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Case Report

Ascorbic acid deficiency impairs wound healing in surgical patients: Four case reports

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ABSTRACT

Background: Vitamin C or ascorbic acid (AA) is the antiscorbutic factor preventing scurvy. It is essential for collagen synthesis, serving as cofactor in the enzymatic conversion of procollagen into collagen.

Scurvy is regarded as something from the past; however, patients with low or subclinical levels of AA are frequently seen in our hospital. A subclinical deficiency will not often cause the display of the hallmark symptoms of scurvy, but this may lead to an altered collagen synthesis and have major implications for adequate wound healing, such as in the surgical field.

Case summary: AA was measured by HPLC using UV detection (Recipe) in a teaching hospital surgical patient group (n = 180) within a week pre- or post-surgery. Over a period of 21 months we found AA levels below the reference limit (25 $\mu\text{mol/L}$) in 65 out of 180 patients (36%). Four patients described in detail initially showed poor wound healing. Their AA levels were 8, 4, and 19 $\mu\text{mol/L}$ respectively. After starting supplementation (1000 mg/day) a dramatic and fast recovery of extensive and complicated wounds was observed by patients and their clinician. Supplementation was ceased after the wounds were completely healed.

Conclusion: AA deficiency is not uncommon in the hospital population, especially in those at risk. Treating deficient patients with AA leads to swift improvement of the wound healing process post-surgery, thereby reducing the costs of extensive wound treatment and extended stay in hospital.

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1. Introduction

Classically, major complications caused by AA deficiency are seen in scurvy patients; however, patients nowadays often do not display these hallmark characteristics. Individuals suffering from vascular disease, elderly people, pregnant women, smokers and substance abusers, and malnourished people are especially prone to AA deficiency. This is demonstrated by the four cases reported below. These patients were all at increased risk of developing an AA deficiency, which in turn resulted in poor wound healing. Treatment of these patients with AA resulted in a rapid improvement of wound healing.

2. Case report 1

A 59-year-old man underwent an exploratory laprotomy in our hospital for abdominal pain caused by diverticulitis, for which he received appendectomy and sigmoid colectomy. Postoperatively, he

suffered twice from an abdominal wound dehiscence, which was surgically corrected (Fig. 1A), the second time with polyglactin mesh interposition, for which the wound was left open (wound size 30 × 25 cm). Unfortunately, the healing process did not show improvement, despite optimal wound care with alginate dressings (Fig. 1B and C). After 6 weeks with little result the patient was told to take AA supplementation of 1000 mg dd orally. No changes were made in his wound dressing regime. Healthy granulation tissue was seen after 2.5 weeks, and the wound size was reduced to one third of its original size (Fig. 1D and E). 2.5 months after start of AA supplementation the wound was fully closed (Fig. 1F). As a result of this case, we decided to conduct a retrospective study in a group of surgical patients with poor wound healing that had their AA measured. Three additional cases are described in detail below.

3. Case report 2

A 79-year-old woman with an extensive medical history, including asthma, severe chronic obstructive pulmonary disease, degenerative spondylolisthesis, total left and right hip replacement, rheumatoid arthritis, and chronic venous insufficiency (grade IV) was admitted to the Meander Medical Center with severe leg

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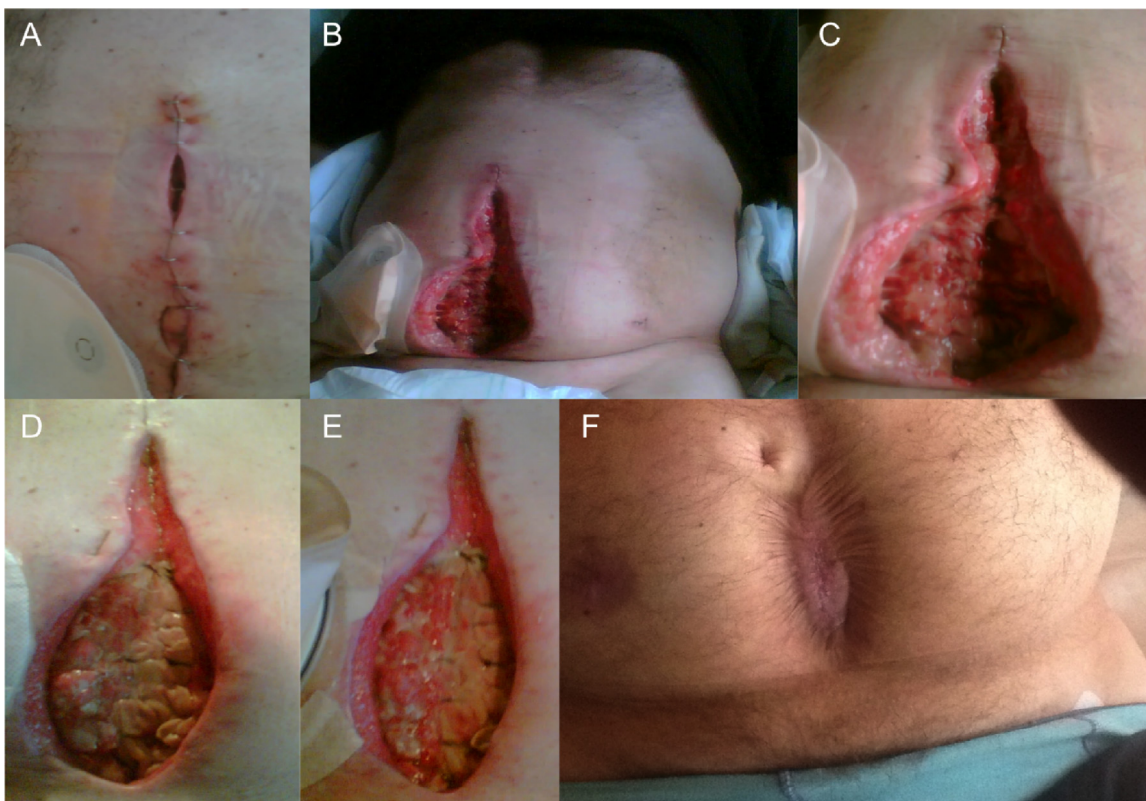


Fig. 1. Post-operation pictures taken by the patient showing an abdominal wound dehiscence and inadequate wound healing (A, B, C), and after ascorbic acid supplementation showing healthy granulation tissue (D, E) and full closure after 2.5 months (F).

ulcers. She underwent a surgical intervention to remove necrotic tissue and her wounds were treated by pinch grafting. Her wounds were dressed post-operatively with Aquacel Ag and dressings were changed when necessary. Unfortunately her post-operative wounds remained ulcerative and showed no progression toward healing. Her treatment was continued with Fluocinonide and Aquacel Ag three times weekly, and her wounds were additionally dressed with foam dressing, and after a month of treatment her wounds seemed to heal accordingly. After two months, however, she returned with a new wound, which was treated with a foam dressing and Cutimed Sorbact. After 9 months of extensive and optimal wound care with disappointing results her vitamin status was measured. Vitamin D (100 nmol/L), B12 (240 pmol/L) en folate (10.5 nmol/L) levels were in the normal range, but her AA level was very low (8 $\mu\text{mol/L}$, reference range 25–85 $\mu\text{mol/L}$). Other laboratory parameters showed a slight normocytic anemia, but no further abnormalities. The patient was immediately started on AA supplementation, 1000 mg a day (effervescent tablet), and after 3 to 4 weeks the patient noticed a significant improvement. After 8 weeks her ulcers were completely healed and supplementation was discontinued.

4. Case report 3

A second case involves a 68-year-old woman, again with an extensive medical history, including Crohn's disease, hypertension, diabetes type 2, cardiovascular disease, and thyroiditis as a result of amiodarone use. She had undergone an ileocecal resection correcting a perforation of the terminal ileum and as a result developed a severe case of peritonitis. Her post-surgery AA level was found to be 4 $\mu\text{mol/L}$; other vitamins measured were active vitamin B12 75 pmol/L (ref. >21 pmol/L), B1 was 179 nmol/L (ref. 88–157 nmol/L), B6 was 83 nmol/L (ref. 35–110 nmol/L), and D3 27 nmol/L (ref.

50–132 nmol/L). Due to her Crohn's disease she had a slightly decreased albumin level (23 g/L, ref. 29–46 g/L), and a history of anemia of the chronic disease. After 2 months she had to undergo another emergency laparotomy because of an anastomotic leakage, resulting in the construction of a loop ileostomy. Surprisingly, a poorly healed laparotomy closure from her previous surgery was observed and the abdominal fascia hardly showed any closure at all. She also suffered from multiple perforations of the transverse colon for which a wedge resection and side-to-side anastomosis was performed. Shortly after, she was started on 2 \times 500 mg AA intravenously during two weeks and 2 \times 500 mg AA orally for two weeks after which no further surgery was needed.

5. Case report 4

The last patient being discussed is a 56-year-old man who was diagnosed with thromboangiitis obliterans (Buerger disease) as a result of nicotine abuse. He suffered from a deep, indolent, and ulcerative wound on the lateral surface of his right ankle (Fontaine stage IV). The wound was ischemic due to arterial insufficiency caused by his disease, and was intensely painful. Furthermore, a wound culture showed the presence of several bacteria (*Staphylococcus aureus*, *Streptococcus dysgalactiae*, *Pseudomonas aeruginosa*, and *Escherichia coli*). Unfortunately, no revascularization surgery was possible, because of far advanced vascular damage to his lower leg arteries. The patient was told to quit smoking and was started on 1 ng/kg/min iloprost (prostacyclin analogue) i.v. therapy for a total of three weeks in order to improve wound healing by relieving ischemic symptoms. In the first week of treatment his laboratory results showed a low AA level of 19 $\mu\text{mol/L}$. Vitamin B12 (202 pmol/L), folic acid (8.4 nmol/L), vitamin D (90 nmol/L), and other laboratory parameters (hemoglobin, platelets, creatinine, CRP) were normal. This

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