Scurvy is one of the earliest recorded diseases in humans, was first described in the Ebers papyrus in 1550 BC. Historically, scurvy is known as an illness affecting sea voyagers. Between 1500 BC and 1800 AD, scurvy killed more sailors than all other diseases and disasters combined. Its successful treatment with oranges and lemons was established by the Scottish surgeon James Lind in one of the first recorded clinical controlled trials, published in 1753. It was not until 1931 that Albert Szent-Györgyi discovered and identified the anti-scorbutic factor in citrus fruits and potatoes. The anti-scorbutic factor was initially called hexuronic acid and was subsequently renamed vitamin C [1].

Vitamin C deficiency is rarely seen today. When it occurs, diagnosis might be difficult as the condition can mimic other disorders. It is crucial to identify the classic signs and symptoms associated with scurvy since it is a fatal but easily curable disease.

We describe the signs and symptoms of a patient with scurvy, and discuss the causes of vitamin C deficiency, the differential diagnosis and the treatment.

**PATIENT DESCRIPTION**

A 43 year old woman was admitted due to right knee pain and recent onset of a rash on the lower limbs. She suffered chronic leg pain that had recently worsened and was accompanied by extensive bruising of the legs. In the preceding 2–3 months she had also experienced increased fatigue. She did not have fever, night sweats, dysphagia, nausea, emesis, dyspnea, or cough. There had been no exposure to insects and no recent travel. She denied any history of trauma. Her family reported that she suffered from an eating disorder since adolescence.

On physical examination, she appeared cachectic with very poor dentition and marked gingival hypertrophy. Examination of the heart, lungs and abdomen was normal. Ecchymosis on the lower extremities and an erythematous rash, not painful or itchy, from the dorsa of the feet to the tops of the thighs was evident. The rash was not raised or excoriated [Figure]. The right knee was swollen and painful but there was full range of passive motion in all joints of the arms and legs. Reflexes were normal, but she had difficulty standing on her feet.

Laboratory test results revealed normocytic anemia with hemoglobin of 8.4 g/dl, hematocrit 25.5% and mean corpuscular volume 79.9 fl. Platelet count was 320,000 µl, prothrombin time 24 seconds, and international normalized ratio 1.09. Serum electrolytes, lactate dehydrogenase, albumin, total protein, renal and liver function tests, as well as ferritin, vitamin B12 and folate levels were all within normal ranges. Anti-nuclear antibody titer, rheumatoid factor, and complement C3 and C4 levels were normal. Tests for perinuclear antineutrophil cytoplasmic antibodies, cytoplasmic ANCA, and cryoglobulinemia were negative. Radiographic studies of the right knee showed metaphyseal irregularities and periosteal reactions along the metaphysis.

The combination of acquired limb pain, non-palpable non-thrombocytopenic purpuric rash and gingival hypertrophy raised several differential diagnoses. Coagulation disorders were ruled out due to the normal platelet count and prothrombin time and partial thromboplastin time values. There were no blasts on blood smear. Since the purpuric rash was not palpable and the serological markers were negative, vasculitis and cryoglobulinemia were ruled out. Because of her symptoms, physical signs and social history, the level of vitamin C was measured. It was almost undetectable at 0.1 mg/dl (normal 0.6–2 mg/dl).

Once the diagnosis of scurvy was established, the patient was started on vitamin C, 500 mg twice a day. After only 3 days of supplementation, she was able to stand up and walk. The ecchymoses and petechiae subsided.

**COMMENT**

Although much decreased in prevalence, scurvy still exists in industrial-
organized societies. The diagnosis of scurvy is generally based on clinical features, dietary history, and the rapid resolution of signs and symptoms after vitamin C supplementation. Laboratory investigations may not be necessary to diagnose scurvy but are useful to confirm complicated cases. A serum level below 0.15 mg/dl is suggestive for scurvy [1].

Many signs and symptoms of vitamin C deficiency are related to its essential role in collagen synthesis. Mature collagen is composed of three polypeptide molecules in a triple helix. The polypeptides lysyl and prolyl use vitamin C as a cofactor for hydroxylation. The absence of hydroxylysyl and hydroxyprolyl residues renders the polypeptide unstable and unable to self-assemble into rigid triple helices [1]. This defect in collagen results in blood vessel fragility and poor wound healing, leading to the most common symptoms, bruising and pedal edema. Systemic symptoms include lassitude and fatigue (as was noted in this case), and neurologic symptoms such as depression and vasomotor instability. Gingival swelling, hemorrhage, and bone disease due to subperiosteal bleeding are also common [1,2].

More than 90% of the vitamin C in western diets derives from fruits and vegetables. A single orange contains 50 mg of vitamin C. Dietary surveys indicate that the average daily vitamin C intake in the United States is about 75–85 mg in adults. Opinions regarding the recommended daily intake differ, with values ranging from 30 to 200 mg. The United Kingdom and the World Health Organization suggestion of 30 mg rests on the belief that an amount three times the minimum necessary to prevent scurvy should provide sufficient safeguards for the population. The minimal daily requirement of vitamin C to prevent scurvy, based on the British experiments, is 10 mg or less [3]. The treatment of scurvy involves increased vitamin C intake. Correcting the deficit and replenishing body stores requires 100 mg three times a day [4].

Olmedo et al. [5] conducted a retrospective record review to identify patients with scurvy treated between 1976 and 2003 at the Mayo Clinic. Eight of the 12 patients were women and the average age was 48 years. Follow-up was available for six who were treated with vitamin C supplementation; five showed complete resolution of symptoms. The most common causes were concomitant gastrointestinal disease (e.g., colitis), poor dentition, food faddism, and alcoholism. Cancer patients on chemotherapy who have increased nausea and diarrhea are also at risk, as are patients on hemodialysis since vitamin C is not reabsorbed by the kidneys. Psychiatric disorders (e.g., depression, schizophrenia, or anorexia as our patient had) have also been recognized as putting patients at risk for insufficient vitamin C intake [4].

Scurvy is rarely seen in modern times and is often underdiagnosed. Nevertheless, its signs and symptoms should be recognized since it is a fatal but curable disease.

References

**Capsule**

**CAMP promotes axon formation**

How do neurons initiate one axon and lots of dendrites? Using an *in vitro* assay involving stripes of cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP), Shelly and co-workers show that an increase in cAMP initiates axon formation while an increase in cGMP initiates dendrites. Moreover, cAMP and cGMP reciprocally inhibit each other via the activation of specific phosphodiesterases, as well as protein kinase A and protein kinase G. Finally, long-range self-inhibition of cAMP can explain why only one axon, yet multiple dendrites, is initiated in single hippocampal neurons in culture. Locally increasing cAMP in one neurite causes long-range cAMP reduction in the rest of the neurites, accompanied by corresponding reciprocal changes in cGMP.

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"The highest result of education is tolerance"

Helen Keller (1880-1968), American author, political activist and lecturer. She was the first deaf-blind person to earn a Bachelor of Arts degree. The story of how Keller’s teacher, Anne Sullivan, broke through the isolation imposed by a near complete lack of language, allowing the girl to blossom as she learned to communicate, has become known worldwide through the dramatic depictions of the play and film *The Miracle Worker*