Ascorbic Acid Deficiency: A Case Report

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ABSTRACT

Scurvy is well known since ancient times, but it is rarely seen in the developed world today owing to the discovery of its link to the dietary deficiency of ascorbic acid. It is very uncommon in the pediatric population, and is usually seen in children with severely restricted diet attributable to psychiatric or developmental disturbances. The condition presents itself by the formation of perifollicular petechiae and bruising, gingival inflammation and bleeding, and, in children, bone disease. We report a case of scurvy in a 10-year-old developmentally delayed boy who had a diet markedly deficient in vitamin C resulting from extremely limited food choices. He presented with debilitating bone pain, inflammatory gingival disease, and perifollicular hyperkeratosis. The diagnosis was made based on clinical and radiographic findings. The importance of diet history is emphasized. We present this case with the aim to help the clinician identify scurvy and implement treatment for a potentially fatal but easily curable disease.

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Scurvy, which is considered an inborn error of metabolism, has received OMIM (Online Mendelian Inheritance in Man) no. 240400. It gets its name from the Latin word "scorbutus." It is synonymous with scorbutus, hypoascorbemia, Moeller's disease, and Cheadle's disease. In infants, scurvy is sometimes referred to as Barlow's disease or Moeller-Barlow disease, named after Sir Thomas Barlow (1845-1945), a British physician who described it.[1]

Scurvy was described as early as 460 to 380 B.C. by Hippocrates. It was a common ailment aboard European seagoing ships in the early days of world exploration and was a serious problem on long voyages. Among the first descriptions of scurvy was that from a voyage by Portuguese sailor Vasco da Gama, who lost no fewer than 100 of his original crew of 160 to scurvy. This was attributed to the lack of fresh fruits and vegetables onboard. The first controlled clinical trials were reported in 1753 by James Lind, a Scottish surgeon in the British Royal Navy who first proved scurvy could be treated with citrus fruits like lemon and lime in his book *A Treatise of the Scurvy*.[2]

Humans, other primates, and guinea pigs are among the exceptional species who are unable to synthesize L-ascorbic acid from D-glucose due to a lack of L-gulono-gamma-lactone oxidase in the liver, rendering its ingestion from exogenous supplements or diet necessary. This enzyme is responsible for catalyzing the last step of L-ascorbic acid biosynthesis in many higher animals.[3]

Since the discovery of ascorbic acid, the incidence of scurvy has declined. Due to the varying dietary patterns, however, isolated cases continue to occur. Populations at

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risk include single adults and the elderly with deficient diets.[4-8] Scurvy also has been reported in pediatric patients with dietary deficiency and end stage organ disease.[9] This disease is extremely rare in the pediatric population and usually is seen in children with severely restricted diets attributable to psychiatric or developmental problems. Scurvy is uncommon worldwide, and most physicians do not consider this disease process in differential diagnoses. Thus, the purpose of this report was to help the practitioner identify and treat scurvy.

CASE REPORT

A 10-year-old boy was referred by a local physician to the Department of Pediatric and Preventive Dentistry, P.M.N.M. Dental College and Hospital, Bagalkot, Karnataka, India, for clinical evaluation of the oral cavity (Figure 1). The child's mentally handicapped status compromised his ability to provide useful historical information. His past medical history was remarkable for mental retardation, moderate developmental delay, and a seizure disorder. He had suffered from seizure episodes since soon after birth, which continued for 4 years. The child was hospitalized 3 years earlier with hemolytic anemia and had received a blood transfusion for the same.

The parents reported a recent 10-day history of progressive swelling in the upper left region of the mouth with spontaneous bleeding, which caused the child to refuse to eat. They also provided a history of fatigue, leg and knee pain, apparent light-headedness, generalized weakness and refusal to walk. Additionally, the parents commented on the patient's apparent decline in function during the past 10 days before coming to the department. A similar swelling in the same area was observed by them 1 year prior, for which they visited a local physician, who diagnosed the patient with aplastic anemia. He was prescribed multivitamins, after which the swelling subsided. The patient's diet had limited varieties of food due to specific preferences and was devoid of fresh fruits and vegetables.

On a review of symptoms, no abnormality was detected. He had no apparent joint swelling, but there was decreased range of motion of his knees bilaterally, which were tender on palpation. His vital signs coincided with age appropriate baseline values. An eye examination revealed pale conjunctiva and upslanting palpabral fissures, and his skin examination showed perifollicular hyperkeratosis of the lower extremities (Figure 2A).

On oral examination, we observed that the patient had a permanent dentition. Atrophy of papillae on his tongue gave it a "bald appearance." Generalized gingivitis with spontaneous hemorrhage was present. Clinically, the gingiva on the buccal and palatal aspects of the maxillary left first premolar, second premolar, and first molar showed severe inflammation and covered the occlusal tooth surfaces (Figure 3). It was soft, red, and nodular.

Laboratory studies performed at the time of examination disclosed the following values: hemoglobin 6.9 g/dL and hemotocrit 21.7%, with a mean corpuscular volume of 103.3 μm, mean corpuscular hemoglobin 32.9 pg, and mean corpuscular hemoglobin concentration of 31.8 g/dL. Prothrombin time, activated partial thromboplastin time, Ivy bleeding time, and platelet count were normal. His vitamin C level was requested, but since the result would not be available for several

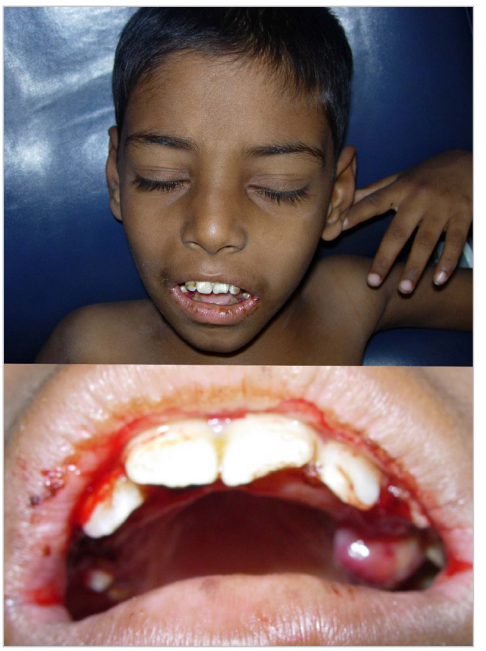

Figure 1. Facial photograph of the child as he presented to the department.

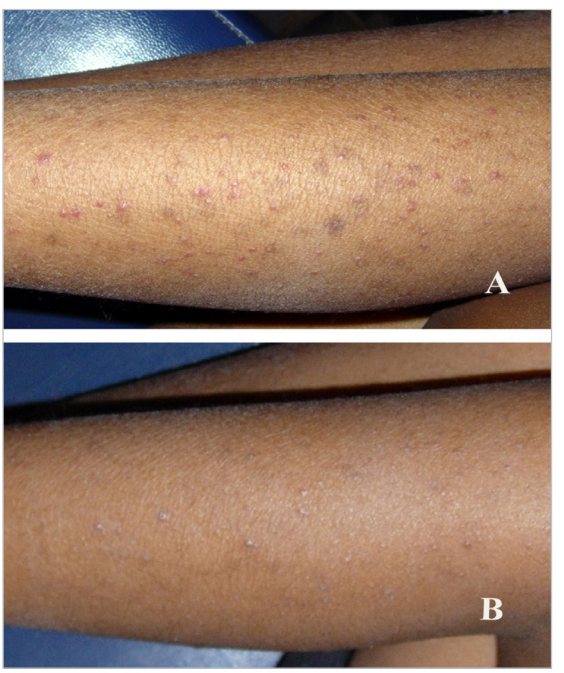

Figure 2. Skin of the lower extremities showing perifollicular hyperkeratotic lesions (A) before vitamin C therapy and (B) after vitamin C therapy.

days, we proceeded with other examinations. Radiographs of the knees showed bone demineralization, revealing a fine white line (Winberger ring) outlining the epiphysis and white line of Frankel (Figure 4).

The clinical findings of perifollicular hyperkeratosis, joint pain, and gingival erythema all were consistent with the pathophysiologic effects of scurvy. We reviewed the patient's history with the parents and asked them to record a 7-day diet diary. From the dietary analysis, we concluded that his diet consisted exclusively of rice and pulses (leguminous crops harvested for their dry grain) in a semisolid form with yogurt occasionally. No vitamin supplements, fresh fruits, or vegetables were recorded from his diet. Thus, we added scurvy to the differential diagnosis. An extensive evaluation excluded trauma, coagulopathies, neoplasia, and vasculitides. An oral regimen of 200 mg vitamin C twice daily was initiated.

The patient's clinical condition improved gradually. Gingival bleeding stopped 1 week after vitamin C supplementation, and there was an improvement in his general health. An increase in his energy and activity levels was noted. There also was a significant improvement and almost a full range of motion in his knees. To correct the anterior open bite and tongue-thrusting habit, a myofunctional trainer was provided. Subsequent follow-up examinations noted a disappearance of symptoms, and the patient remained well (Figures 2B and 5).

DISCUSSION

Human beings lack the ability to convert glucose to ascorbic acid (vitamin C) via gulonolactone oxidase. This metabolic defect is said to have occurred during evolution. This function was lost because of adequate dietary intake of vitamin C. The accumulation of random mutations in the gene for the relevant enzyme might have destroyed the functional capacity of the enzyme over time, ultimately removing the constraint of enzyme selection.[3] The population at risk for scurvy includes: elderly individuals; alcoholics; cigarette smokers; food faddists; pregnant and lactating women; infants fed on boiled evaporated milk; type I diabetes patients; hemodialysis and peritoneal dialysis patients; patients with diseases of the small intestine; and children with dietary restrictions stemming from psychiatric or developmental disorders such as the child described in the present report.

In 1927, a Hungarian scientist Albert Szent Gyorgyi isolated a chemical, which was found in high concentrations in the adrenal cortex, oranges, and cabbages, and termed it hexuronic acid. Its effectiveness in preventing scurvy was identified by King and Waugh in 1932. The following year, Szent Gyorgyi and Norman Haworh, who delineated its precise chemical structure, renamed it "ascorbic acid," meaning a substance effective against scurvy.[10,11] It is a stable, odorless, water-soluble white solid that is readily absorbed from the gastrointestinal tract and excreted by the kidneys into the urine. The total vitamin C body pool is 20 mg/kg or approximately 1,500 mg. The average serum half-life of vitamin C is 16 to 20 days. An obligatory dietary source of ascorbic acid is needed to maintain body stores in humans, other primates,and guinea pigs. It serves as an enzyme or cofactor for many biochemical reactions, the best being collagen cross-linking. Production of collagen by the fibroblast requires vitamin C as a coenzyme for the proper hydroxylation of proline and lysine residues of procollagen.

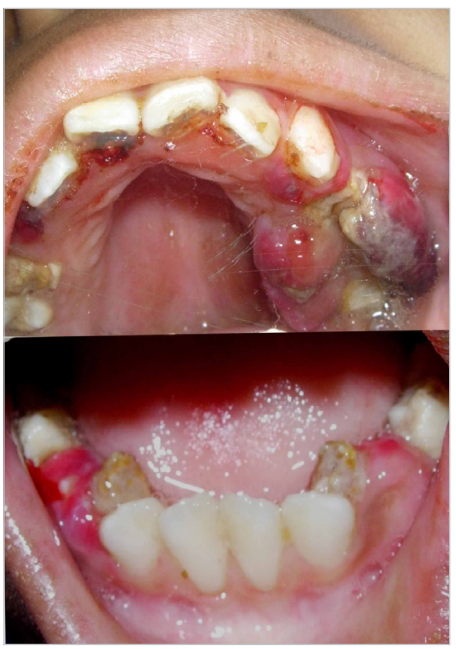

Figure 3. Occlusal view of the gingival enlargement and bleeding in the maxillary and mandibular area.

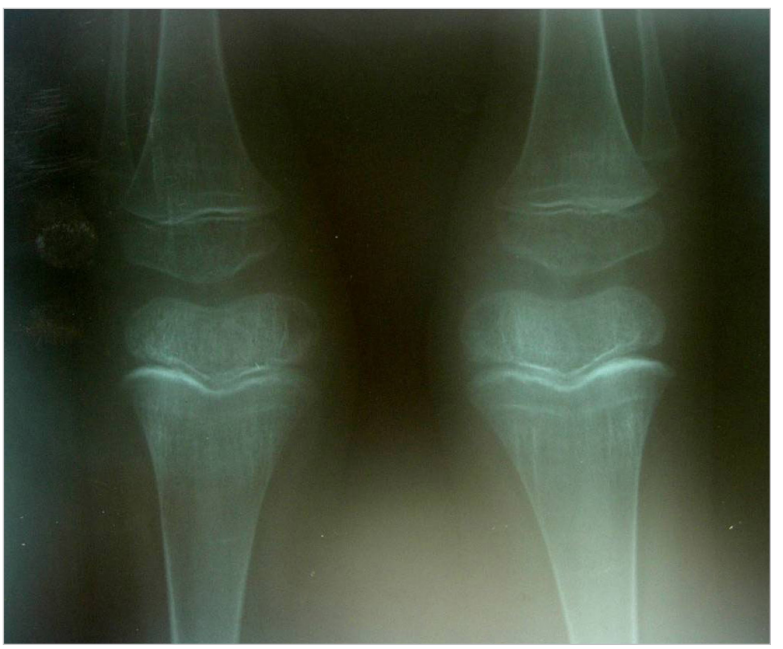

Figure 4. Anteroposterior radiograph of the knees showing a dense white line at the proximal end of the tibial metaphysis, with adjacent lucent band (white line of Frankel).

In the absence of sufficient vitamin C levels, collagen is not hydroxylated, which creates an unstable, uncrosslinked, nonhelical configuration. Such collagen lacks tensile strength and is susceptible to enzymatic degradation. Vitamin C also is required for carnitine biosynthesis in muscle, neurotransmitter synthesis, including dopamine and seratonin, cholesterol degradation and iron absorption. It has been shown to have immune-enhancing, anticariogenic, and antioxidant effects.

Clinical manifestations are attributable to the depletion of pericapillary collagen.[12] Complete cessation of oral intake of vitamin C produces clinical signs of deficiency within 1 to 3 weeks. The earliest symptoms of vitamin C deficiency include fatigue and anemia. Other manifestations include ecchymoses, bleeding gums, corkscrew hairs, perifollicular hyperkeratosis, myalgias, arthralgia, and death. Iron deficiency anemia is common and may be secondary to a combination of bleeding or other dietary deficiencies and decreased absorption.

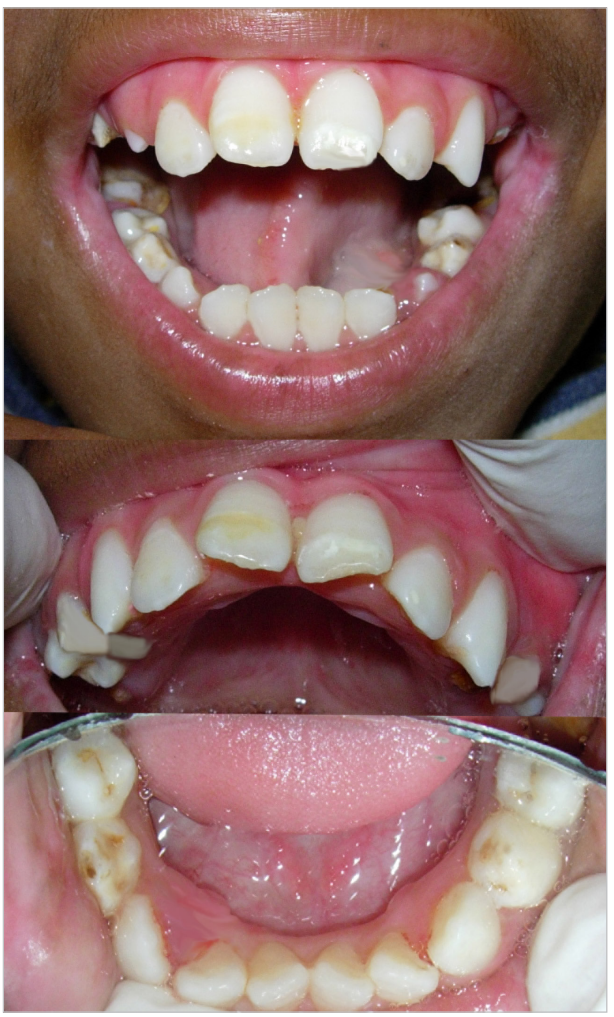

Figure 5. Photograph demonstrating complete resolution of the gingival enlargement and bleeding 1 month after treatment with vitamin C.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of scurvy includes various abnormalities like hematological disorders, medication side effects (antiplatelet agents, anticoagulants, nonsteroidal anti-inflammatory drugs), infections, collagen vascular disorders, ulcerative gingivitis, vitamin deficiencies (vitamin K and D), and trauma to the legs and joints. An appropriate history—together with physical examination, basic laboratory examination, and radiographs—aids in reaching a final diagnosis. Local physicians failed to diagnose this condition, which led to the repeated recurrence of the same. Systemic manifestations, oral manifestations, and a detailed diet history helped us to arrive at a provisional diagnosis of scurvy.

A low level of plasma vitamin C would have been specific in this condition, but the results would be normal if there was a recent ascorbic acid intake—making it an insensitive diagnostic test for vitamin C deficiency. Measuring vitamin C levels in buffy-coated leukocytes better reflects body stores,[13] but this is technically more difficult and was not readily available in our case. Another indicator of measuring body stores is the measure of urinary excretion after parental ascorbic acid infusion. After 100 mg of an intravenous dose of vitamin C, 80% should be excreted within 5 hours in the setting of adequate body stores.[14,15] Finally, the best evidence of the presence of scurvy is the resolution of the manifestations of the disease after ascorbic acid treatment.

No single replacement regimen for vitamin C deficiency has been published in the literature. The daily intake needed to prevent scurvy is approximately 10 mg. The daily allowance recommended by health authorities for an adult ranges from 20 mg to 75 mg. The Food and Nutrition Board of the U.S. National Research Council recommends values ranging from 35 mg for an infant to 60 mg for a 70 kg man.[16] The requirement increases to 70 mg/day during pregnancy and to 90 to 95 mg/day during lactation. The requirements may also increase in smokers, patients undergoing hemodialysis, and in cases of infection and trauma. Individual needs may vary, however, so the biochemical individuality also should be considered. Vitamin C recommendations vary for the treatment of acute scurvy. An intake of 200mg/day results in marked improvement in symptoms within a few days.[17] Taking 1 gm/day for the first 3 to 5 days followed by 300 to 500 mg/day for at least 1 week also has been suggested.[18,19] Appropriate dietary adjustments with an emphasis on an antiscorbutic diet consisting of citrus fruits, green vegetables, tomatoes, and potatoes also should be implemented.

A diagnosis of scurvy often can be overlooked because it is rarely encountered in present day society. Many people have dietary or medical factors that place them at risk for vitamin C deficiency. A nutritional

history is important, especially in the elderly, institutionalized, those with eating disorders, or psychiatric patient. It is important for clinicians to include scurvy in the differential diagnosis of patients who present with purpuric lesions, joint pains, and bleeding gums. Appropriate diagnosis and treatment can be life-saving, even when a patient presents in the most advanced stage. This case emphasizes the importance of nutritional screening as a part of every child's general health care, illustrates the necessity of identifying the population at high risk, and recognizes the clear and classic signs and symptoms associated with scurvy. If such a case is diagnosed successfully, it can prevent expensive and unnecessary medical tests and be treated simply.

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