyte count within 2 weeks of initiating vitamin C points out to scurvy as the etiology. Blood smear was not repeated. With oral vitamin C and diet rich in citrus fruits, levels of vitamin C normalized and he sustained stable blood counts, along with the improvement in rash.

Discussion

Scurvy is a nutritional deficiency that has been described in history dating back to 1500 BC in Ebers Paperus. It was a common disease that killed sailors in seventeenth and eighteenth Century [6]. James Lind, a naval surgeon on HMS Salisbary in 1747 treated scurvy patients with citrus fruits and described his finding in The Treatise of scurvy in 1753 [7].

The clinical features of scurvy are varied and relate to the functions disturbed by lack of vitamin C. It is an essential nutrient required for hydroxylation reactions including procollagen synthesis [8]. Loss of collagen synthesis leads to blood vessel fragility leading to cutaneous manifestations that include hyperkeratosis, parafollicular hemorrhage, petechiae and ecchymosis. Gum diseases including hyperplastic ulcerative gingivitis and periodontitis are also reflective of defective collagen synthesis. Inability to make disulfide bridges results in corkscrew hair. Muscle weakness, myalgia and leg edema, dyspnea, pulmonary hypertension, leukopenia, and hypotension are other manifestations of scurvy, and the deficiency can eventually progress to death [9]. Symptoms of deficiency of vitamin C can appear as early as in 4 weeks of last oral intake, [10], but the dermal lesions can take months to appear [11].

Anemia in scurvy can affect up to 80% of patients [12]. It can be through one of the various mechanisms, including occult gastrointestinal bleeding, impaired erythropoiesis, concurrent folate deficiency, intravascular, or extravascular hemolysis [12, 13]. Majority of the patients have normochromic, normocytic peripheral blood picture with reticulocytosis, normal white cell counts, and platelets [12]. Bleeding into the tissues caused by fragility of collagen fibers in vascular walls results in bleeding in skin and joints, [12, 14] and if severe can progress to cerebral hemorrhage and hemopericardium [4]. In addition, scurvy also causes reduced red blood cell survival. Merskey demonstrated reduced life span of red blood cells transfused to patients with scurvy using Ashby technique [15]. Similar findings were also demonstrated by Goldberg using radiolabeled RBCs [13].

The recommended dose of vitamin C for scurvy is 300 mg daily in divided doses [13]. With vitamin C replacement, the clinical recovery is prompt and the symptoms improve rapidly within 24–48 h [9], while the anemia improves within weeks of treatment [16, 17]. Rapid resolution of rash and hemolytic anemia in our patient with repletion of vitamin C confirmed the diagnosis.

Conclusion

This case highlights that although rare in developed countries, vitamin C deficiency is possible in twenty-first century and can be easily missed if not sought for in high-risk populations. Being a reversible condition, with potential for rapid recovery with supplementation, the condition should be diagnosed early and treated aggressively.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests to disclose.

References

1. Fazio V, Flint DM, Wahlqvist ML. Acute effects of alcohol on plasma ascorbic acid in healthy subjects. Am J Clin Nutr. 1981;34(11):2394–6.
2. Leung FW, Guze PA. Adult scurvy. Ann Emerg Med. 1981;10(12):652–5.
3. Malmauret L, Leblanc J, Cuvelier I, Verger P. Dietary intakes and vitamin status of a sample of homeless people in Paris. Eur J Clin Nutr. 2002;56(4):313–20.
4. Fraser IM, Dean M. Extensive bruising secondary to vitamin C deficiency. BMJ Case Rep. 2009. https://doi.org/10.1136/bcr.08.2008.0750.
5. Reuler JB, Broudy VC, Cooney TG. Adult scurvy. Jama. 1985;253(6):805–7.
6. Major RH, A history of medicine. A history of medicine. Charles C. Thomas; 1954.
7. Lind J, A treatise on the scurvy: in three parts, containing an inquiry into the nature, causes, and cure, of that disease. A. Millar; 1757.
8. Smith A, Di Primio G, Humphrey-Murto S. Scurvy in the developed world. Cmaj. 2011;183(11):E752-5.
9. Lau H, Massasso D, Joshua F. Skin, muscle and joint disease from the 17th century: scurvy. Int J Rheum Dis. 2009;12(4):361–5.
10. Padayatty SJ, Levine M. New insights into the physiology and pharmacology of vitamin C. Cmaj. 2001;164(3):353–5.

11. Baradhi KM, Vallabhaneni S, Koya S. Scurvy in 2017 in the USA. Proc (Bayl Univ Med Cent). 2018;31(2):227–8.
12. Cox EV. The Anemia of Scurvy. In: Harris RS, Wool IG, Loraine JA, Thimann KV (eds). Vitamins & hormones. Cambridge: Academic Press, 1969, pp 635–652.
13. Goldberg A. The anaemia of scurvy. Q J Med. 1963;32:51–64.
14. Stefanini M, Dameshek W. The hemorrhagic disorders. New York: Grune & Stratton. Inc; 1955.
15. Merskey C. Survival of transfused red cells in scurvy. Br Med J. 1953;2(4850):1353–6.
16. Yalcin A, Ural AU, Beyan C, Tastan B, Demiriz M, Cetin T. Scurvy presenting with cutaneous and articular signs and decrease in red and white blood cells. Int J Dermatol. 1996;35(12):879–81.
17. Vilter RW, Woolford RM, Spies TD. Severe scurvy; a clinical and hematologic study. J Lab Clin Med. 1946;31:609–30.