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Case Report

Digital Ulcers in an 11-Year-Old Boy: An Unusual Presentation of Protein S Deficiency

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Abstract

Protein S deficiency is characterized by decreased activity of Protein S, a serine protease complex with role in coagulation, apoptosis and inflammation. Protein S deficiency can be congenital or acquired. Protein S deficiency can be due to multiple causes including Vitamin K antagonists, hepatic diseases, SLE, myeloproliferative disorder and DIC. It commonly presents as venous thrombotic events such as deep venous thrombosis and pulmonary embolism. We present a case of an 11-year-old boy who presented to the OPD of tertiary care hospital with a two-month history of multiple painful erosions and ulcers on both feet, predominantly involving toes. He had previously lost the distal phalanx of the third toe following a similar episode one year earlier. Extensive laboratory investigations revealed decreased levels of protein S, thereby confirming the diagnosis. This case highlights an unusual presentation 'digital ulcers' in a pediatric patient with underlying Protein S deficiency. This underscores the importance of considering coagulation disorders in the differential diagnosis of recurrent ulcers in young patients.

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Introduction

Protein S deficiency is characterized by decreased activity of Protein S, a serine protease complex with role in coagulation, apoptosis and inflammation.[1] This leads to impaired coagulation control and development of multiple blood clots and venous thromboembolism in the body.[2]

Protein S is normally produced by the hepatocytes and undergoes Vitamin-K dependent gamma carboxylation.[1] It exists in bloodstream in two forms: free form and complement component C4b binding protein-bound form. The free form constitutes 30-40% of total Protein S and acts as a cofactor for activated protein C, which in turn inactivates factor Va and VIIIa, reducing thrombin production.[3]

Protein S deficiency can be congenital due to mutations in PROS1 gene.[4] Acquired Protein S deficiency can be due to multiple causes including Vitamin K antagonists, hepatic diseases, SLE, myeloproliferative disorder and DIC.[5] It most commonly presents as venous thrombotic events such as deep venous thrombosis and pulmonary embolism.[6] Here, we present a case of digital ulcers as an unusual presentation of Protein S deficiency.

Case Report

An 11-year-old boy presented to the outpatient department with complaint of multiple ulcers involving toes and both feet for two months. These were gradual in onset, started on a background of bluish discoloration on left three toes two months ago, with no preceding skin erythema, followed by development of erosions progressing to ulcers over a period of two months. The ulcers were painful,

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Figure 1 a) Ulceration over medial border of foot; **b)** Erosions and ischemia of toes with loss of distal phalanx of right 3rd toe **C)** Ulceration and crusting over medial malleolus and lateral border of foot.

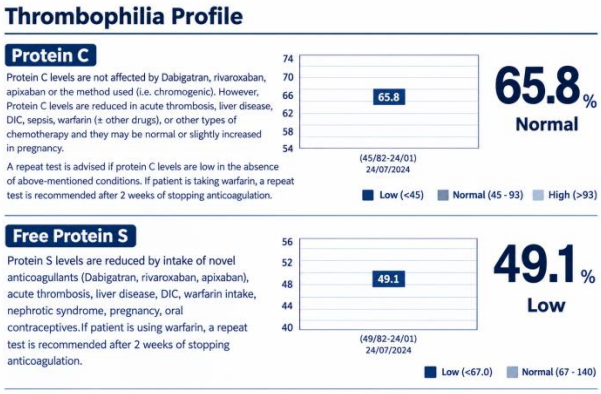

Figure 2 Lab report showing decreased Protein S levels

asymmetrical, irregular in shape, approximately half the size of the involved phalanx, covered with serous to some purulent exudate with some itching and surrounding erythema. These were not associated with trauma, pressure or insect bite. There was history of low grade fever for one week associated with abdominal pain and loose stools that settled with medication from community hospital (record was not available). There was history of painful bluish discoloration of fingers in cold that settled in a few minutes. There was no history of malaise, weight loss, night sweats, oral ulcers, photosensitivity, joint pains, myalgia or any lymphadenopathy in the body. There was no history of difficulty in swallowing of food, dry eyes or any redness of eyes.

There was history of similar ulcer development on right third toe followed by dry gangrene and loss of distal phalanx of third toe one year back. These were treated with oral and topical antibiotic medications at that time.

Physical examination revealed a young anxious boy with obvious mottled pigmentation of both lower legs including the feet. 2×2 cm irregular ulcer having ill-defined borders with granulation tissue in base and covered with hemorrhagic exudate was seen just behind the medial malleolus of left leg. Erosions with crusted exudate were seen in involving middle three toes of left foot with surrounding dark discoloration. A 3×2cm erosion was noted on lateral border on left foot. There was also blackish discoloration on right third toe along with loss of distal phalanx. All peripheral pulses, specifically the distal pulses (i.e. dorsalis pedis and posterior tibial), were palpable, and nerve sensations in both legs were normal. There was no associated lymphadenopathy. Chest and abdominal examination was unremarkable.

Baseline investigations and workup for systemic involvement was done which included complete blood count showing an Hb level of 10g/dL with slight decreased MCV of 72fL and platelet count of 380×109 /L. Liver function tests, renal function tests, urine complete examination and coagulation profile was normal. Hepatitis B and C screening was negative. ANA (Antinuclear Antibody) levels, RA (Rheumatoid Arthritis) factor, p-ANCA (perinuclear

antineutrophil cytoplasmic antibodies) and c-ANCA (cytoplasmic antineutrophil cytoplasmic antibodies) were also negative. Doppler ultrasound of both legs was unremarkable.

Protein C levels were 65.8% (normal); however, Free Protein S activity was 49%, which is significantly below the normal reference range (67-140%).

Patient was started on anticoagulant Rivaroxaban 5mg daily along with nifedipine 10mg daily orally after liaison with the pediatric department. Topical antibiotics to clear the infection were applied and topical 2%GTN (Glyceryl trinitrate) was applied as vasodilator. Patient's lesions showed significant improvement at the follow-up in OPD after two weeks.

Discussion

This case describes an unusual presentation of digital ulcers due to underlying Protein S deficiency in a young patient, highlighting the importance of a broad differential diagnoses when evaluating non-healing ulcers, particularly in individuals without typical risk factors such as diabetes, smoking, or occupational trauma. The presentation was insidious, and the absence of systemic symptoms or congenital symptoms initially delayed consideration of an underlying hereditary, vasculopathic or autoimmune etiology.

Digital ulcers in young individuals are rare and often serve as a cutaneous marker for systemic disease. Common causes include connective tissue disorders such as systemic sclerosis,[7] vasculitis, thromboangiitis obliterans, and hypercoagulable states like antiphospholipid syndrome or inherited thrombophilias (e.g. Protein S or C deficiency).[7] One article by Hughes *et al*. explains the clinical importance of digital ulcers being the most common complication of systemic sclerosis and adding to the burden of patients and communities.[8] In our patient, initial work-up ruled out infectious, traumatic and autoimmune causes, and further investigations revealed low levels of free Protein S, supporting a diagnosis of Protein S deficiency.

Protein S deficiency is typically associated with deep vein thrombosis and pulmonary embolism. Cerebral venous sinus thrombosis, though rare, has been described in a few isolated reports. One study by Hincapié *et al*. reported mesenteric ischemia as a rare presentation of Protein S deficiency.[9] Another case report by Nanda *et al.* revealed stroke in a 16-year old patient as a presentation.[10] Another case report documented a 74-year-old female admitted to the ICU after collapsing. Her MRI revealed a thrombus in distal right transverse sinus and sigmoid sinus. Her hematological workup showed decreased protein S levels of 24%.[11]

Timely recognition and management are critical, as digital ulcers are associated with pain, risk of infection, tissue necrosis, and functional impairment. In our case, early initiation of vasodilator therapy (oral calcium channel blockers and topical nitrates) along with oral anticoagulation led to significant clinical improvement, highlighting the need for prompt intervention.

This case reinforces the need for clinicians to maintain a high index of suspicion when encountering digital ulcers in young patients. A multidisciplinary approach involving dermatology, pediatric hematology, rheumatology, and vascular medicine may be required. Diagnostic workup should include autoimmune screening, coagulation profile, Doppler ultrasound, and where indicated, nail fold capillaroscopy or biopsy.

In summary, digital ulcers, though rare in the young, can be the first sign of a coagulation disorder. Our case contributes to the growing awareness of atypical presentations and emphasizes the role of comprehensive evaluation in reaching an accurate diagnosis and initiating timely treatment.

Conclusion

This case emphasizes the diagnostic challenge and

clinical significance of digital ulcers in young patients, especially in the absence of conventional risk factors. Such ulcers may be representative of underlying coagulation disorders. A thorough and systemic evaluation is crucial to identify the cause and initiate timely targeted therapy. Early identification not only aids in preventing ulcer-related complications but also enables the early diagnosis of potentially serious systemic conditions. This case reinforces the importance of maintaining a comprehensive differential diagnoses and multidisciplinary assessment when evaluating atypical presentations in young individuals.

Limitations of study The diagnosis of Protein S deficiency was established on low levels of free protein S antigen. However, genetic testing to determine hereditary or acquired Protein S deficiency could not be performed due to financial constraints. A repeat Protein S level after 8-12 weeks to confirm baseline deficiency vs. transient drop could not be performed due to financial liabilities

Declaration of patient consent Author certify that they had obtained all appropriate patient consent.

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Author's contribution

HK: Identification, diagnosis and management of the case. Manuscript writing and critical review of the manuscript.

SS: Identification, diagnosis and management of the case. Critical review of the manuscript.

MUS: Diagnosis of case, manuscript writing.

All authors have given final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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