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Single Case

Characteristic Skin Eruptions with a Distinct Histological Pattern Allow Early Diagnosis of Vitamin C Deficiency

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Keywords
Vitamin C deficiency · Hemorrhagic diathesis · Histology · Nutrition · Ascorbic acid

Abstract
Introduction: Scurvy has become a rare disease in western countries with potentially high morbidity. Early diagnosis is crucial and can be challenging. ***Case Presentation:*** We present the case of a 56-year-old male patient who developed hemorrhagic diathesis after trivial impact trauma. Previously, the patient suffered from fatigue and loss of appetite. Characteristic skin eruptions and a distinct skin histology along with a decreased serum vitamin C level led to the diagnosis of scurvy. Following vitamin C supplementation, symptoms improved rapidly. ***Conclusion:*** In conclusion, vitamin C deficiency should be considered in cases with unclear hemorrhagic diathesis and a medical history of nutritional irregularities. Especially in cases of scurvy that do not yet show the full clinical spectrum of symptoms or have only moderately decreased serum vitamin C levels, thorough clinical dermatological examination and a skin biopsy are essential for early diagnosis and to prevent complications.

Introduction

Even though the prevalence of scurvy is nowadays much lower in western countries than it used to be in the last century, it is a severe disease with high morbidity that can cause a high financial burden on the health care system if the diagnosis is missed or if the diagnostic approach starts with inappropriate expensive tests. Especially in cases of scurvy that do not

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yet show the full spectrum of symptoms such as also bleeding of the gums or in cases that are associated with only slightly to moderately decreased serum vitamin C levels, early correct diagnosis can be challenging.

The skin is an easily accessible organ and reveals important macroscopic, dermatoscopic, and histological clues in scurvy. Besides measurement of vitamin C serum level, thorough clinical examination, dermoscopy and a skin biopsy are simple inexpensive steps to make an early diagnosis of scurvy and to rule out other causes of hemorrhages such as vasculitis. Vitamin C substitution is simple, inexpensive and leads to rapid disappearance of the symptoms.

Case Presentation

A 56-year-old male patient presented on our emergency unit with progressive swelling and throbbing pain in the left leg for about 2 months with extensive ecchymoses following a trivial impact trauma of the left knee when his leg got slightly trapped in a closing train door. Before that event, he had already noticed painless tiny red spots on both legs. The patient reported gait instability since that trauma and fatigue, loss of appetite, and a weight loss of about 8 kg over the past 3 weeks. At the time of admission, the patient went on walking sticks and needed a wheelchair for longer distances. Patient history revealed an unbalanced diet devoid of fresh fruit, vegetables, or meat for several months. Furthermore, the patient had a history of previous intravenous drug abuse and hepatitis C virus-infection in complete remission. He was an active smoker and drank about 2 L of beer a day.

On clinical examination, the patient presented in reduced general and nutritional condition with an increased circumference of the left leg with large confluent reddish livid ecchymoses (Fig. 1). In addition, disseminated reddish brown follicular papules were found on both legs (Fig. 2, 3). Muscle strength was decreased – predominantly in the left leg. Orally, there was no gingival hyperplasia or evidence of hemorrhage.

Laboratory analysis revealed chronic preexisting but currently aggravated pancytopenia with marked macrocytic hyporegenerative normochromic anemia with a hemoglobin level of 61 g/L, as well as mild hyponatremia and an elevated D-dimer level. Levels of folic acid and vitamin B12 were decreased. The coagulation profile was normal with an activated partial thromboplastin time of 27 s (normal range (NR): 23–33 s), a thrombin time of 21 s (NR: 16–25 s), and serum fibrinogen of 3.1 g/L (NR: 1.7–4.0 g/L). The patient was not on any medication that affects the coagulation system. Computed tomography ruled out pulmonary embolism. X-ray did not reveal any fractures of the left leg. Duplex sonography of the left leg showed no evidence of deep vein thrombosis. Fluorescence-activated cell sorting analysis of the peripheral blood was normal. An abdominal ultrasound and a magnetic resonance cholangiopancreatography ruled out an abdominal neoplasia.

The chronic component of anemia was interpreted as a result of folic acid and vitamin B12 deficiency and therefore substituted. Also, zinc was administered empirically. The acute component of the anemia with symptomatic hemoglobin loss was best explained by a hemorrhagic diathesis of the left leg. A cutaneous vasculitis could not be confirmed – neither serologically nor by skin histology. Skin histology and serology showed no signs of a vaso-occlusive disease such as cryoglobulinemia. Since the hemorrhagic diathesis as well as the weight loss still remained unexplained and had not improved following substitution of zinc, folic acid, and vitamin B12, we measured vitamin C in the serum, which was decreased (14 μmol/L, standard value >24 μmol/L). Skin biopsies from the lower extremities showed follicular hyperkeratosis, coiled hair shafts, extravasated erythrocytes around vessels in the upper dermis and around hair follicles and siderophages as a sign of previous hemorrhage, all of which are characteristic morphological changes in scurvy.

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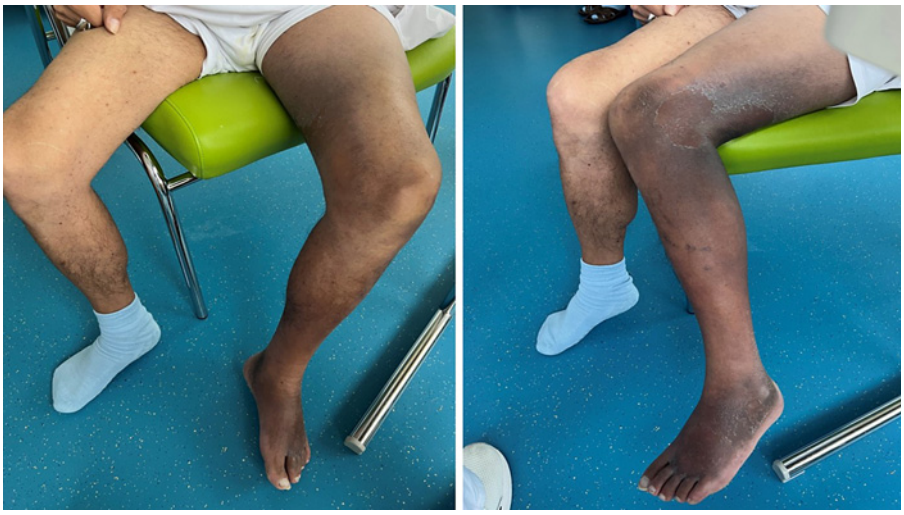

Fig. 1. Increased leg circumference on the left side with large confluent reddish livid ecchymoses.

We started vitamin C substitution at 1,000 mg daily and saw a rapid improvement of the patient's symptoms, further supporting the diagnosis. At the time of discharge, the patient could walk again for longer distances without assistance and had no difficulties in climbing stairs. Furthermore, we were informed by patient's general practitioner that his well-being has improved and that the above-noted symptoms have completely disappeared.

Discussion

Vitamin C is an essential dietary vitamin. Important dietary sources for humans include fresh fruits and vegetables. The most frequent cause of scurvy is inadequate intake. Scurvy was common among sailors in the past due to lack of fresh food. Certain conditions such as excessive consumption of alcohol, eating disorders but also increased need during growth, infections, pregnancy, and breast-feeding can further enhance vitamin C deficiency [1, 2]. Vitamin C is a reversible reducing agent that acts as an essential electron donor in several biochemical reactions and enzymatic activities such as in collagen synthesis where proline and lysine residues in the collagen structure must be enzymatically hydroxylated using ascorbic acid as an electron donor. The inability to finish this step of collagen synthesis has adverse effects on fibroblast functions, stability of collagen rich soft tissues, stability of small blood vessels, enhancing the risk of bleeding and impaired wound healing. Furthermore, vitamin C, together with vitamin A and vitamin E are antioxidants, protecting cellular systems from the harmful effects of free radicals [1].

The full clinical spectrum of scurvy comprises fatigue, muscle weakness, malaise, arthralgias, loss of appetite, mood changes, peripheral neuropathy, vasomotor instability, musculoskeletal pain due to bleeding into the periosteum or muscles, gingivitis and conjunctivitis with bleeding, receding gums as well as caries [2]. This full clinical picture of scurvy is typically seen, if serum levels of vitamin C fall below 11 μmol/L (normal value >24 μmol/L), but there is sufficient published evidence that symptoms of scurvy start already in the range between 11 and 24 μmol/L [3]. Our patient had symptoms of scurvy along with a significantly decreased serum vitamin C level of 14 μmol/L even though he did not show the full picture of scurvy.

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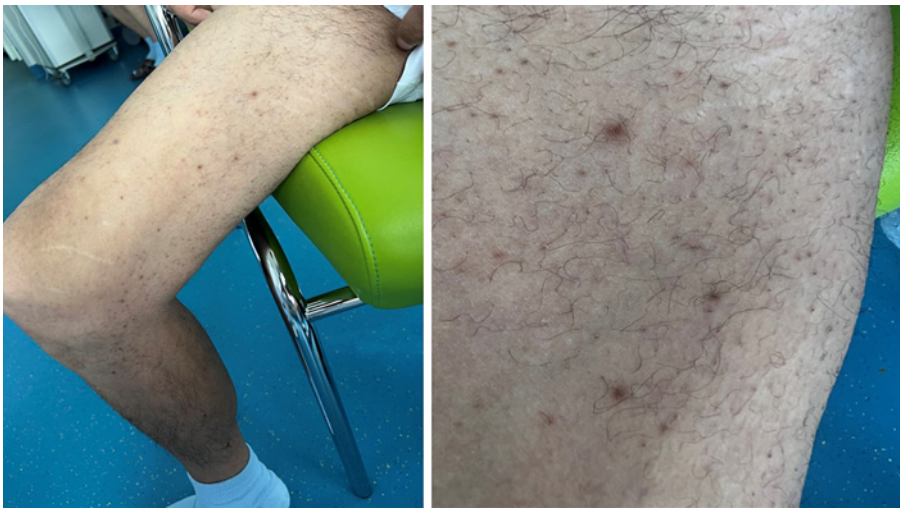

Fig. 2. Multiple livid follicular macules and papules predominantly on the extremities.

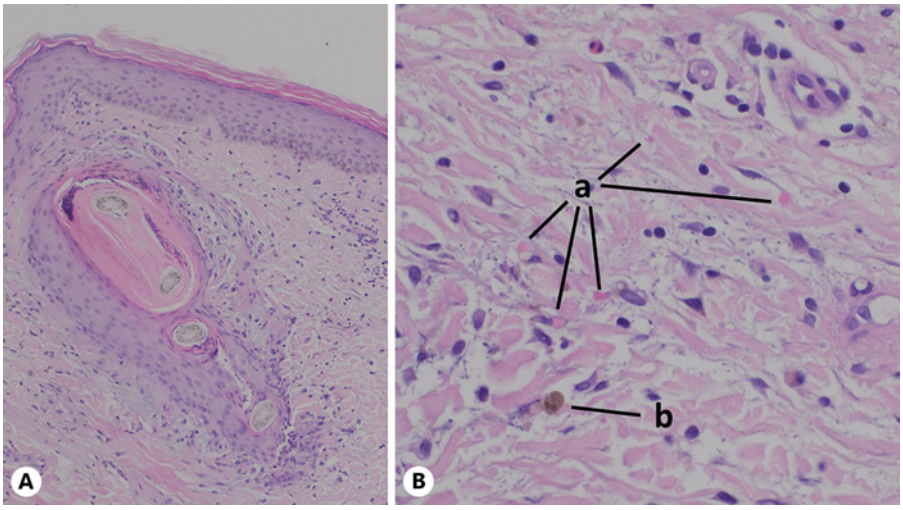

Fig. 3. Skin biopsy revealed follicular hyperkeratosis with coiled, distorted hair shafts (**A**) and in the upper dermis (**B**) perivascular and perifollicular extravasated erythrocytes (**a**) and siderophages (**b**). Hematoxylin and eosin (HE)-staining, ×40 (**A**) and ×100 (**B**) magnification, respectively.

Skin biopsy plays an essential role in the diagnostic work-up of cutaneous bleeding disorders. Histology was able to rule out cutaneous vasculitis and cutaneous vaso-occlusive disease in the context of the previous hepatitis C infection in our patient. Skin histology showed coiled, distorted hair shafts, follicular hyperkeratosis, and perifollicular hemorrhages, all of which are distinct clues for vitamin C deficiency [4]. Dermoscopy was not done in this case since at admission there had not yet been a suspicion of scurvy. However, dermoscopy in scurvy may be another simple and helpful test that shows perifollicular erythematous macules that will not disappear diascopically and together with the presence of coiled hair are the dermoscopic correlates of the characteristic histological findings described above. Patients with vitamin C deficiency and neurological symptoms should also be evaluated for zinc deficiency as synergistic actions between these two occur. In our case, zinc was not measured but administered empirically on admission. Zinc

supplementation alone showed no effect, but vitamin C supplementation later on led to a rapid improvement of symptoms. We therefore assume that the patient's symptoms were caused by vitamin C deficiency alone and not by an unknown zinc deficiency. Especially, if vitamin C levels are decreased but not yet extremely low, thorough clinical skin examination and skin histology are important diagnostic measures to establish the diagnosis of scurvy early and thereby prevent complications such as excessive bleeding, gait instability, falls and accidents.

Vitamin C supplementation is simple, inexpensive and further supports the diagnosis by rapid disappearance of the symptoms. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000538916).

Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Goran Mirkovic contributed significantly to the design of the study, collection of data, analysis of data, and paper writing. Markus Reinhold Mutke and Beda Muehleisen contributed significantly to the design of the study, collection of data, analysis of data, and paper writing.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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