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Case Report

Clinical, laboratory, radiologic and ex juvantibus diagnosis of pediatric scurvy: A case report

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Abstract This case report highlighted diagnosis of pediatric scurvy from clinical, laboratory, radiologic examination and excellent response after vitamin C supplementation. A 3-years-old boy presented with painful edematous knees and feet and pseudoparalysis for 2 months, palpable perifollicular petechiae and corkscrew hairs on legs for 11 days and petechiae on feet and edematous easily-bleeding gums for 3 days. His diet lacked fruits and vegetables. Laboratory investigations showed anemia, elevated erythrocyte sedimentation rate, decreased iron and hematuria. Plain radiograph of knees showed osteopenia and joint effusion. Initial diagnosis made was cutaneous vasculitis. Complaints persisted despite treatment with ibuprofen and prednisone, but improved rapidly after vitamin C supplementation. Histopathology of skin lesion showed no vasculitis. Final diagnosis of scurvy was made. Vitamin C supplementation was continued which led to resolution and no recurrence of signs and symptoms. Prominent musculoskeletal findings and vasculitis-like skin lesions often cause misdiagnosis of pediatric scurvy. Perifollicular petechiae, corkscrew hairs, gingival edema, and dietary history are clues for scurvy. Diagnosis of scurvy can be established by clinical and supporting examination, or in ex juvantibus, when ascorbic acid level measurement is unavailable.

Key words
Scurvy, vitamin C, musculoskeletal, ex juvantibus, human & health.

Introduction

Scurvy is a disorder of vitamin C deficiency which is uncommon among children. Scurvy has nonspecific initial manifestations of mild fever, decreased appetite and irritability, which are followed by dermatologic and musculoskeletal complaints.[1,2] Dermatological manifestation of scurvy include follicular hyperkeratosis, corkscrew hair, skin and mucosal bleeding. Musculoskeletal features, such as arthralgia, joint swelling and pseudoparalysis, are more prominent and noticeable than dermatological findings in pediatric scurvy. Thus, pediatric scurvy is often misdiagnosed as rheumatological disease or bone tumors.[1,3] Gold standard confirmatory test for scurvy is ascorbic acid level determination.3 Because this examination is not always available, diagnosis of scurvy can also be established by clinical, laboratory or radiology examination or ex juvantibus.[2,4]

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Case report

A 3-years-old boy was referred to Dermatology and Venereology Department as a suspected

case of juvenile idiopathic arthritis with differential diagnosis of scurvy with presenting complaint of asymptomatic red bumps on both legs for 11 days. Illness started two months before consultation, with decreased appetite along with swollen and painful knees and feet. The swelling and pain gradually increased in severity and caused the patient to limp and later crawl. One month before consultation, patient eventually refused to move both legs. Three weeks before consultation, patient was admitted at Pediatric Ward as a suspected case of juvenile idiopathic arthritis, anemia and pulmonary hypertension. He was treated with ibuprofen, sildenafil and transfusion of packed-red cells but symptoms persisted. Eleven days before consultation, nonpruritic and painless red bumps were noted on both legs. Three days before consultation, he developed red spots on both feet along with swollen and easily bleeding gums. Treatment was continued but lesions and symptoms persisted. Review of the systems revealed absence of fever, sore throat, abdominal pain, bloody urine or feces, dyspnea, epistaxis, bruising and hair fall. Past and family medical history was unremarkable. Dietary history revealed that patient only consumed rice, meat and water, but did not consume any fruits, vegetables, juices or vitamins.

Physical examination showed normal vital signs and body weight of 20 kg. Patient looked in pain when the knees or feet were moved or touched. Dermatological examination showed multiple 1-2mm perifollicular palpable petechiae, corkscrew hair and xerosis on both legs, multiple nonpalpable petechiae on both feet, edema of knees, legs, feet and gingiva. Diascopy showed nonblanching lesions **(Figure 1)**.

Laboratory examination showed hemoglobin 10.8 g/dL (anemia), erythrocyte sedimentation rate (ESR) 75mm/hour (elevated), serum iron 17 μg/dL (decreased), total iron binding capacity 289μg/dL and transferrin saturation 5.8%. Peripheral blood smear showed normochromic normocytic anemia and anisopoikilocytosis. Urinalysis revealed erythrocytes +2 (hematuria). Fecal occult blood test was positive. Metabolic panel showed albumin 2.9 g/dL (decreased). Other laboratory values such as platelet count, hemostatic function, liver and renal function, electrolyte serum, ANA test and C3 were within normal range. Antistreptolysin O, anti double-stranded DNA, rheumatoid factor and antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were negative.

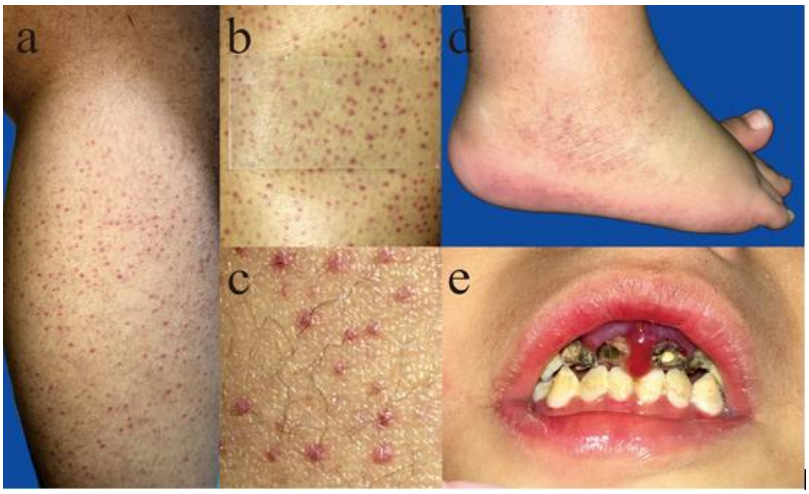

Figure 1 (a) Perifollicular palpable petechiae, (b) which did not blanch on diascopy, (c) with corkscrew hair, (d) on both legs, nonpalpable petechiae and edema, (e) on both feet, and gingival edema.

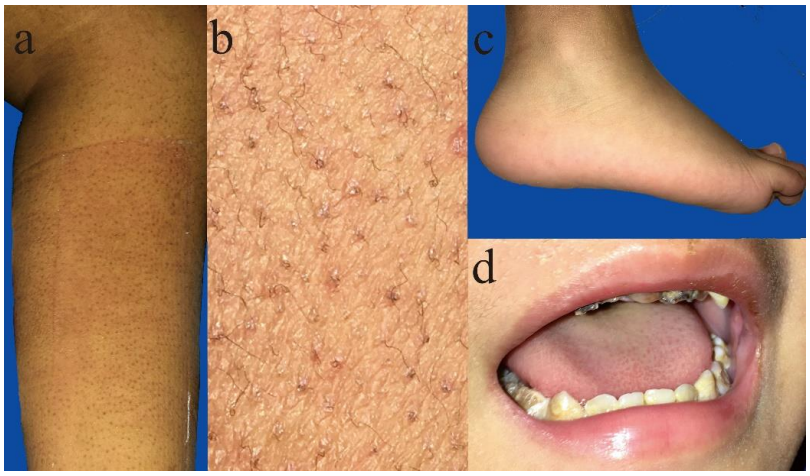

Figure 2 (a) Disappearance of petechia (b) leaving multiple skin-colored hyperkeratotic follicular papules with corkscrew hairs (c) on both legs, and improvement of feet (d) and gingival edema after 5 days course of vitamin C supplementation.

Plain radiograph of both knees showed juxtaarticular osteopenia of both femora, tibias and fibulas, distal epiphyseal irregularity of both femora and tibias, bilateral anterior and posterior femorotibial joint opacity which led to diagnosis of systemic illnesses with joint involvement and suspected joint effusion. Plain radiograph of pelvis and ankle was normal. Electromyography (EMG) did not support muscular disorder, but could not rule out myelopathy. Magnetic resonance imaging (MRI) did not show any lesion on spinal canal or spinal cord.

Patient was diagnosed as suspected case of cutaneous vasculitis with differentials of scurvy and juvenile idiopathic arthritis, xerosis cutis, anemia and pulmonary hypertension. Diagnostic plan included skin punch biopsy and referral to Orthopaedic Department. Serum Ascorbic acid level was planned but not available. Prednisone 20 mg daily for 5 days, ibuprofen 150 mg twice a day, sildenafil 5 mg thrice a day and 10% urea cream twice a day were given.

After 5 days of prednisone, lesions and symptoms showed no improvement. Patient was then reassessed as suspected case of scurvy. Joint fluid aspiration was planned and both legs were splinted. Vitamin C 50mg twice a day was added, prednisone was stopped and other treatment was continued.

After 5 days treatment with vitamin C, petechiae disappeared leaving hyperkeratotic follicular papules. Edema and pain of both knees, legs and feet decreased. Edema of the gingiva also improved **(Figure 2)**. Repeat laboratory examination showed improvement in hemoglobin (11.6 g/dL), ESR (28mm/hour) and hematuria (1+). Cytology of joint fluid revealed red fluid macroscopically and erythrocytes, lymphocytes, neutrophils without malignant cells microscopically. Histopathology revealed widespread erythrocytes extravasation and perifollicular and perivascular lymphocytic infiltrate without vasculitis consistent with scurvy **(Figure 3)**. Patient was then diagnosed as scurvy (improving), xerosis cutis, anemia (improving) and pulmonary hypertension. Patient was discharged on same treatment. Parents were educated to include fruits and vegetables in patient's diet.

After 30 days course of vitamin C, swelling and pain of both knees, legs and feet disappeared. Patient was able to walk and willing to eat fruits

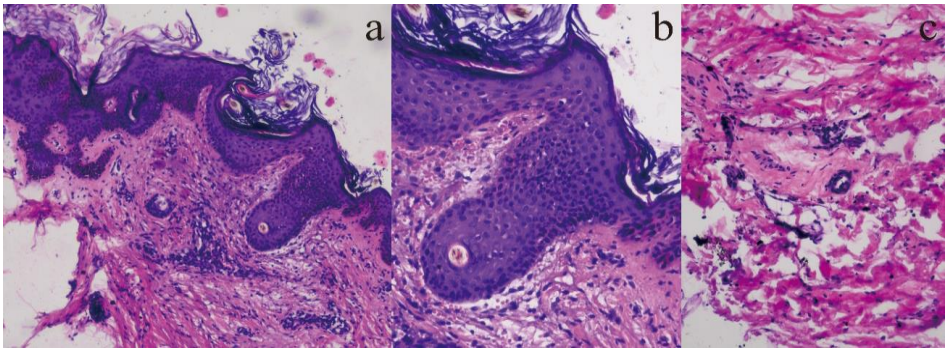

Figure 3 Histopathology showed follicular hyperkeratosis and plugging without corkscrew hair (a, H&E, 10x), widespread erythrocyte extravasation and perifollicular (b, H&E, 20x) and perivascular (c, H&E, 20x) lymphocytic infiltrate without vasculitis.

and vegetables. Dermatologic examination showed few skin-colored hyperkeratotic follicular papules. Complete blood count, ESR and urinalysis were within normal range. Patient was diagnosed as scurvy (improved). Vitamin C was continued for 3 months. No recurrence of lesions or symptoms was noted.

Discussion

Vitamin C is not produced by human body. Vitamin C requirement is met from intake of fruits and vegetables such as oranges, lemons, tomatoes and potatoes. Vitamin C requirement may increase during inflammation or infection. Vitamin C deficiency or scurvy is uncommon among pediatric population. Risk factors for scurvy in children include exclusive meat intake, dietary restriction in neuropsychiatric patients, intestinal malabsorption syndrome, cancer, chronic hemodialysis and even imbalanced diet in a healthy-appearing child. Therefore, dietary history must be inquired routinely in every pediatric patient.[1,3]

Vitamin C has a role in collagen and bone formation, iron reduction and prostaglandin metabolism.[1,2] Vitamin C deficiency results in defect in osteoid matrix formation leading to osteopenia, bone fragility, epiphyseal fracture and subperiosteal bleeding.[1,3] It also results in collagen deficiency and capillary fragility leading to hemarthroses, cutaneous hemorrhage and mucosal bleeding.[1] Cutaneous, mucosal and joint hemorrhage along with reduced iron absorption results in anemia which further leads to pulmonary hypertension.[1] Dysregulation of prostaglandin metabolism resulting in inflammation and elevated inflammatory markers.[1,2]

All of the defective processes above are responsible for the manifestations of scurvy. Dermatologic manifestations of scurvy include follicular hyperkeratosis, corkscrew hairs and cutaneous and mucosal hemorrhage. Cutaneous hemorrhage due to capillary fragility often occurs on legs due to high hydrostatic pressure, and on perifollicular area due to traction by follicular hyperkeratosis or mechanical trauma on hairs.[5,6] Perifollicular petechiae are initially flat, but gradually become palpable which and are often misdiagnosed as vasculitis, They may coalesce into ecchymoses.[1,3,7] Mucosal bleeding may appear as edematous and easily bleeding gums, nosebleed or gastrointestinal hemorrhage.[1,5] Musculoskeletal manifestation are more prominent and observed in 80% of pediatric scurvy. These include myalgia, arthralgia, joint edema, hemarthroses and subperiosteal hematoma. These findings are symmetric and often affect legs and ankles.[1] Epiphyseal fractures due to bone fragility, subperiosteal bleeding and hemarthroses

produce severe pain resulting in refusal to walk or pseudoparalysis.[1,3] Other manifestations of scurvy include alopecia, pulmonary hypertension and death due to cerebral or pericardial hemorrhage.[1,3]

Supporting investigations in scurvy involve laboratory, radiology and histopathology. Laboratory investigations often showed anemia due to hemorrhage and iron deficiency and elevated inflammatory markers.[1,2] Plain radiographs in scurvy most often show osteopenia. Other radiologic findings include pencil-line like cortical thinning, Fraenkel white lines (thick irregular white lines of the metaphyses), Trummerfeld zone (metaphyseal rarefaction zone below Fraenkel line), Pelkan spur (calcification spur at peripheral metaphyses), Wimberger ring (circular opaque shadow on the growth center surrounded by white lines at epiphyses), subperiosteal hematoma and soft tissue edema.[1,3] Histopathology helps to rule out vasculitis. Follicular hyperkeratosis, corkscrew hairs and widespread erythrocyte extravasation in superficial dermis are observed. Perivascular fibrosis and inflammation may be seen, but vasculitis is not present in scurvy.[7]

Pediatric scurvy is often misdiagnosed as other disorders presenting with petechiae and purpura such as cutaneous vasculitis like Henoch-Schonlein purpura or vasculopathy due to SARS-CoV-2 infection.[1,8-10] It is also frequently misdiagnosed as rheumatological disorders such as juvenile idiopathic arthritis, dermatomyositis and myasthenia gravis, or neuropathies due to prominent musculoskeletal findings which may appear earlier than dermatological findings, such as in our case.[3,11-13] These differential diagnoses were ruled out in our case by investigations such as negative antibodies to SARS-CoV-2, absence of vasculitis on histopathology, normal EMG and lack of response to nonsteroidal anti-inflammatory drugs and corticosteroids.

Gold standard diagnosis of scurvy is ascorbic acid level determination.[3] Plasma ascorbic acid less than 11μmol/L indicates deficiency. Buffy-coat level of ascorbic acid is more accurate.[1,2] Because this investigation is not always available, scurvy can be diagnosed by clinical, laboratory or radiology examination or ex juvantibus by demonstration of rapid clinical improvement after empirical supplementation of vitamin C.[2,3] Treatment of pediatric scurvy is supplementation of vitamin C 100-300 mg/day for 1 month or until complete resolution of signs and symptoms. Spontaneous bleeding, oral lesions and constitutional symptoms usually show dramatic improvement within days, while ecchymoses and musculoskeletal manifestations resolve within weeks after supplementation. Other symptomatic treatments for scurvy include analgesics and splinting.[1]

In our case, musculoskeletal findings such as edema and arthralgia of knees and ankles and pseudoparalysis were more prominent. Dermatological manifestations such as palpable and nonpalpable perifollicular petechiae and edematous and easily bleeding gums appeared few weeks after musculoskeletal complaints. These prominent musculoskeletal findings and vasculitis-like skin lesions often causes misdiagnosis of pediatric scurvy. Perifollicular petechiae, follicular hyperkeratosis, corkscrew hairs, and gingival abnormalities supported clinical diagnosis of scurvy. Diagnosis of scurvy can be established by dietary history, clinical, laboratory and radiology examination and in ex juvantibus by rapid improvement after vitamin C supplementation if determination of ascorbic acid level is not available. Histopathology helps to rule out differential diagnosis of vasculitis.

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