Perifollicular hemorrhagic lesions and broken twisted hairs on legs

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Abstract

A 17-year-old girl presented with multiple perifollicular hemorrhagic lesions on legs for 2 weeks. There was history of intermittent gum bleeding for last 2 months. Clinical examination revealed follicular keratosis and broken twisted hair (corkscrew hair), in addition to hemorrhagic lesions. Perifollicular hemorrhagic lesions and corkscrew hair are virtually pathognomonic for scurvy. When specifically asked, mother revealed that the girl was on self-imposed diet with almost no citrus fruits. Based on history and clinical findings, diagnosis of scurvy was made. The response to vitamin C supplementation was very good and all the lesions disappeared within one month. Scurvy has been reported in increasing numbers in recent literature; hence, recognition of scurvy is essential to avoid many serious complications including internal bleeding and even, death.

Key words
Scurvy, perifollicular hemorrhage, corkscrew hairs, bleeding gums, vitamin C.

Introduction

Scurvy has been known to mankind since ages; link with vitamin C was not established until in 1747 Sir James Lind established the fact that oranges and lemons were effective in curing scurvy. Later in 1931, Albert Szent-Gyorgyi identified the active substance as ascorbic acid, also known as vitamin C. Since the recognition of the role of vitamin C in preventing and treating scurvy, it has been considered as a disease of past, prevalent among sailors and soldiers with limited access to fresh citrus fruits. However, recognition of many new cases and identification of several risk factors (food faddists, chemotherapy patients, anorexia nervosa, major depression disorder, alcohol abuse, etc.), not so uncommon in the modern world, have renewed interest in scurvy.

Case report

A 17-year-old girl presented with asymptomatic red eruption on legs for 2 weeks. The lesions started all of a sudden on legs and had been increasing in number. There was history of intermittent gum bleeding for the last 2 months. Rest of the history was non-contributory and no other family member was suffering from similar disease. On examination, multiple perifollicular hemorrhagic lesions were found on both lower limbs (Figure 1). Most of them were blanchable on diascopy; however, few of them were brownish and were non-blanchable. Apart from hemorrhagic lesions, follicular keratosis was noted and hair was twisted and fragmented (Figure 1, marked with arrow). Gums, at places, were swollen and blood was noted at its margin. Rest of the mucocutaneous examination was unremarkable. Routine blood investigations including haemoglobin, erythrocyte sedimentation rate, and platelet count as well as bleeding time and clotting time were within normal limits. Considering
clinical presentation and normal laboratory investigations, clinical diagnosis of scurvy was made. On enquiry, mother revealed that girl was on self-imposed diet that contained almost no citrus fruits. She was asked to take plenty of citrus fruits and was given oral vitamin C supplementation. There was complete clinical recovery within a month.

**Discussion**

Skin frequently bears the brunt of deficiency of various nutrients and often has telltale signs, specific enough to allow a diagnosis. The characteristic cutaneous findings of scurvy are follicular keratotic papules and perifollicular hemorrhages, purpura, and ecchymoses.\(^1\)\(^2\) These are seen most commonly on the legs and buttocks where hydrostatic pressure is the greatest.\(^1\) Another specific finding is ‘corkscrew hairs’- hair on legs is twisted like corkscrews, and is sometimes fragmented.\(^2\) Many other manifestations result from vessel wall fragility and include splinter hemorrhages in nails, gum bleeding, painful hemarthroses, subperiosteal hemorrhage, subconjunctival hemorrhage, bleeding within the optic nerve sheath, bleeding into the periorbital area, eyelids, and retrobulbar space, hematuria, hematochezia, melena, and rarely, fatal bleeding into the myocardium and pericardial space.\(^1\)\(^2\) Rumpel-Leede sign (petechial hemorrhages occurring below the site of tourniquet application) may be elicited.\(^8\)

Changes in the gums are most noticeable after teeth have erupted and are manifested as bluish purple, spongy swellings of the mucous membrane, especially over the upper incisors.\(^1\) Extracutaneous findings include scurbutic rosary, fractures, pain and tenderness of bones, pseudoparalysis, and normochromic normocytic anemia.\(^1\)\(^7\) In advanced cases, hypotension and high-output cardiac failure may be seen.\(^1\) Neuropsychiatric manifestations may be seen and include depression, lethargy, Irritability, emotional changes, and convulsions.\(^2\) Scurvy can occur at any age; the incidence of scurvy peaks in children aged 6-12 months as well as in elderly populations.\(^1\)

Infantile scurvy, also known as Barlow’s disease, Moeller's disease and Cheadle's disease, usually presents after weaning and is different from adult scurvy in having prominent musculoskeletal system involvement. Initial manifestations are vague and include irritability, decreased appetite, fever, and delayed development. As the disease progresses, generalized tenderness due to subperiosteal hemorrhage develops and child lies still with little movement and legs in ‘frog leg’ position. Swelling may be noted.
along the shafts of long bones. Mucocutaneous findings are similar to adult scurvy.\(^5\)

Humans like other primates are unable to synthesize L-ascorbic acid (vitamin C); therefore, they require it in their diet. Foods high in vitamin C include citrus fruits (grapefruit, lemon, berries, cantaloupe), and vegetables (broccoli, spinach, green peppers, tomatoes, potatoes, cauliflower, and cabbage). This nutrient is absorbed by active transport in the ileum. Approximately 85% of the ingested vitamin is absorbed, but the transport mechanism can become saturated. Recommended daily dietary allowance of vitamin C is 30–40 mg for infants, 45–60 mg for children and adults, 70 mg for pregnant women and 90-95 mg for lactating mothers. Ascorbic acid is metabolized in the liver by oxidation and sulfation. The renal threshold for excretion by the kidney in urine is approximately 1.4 mg/100 mL plasma. Excess amounts of ascorbic acid are excreted unchanged or as metabolites. The total body pool of vitamin C is approximately 1500 mg. The absorbed vitamin is found ubiquitously in body tissues, with the highest concentrations in glandular tissue and the lowest concentrations in muscle and stored fat. Scurvy occurs after vitamin C has been eliminated from the diet for at least 3 months and when the body pool falls below 350 mg.\(^1,2\)

One study has identified a genetic polymorphism of the human plasma protein haptoglobin, Hp 2 associated with scurvy. It may represent an important non-nutritional modifying factor in the pathogenesis of scurvy. Hp 2-2 polymers are less efficient inhibitors of hemoglobin-driven oxidative stress, leading to ascorbic acid depletion. The Hp 2-2 phenotype is present in 35% of whites and 50% of South Asians and East Asians.\(^9\) The full clinical implications of this finding are yet to be recognized.

Though vitamin C has diverse biological functions, yet it is functionally most relevant for the triple-helix formation of collagen. Therefore, a vitamin C deficiency results in impaired collagen synthesis. The typical pathologic manifestations of vitamin C deficiency, including poor wound healing, are noted in collagen-containing tissues and organs, such as skin, cartilage, dentine, osteoid, and capillary blood vessels. Increased blood vessels fragility accounts for hemorrhage, a hallmark feature of scurvy and it can occur in any organ. Hair follicles are one of the common sites of cutaneous bleeding. Hair follicles of lower limbs and buttock are preferentially involved as hydrostatic pressure is the greatest at these sites. Pathologic changes of bones affect the rate of growth; therefore, the bone changes are often observed only in infants during periods of rapid bone growth. Apart from collagen synthesis, vitamin C has an important role in the metabolism of tyrosine and cholesterol and the synthesis of carnitine, neurotransmitters (e.g. norepinephrine), peptide hormones, corticosteroids, and aldosterone. It also affects hematopoiesis by enhancing the absorption of iron from the small intestine by reducing dietary iron from the ferric form to the ferrous form. It is also necessary to convert folic acid to its active metabolite, folinic acid. Impaired iron absorption and less conversion of folic acid into its active metabolite may account for anemia, a frequent finding in scurvy. It is also required for the disulfide bonding of hair. This may explain ‘corkscrew hairs’ and alopecia.\(^1,2,6\)

The most important cause is reduced dietary intake. It includes babies who are fed only cow’s milk during the first year of life, food faddists, widowers, those suffering from anorexia nervosa and anorexia from other diseases such as acquired immunodeficiency syndrome (AIDS) or cancer, individuals with major depression disorder, and schizophrenics. Economically deprived persons and refugees also are susceptible to develop scurvy. People with disease of the small intestine such as
Crohn, Whipple, and celiac disease may have vitamin C deficiency, as vitamin C is absorbed in the small intestine. Another important risk group includes persons with increased demand for vitamin C and they include pregnant and lactating women, those with thyrotoxicosis, type 1 diabetes and those on hemodialysis and peritoneal dialysis. Alcohol abuse, tobacco abuse, and individuals with iron overload disorders (hemochromatosis, thalassemia etc) are other risk factors.1,2,6,7

The list of differential diagnosis is exhaustive and some important ones include hypersensitivity vasculitis (leukocytoclastic vasculitis), Henoch-Schönlein purpura, clotting factor deficiencies, disseminated intravascular coagulation, hematologic malignancies (e.g. acute lymphoblastic leukemia), necrotizing gingivitis, platelet dysfunction disorders (e.g. immune thrombocytopenic purpura), senile purpura in old age, and vitamin D deficiency and physical abuse in a child.12

The diagnosis is mainly clinical. Plasma ascorbic acid level may help in establishing the diagnosis, but this level tends to reflect the recent dietary intake rather than the actual tissue levels of vitamin C. Therefore, normal or increased levels do not rule out the diagnosis, but a low level of serum ascorbic acid is diagnostic. Scurvy generally occurs at levels less than 0.1 mg/dl; while a fasting level greater than 0.6 mg/dl rules out scurvy. The level of ascorbic acid in leukocytes more accurately correlates to tissue stores compared with serum levels. A level greater than 15 mg/dl reflects a state of nutritional adequacy, whereas a level of 0-7 mg/dl is an indicator of deficiency. Radiographic findings in infantile scurvy are diagnostic. The knee joint, wrist, and sternal ends of the ribs are typical sites of involvement. Osteoporosis of long bones occurs and they develop a ground-glass appearance. The zone of provisional calcification becomes dense and widened (white line of Fränkel). The epiphysis also shows cortical thinning and the ground-glass appearance. Metaphyseal spurs or marginal fractures (Pelkan spur), a transverse band of radiolucency in the metaphysis, subjacent to the zone of provisional calcification (scurvy line or Trümmerfeld zone), ring of increased density surrounding the epiphysis (Wimberger ring); and periosteal elevation (due to subperiosteal hemorrhage) are other important findings. As scurvy becomes advanced, a zone of rarefaction occurs at the metaphysis under the white line of Fränkel. This zone of rarefaction typically involves the lateral aspects, resulting in triangular defects called the corner sign of Park. Subperiosteal hemorrhages organize and later become calcified. Histopathology is nonspecific; nonetheless they are helpful in excluding differentials. Noninflammatory perivascular extravasation of red cells and deposition of hemosiderin near hair follicles with intrafollicular keratotic plugs and coiled hair are the usual findings. The best confirmation of the diagnosis of scurvy remains its resolution following vitamin C administration. With proper treatment, bleeding stops within 24 hours, and perifollicular petechiae resolve in 2 weeks.1,2,5,6

Ensuring adequate vitamin C replenishment with vitamin C rich diets (orange juice) and oral ascorbic acid is mainstay of therapy. Ascorbic acid is usually given at a dose of 100 mg 3-5 times a day until total of 4 g is reached, and then it should be decreased to 100 mg daily. Alternatively, it may be taken at 1 g/d for the first 3-5 days followed by 300-500 mg/d for 1 week. Then, the recommended daily allowance is resumed. Divided doses are preferred as intestinal absorption is limited to 100 mg at one time. Parenteral doses may be necessary in those with gastrointestinal malabsorption. Identifying and treating comorbid nutritional deficiencies (e.g. iron deficiency, iron overload disorders, and vitamin D deficiency) is also important in the treatment of scurvy.
deficiency anemia, folate deficiency, other vitamin deficiencies) and treatment of various complications are integral parts of management. Caution is exercised not to use large doses of vitamin C, more than 1 g/d, as it may increase the risk of kidney stones, particularly oxalate stones.\textsuperscript{1,2,6}

Lethargy, fatigue, and hemorrhagic manifestations associated with scurvy incapacitated or killed more people than enemy action in old times.\textsuperscript{2} However, if the condition is identified and treated adequately with oral vitamin C, bleeding and sore gums heal in 2-3 days and ecchymoses heal within 2 weeks and various other complications can be avoided. Although it is a multi-system disease, initial cutaneous findings are specific enough to make a diagnosis. Scurvy is not a disease of the past as recently scurvy in AIDS\textsuperscript{10} and anorexia nervosa\textsuperscript{11} patients have been reported. So physicians should have a high index of suspicion and look for cutaneous signs in patients presenting with different bleeding manifestations, especially in predisposed individuals.

We considered leukocytoclastic vasculitis, Henoch-Schönlein purpura and scurvy as differential diagnoses. Absence of history of infection or drug intake and no palpable lesions were against the diagnosis of leukocytoclastic vasculitis clinically. Absence of history of abdominal pain, melena, arthralgia and of palpable purpura on clinical examination were against the clinical diagnosis of Henoch-Schönlein purpura. History of self-imposed diet with almost no citrus fruits, bleeding gums, perifollicular hemorrhagic lesions, corkscrew hair and normal laboratory findings were in favour of clinical diagnosis of scurvy. Radiological evaluation was not done as it was not of diagnostic importance in our patient aged 17 years. Serum ascorbic acid estimation was not done as it was not available in our institute. However, complete clinical recovery with vitamin C supplementation confirms the diagnosis of scurvy.

References