

CASE REPORTS

Vitamin C or not to see: A diagnostic dilemma

Zachary M. Zemore*¹, Nathaniel C. Warner²

¹School of Medicine, Virginia Commonwealth University, Richmond, Virginia, USA

²Department of Internal Medicine, Virginia Commonwealth University, Richmond, Virginia, USA

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ABSTRACT

Scurvy is a severe deficiency of vitamin C, or ascorbic acid. Despite its perceived rarity in developed countries, certain populations are at higher risk of developing scurvy, and a delay in diagnosis can lead to significant morbidity and possibly death. In this case, a 46-year-old female was admitted to the hospital with subtle mood changes, memory loss, and generalized failure to thrive. Physical exam revealed a petechial rash. Evaluation and workup by multiple physicians revealed no source for her condition, which continued to deteriorate. Finally, because of the patient's rash, a nutritional history was taken which was highly concerning for scurvy. An ascorbic acid level was ordered and returned at 0 mg/dl (reference range 0.2-2 mg/dl), confirming the clinical diagnosis of scurvy. Ascorbic acid repletion reversed her symptoms and she was discharged home uneventfully. Ascorbic acid is vital for the integrity of skin and soft tissues. Due to its high prevalence in the diets of most developed countries, scurvy has become a rare diagnosis that many providers do not recognize. Despite its rarity, certain populations are still at risk and providers should remain cognizant of the diagnosis, especially when classic manifestations such as a petechial rash or bleeding gums are seen.

Key Words: Scurvy, Ascorbic acid, Malnutrition, Petechial rash

1. INTRODUCTION

Scurvy is one of the most storied and recognizable diseases in medicine. It was described as far back as 1550 BC. In the 15th and 16th century, physicians began to recognize its clinical signs during the ocean voyages of the English and Portuguese. They found that fruits and vegetables alleviated this condition. Possibly the first ever controlled clinical trial was conducted by James Lind, searching for scurvy's cure. In 1927, ascorbic acid was discovered and further research was conducted demonstrating its effects on the human body and its importance as an essential vitamin.^[1] Scurvy is now easily preventable and all too often ignored.

Although widely available and cheap, many Americans are deficient in ascorbic acid. Seven percent of the U.S. popu-

lation has ascorbic acid deficiency based on serum levels.^[2] Furthermore, 20%-30% of Americans consume less than 60 mg of ascorbic acid daily,^[3] well below the recommended daily intake suggested by the National Institute of Health and other major health agencies. Certain populations are at increased risk of ascorbic acid deficiency. Smokers metabolize two times more ascorbic acid compared to nonsmokers.^[4] Without fortified foods or vitamins, 45% of people will consume less than the average estimated requirement of ascorbic acid.^[5] With recent health trends in the United States, this may place a large portion of the population at risk. Other high-risk groups include alcoholics and those with very stringent diets.

Given the large at-risk population, it is important to highlight

*Correspondence: Zachary M. Zemore; Email: zemorezm@vcu.edu; Address: 1730 Porter St. Richmond, Virginia 23224, USA.

this topic and encourage practitioners to obtain a nutritional history in high-risk groups. Physicians are often aware of the clinical signs of scurvy but are delayed in making the diagnosis. The case presented will demonstrate some of these key principles.

2. CASE PRESENTATION

A 46-year-old female with history of right sided fronto-temporal epidermoid tumor presented with her husband to the neurology clinic for routine follow up of her seizures. Her husband noted three-weeks of progressive fatigue, weight loss, memory loss and irritability. She then developed a petechial rash predominately on her extremities and lower extremity edema ten days prior to presentation. On exam, she was disoriented and unable to cooperate in the history. She was admitted to the inpatient neurology service for failure to thrive.

Initial physical examination revealed a BMI of 19. Vital signs were within normal limits. Cardiopulmonary and abdominal examinations were benign. She had 2+ pitting edema in her right lower extremity along with a fine, non-blanching petechial rash over the distal extremities (see Figure 1). Subungual hemorrhages were present on both hands (see Figure 2).

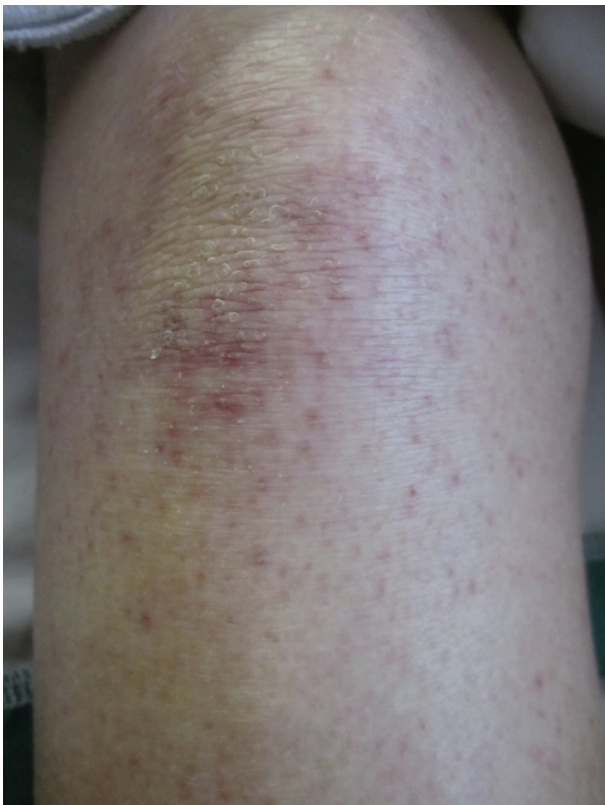


Figure 1. Fine, non-blanching petechial rash

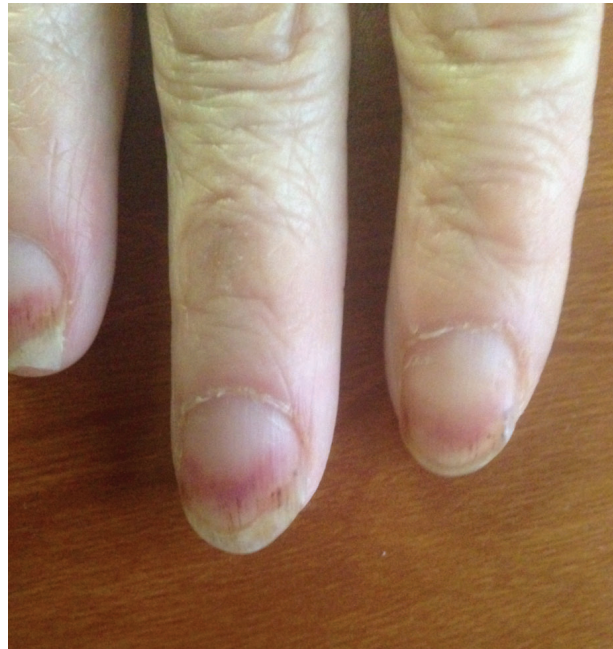


Figure 2. Subungual hemorrhages

Labs demonstrated a megaloblastic anemia, with hemoglobin of 7.2 g/dl (reference range 12-15 g/dl) and a MCV of 100.5 fL (80-100 fL). Folic acid level was 2.5 ng/ml (5-20 ng/ml). Her albumin and prealbumin were low at 3.3 g/dl (3.7-5.2 g/dl) and 7 mg/dl (17-42 mg/dl) respectively. The remaining labs were within normal limits. A KUB simply demonstrated bilateral renal calculi. Further labs and testing had no significant findings. MRI showed no progression of the epidermoid tumor or any new acute abnormalities.

The patient continued to appear ill and the internal medicine consult service was called for additional recommendations. Given the petechial rash, small vessel vasculitis was considered and the patient was transferred to an inpatient medicine team for further workup.

The primary medicine team interviewed the patient, and noting her rash and cachectic appearance, inquired more about her diet. Her diet consisted exclusively of cashews and “Brownie Bites” for the last eight months. Two years prior to that, she had eaten only chicken nuggets. She vehemently denied eating any fruits or vegetables and drank only diet soda. The team quickly became aware that the patient was malnourished, as this type of diet lacks many essential nutrients and vitamins, including ascorbic acid.

Furthermore, on exam her oral mucosa demonstrated a purple hue at the base with occasional small ulcers. She said she had been experiencing soreness of her gums and bleeding while brushing her teeth lately, and had even started using a children’s soft toothbrush. The hair on her scalp was thin and

falling out while the remaining hair on her legs demonstrated a swan neck type appearance.

The medicine team made a clinical diagnosis of scurvy based off these findings and began treatment with intravenous ascorbic acid. The patient was loaded with 1,500 mg IV of ascorbic acid over 24 hours followed by 1,000 mg PO ascorbic acid daily until the clinical resolution of her symptoms. Subsequently, her initial serum ascorbic acid level returned undetectable, at 0 mg/dl (0.2-2 mg/dl).

3. DISCUSSION

Scurvy is an ancient disease that is well described in the literature, although the diagnosis is uncommon and infrequently considered in the United States. Traditionally, the diagnosis of scurvy was made clinically in patients with deficient diets and classic exam findings. The modern diagnosis of scurvy is made by demonstrating a patient has classic clinical features in the setting of ascorbic acid deficiency, which is measured through a serum ascorbic acid level.

The earliest symptoms include lassitude, irritability and anxiety. Unfortunately they are non-specific and rarely lead to a diagnosis of scurvy.^[6] It is not until the physical signs appear that the diagnosis is typically made. Additionally, classic findings of a petechial rash are frequently confused with a vasculitic process,^[4] as was the case in this patient. A petechial rash in adults warrants further workup, and can often be placed into etiologic categories (see Table 1). In this case, traumatic and familial causes were ruled out from the history and clinical setting. A detailed history, physical and blood testing failed to reveal signs of infection such as recent travel, fever, leukocytosis or other concerning findings. Platelet counts and kidney function also remained within normal limits, helping to eliminate other causes. This patient presented classically with scurvy and many physicians evaluated her before the diagnosis was considered.

Table 1. Common components of a differential diagnosis for a petechial rash in adults

Non-Infectious	Infectious
Familial	-Rocky mountain spotted fever
-VonWillebrand's disease	-Bacterial endocarditis
Neoplastic	-Meningococcemia
-Leukemia	-Disseminated CMV
Acquired	-Waterhouse-friderichsen syndrome
-Thrombotic thrombocytopenic purpura	-Measles
-Aplastic anemia	-Hemolytic uremic syndrome
-Disseminated intravascular coagulation	
Autoimmune	
-Idiopathic thrombocytopenic purpura	
-Antiphospholipid syndrome	
-Churg-strauss syndrome	
-Microscopic polyangiitis	
-Polyarteritis nodosa	

The most widely recognized signs of scurvy are petechial hemorrhages. These may appear anywhere on the body, but usually emerge in dependent areas such as the lower extremities. Vessels leak due to an impaired post-translational modification of collagen, which requires ascorbic acid as a cofactor. Up to 30% of cellular proteins are collagen, and without this reaction, the triple helix structure of collagen is unable to form properly and vessel leakage occurs.^[7] Other classic findings include hematoma formation with minimal trauma, bleeding gums, subungual hemorrhages, perifollicular hyperkeratosis, and coiled "corkscrew" or "swan neck" hairs. These are often late findings and patients may have scurvy without these signs.^[6] If untreated, scurvy will eventually lead to death.

In addition to the effects on collagen, ascorbic acid is involved in many other processes that are not typically recognized. It is involved in the formation of several neurotransmitters, amino acids and catecholamines.^[8] It increases the absorption of iron up to 10 times by reducing ferric iron to its absorbable ferrous form.^[9] It also plays a role in the formation of folic acid.^[8] These effects help to explain why many patients including ours present with anemia. There is emerging evidence that ascorbic acid may also be involved in other reactions such as histone demethylation, resultantly helping to regulate genes expression.^[6,10] These examples highlight several of the numerous roles of ascorbic acid.

One final note should be made regarding the overuse of ascorbic acid. Most individuals do not exceed the recommended upper limit of ascorbic acid, and overall it has relatively few adverse reactions associated with it.^[5] However, high levels of ascorbate can precipitate oxalate stone formation. High doses are contraindicated in patients with oxalate stones, as was the case in our patient.^[6]

4. CONCLUSION

Ascorbic acid is widely available, making it easy to preclude its importance as an essential nutrient. Scurvy has now become a rare disease in the United States and many developed countries. Despite this, certain populations including alcoholics, smokers and those with poor diets are at increased risk. Providers in these countries should recognize the signs and symptoms of scurvy so that a detailed dietary history may be obtained to screen for this disease. Additionally, ascorbic acid contributes to many functions of the human body and there is a growing fund of evidence demonstrating it may play a larger and more diverse role than previously thought. Our patient was an example of scurvy that was difficult for many providers to recognize despite classic findings of petechiae, gum bleeding and follicular changes.

CONFLICTS OF INTEREST DISCLOSURE

The authors declare that they have no competing interests.

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