Dactylitis: A Complication in Patients With Sickle Cell Disease

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ABSTRACT:

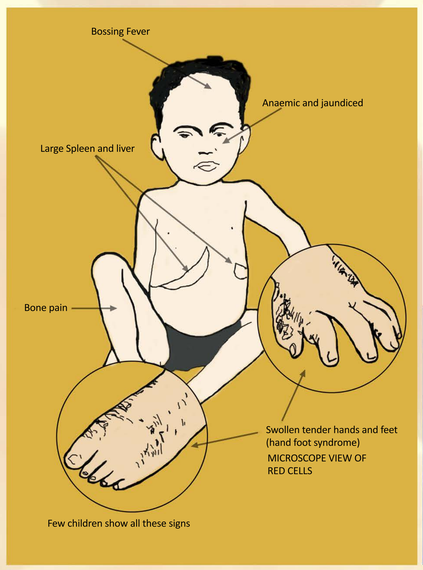
Sickle cell disease (SCD) is a group of disorders that affects hemoglobin, the red pigment in blood erythrocytes responsible for delivering oxygen throughout the body. This is the most commonly inherited blood disorder. One of the most widespread manifestations of SCD is painful vaso-occlusive crises and osteomyelitis. Dactylitis or hand-foot syndrome is the first clinical sign of SCD among children under the age of 6 years, particularly for those aged 1-2 years. Sickle cell dactylitis, an acute vaso-occlusive condition is associated with pain and edema on the dorsum of hands or feet or both simultaneously, along with elevated local temperature and erythema. This review will detail the problems associated with the bone and skeletal involvement in SCD with specific emphasis on dactylitis in children; description of its signs, symptoms, effects, as well as treatment procedure.

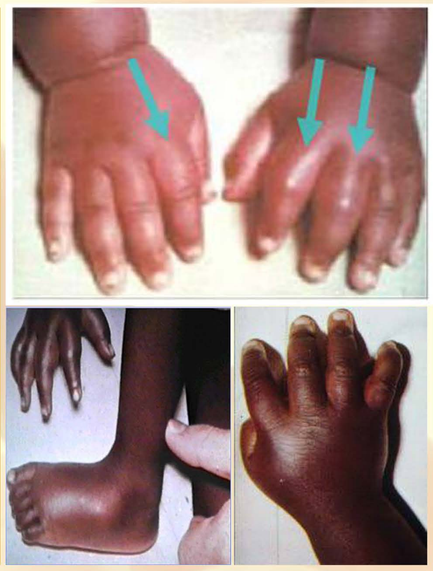
INTRODUCTION:

Sickle cell disease (SCD) is an inherited chronic hematological disorder that affects millions of people across the globe. [1] This is the first monogenic disorder to be elucidated at the molecular level. SCD is characterized by decreased or abnormal production of hemoglobin protein in red blood cells (RBC). Dactylitis or hand-foot syndrome is generally the earliest clinical musculoskeletal manifestation of SCD that affects infants and young children in the age group of 6 months to 6 years, with highest incidence during the first 6-12 months of life.[2] In fact, affected infants normally do not develop symptoms in the first few months (0-4 months) of life due to the presence of fetal hemoglobin (Hbf) produced by the developing fetus, which prevents the RBCs from sickling. Dactylitis has been found to occur in SCD patients with lower Hbf and higher reticulocyte counts. The occurrence of dactylitis was also found to be associated with cold weather. [1]

CLINICAL SYMPTOMS:

The clinical symptoms of dactylitis in children include puffy, tender, warm feet and hands, acute pain, fever, reduction of movement, and refusal to bear weight.[3] Previous studies revealed different opinions regarding the role of dactylitis as a possible predictive factor of adverse outcomes. Studies conducted on Pediatric Cohort of Guadeloupe from 1984-1999[1] and a retrospective study by Miller et al[4] indicated that dactylitis occurring in children at an age less than 6 months could lead to severe consequences in later life, such as recurrent acute chest syndrome, stroke, frequent pain, and even death. On the contrary, the study on Dallas cohort by Quinn et al[5] could not reflect the importance of dactylitis as a possible predictor of adverse outcome, rather the study observed that those subjects predicted to be at high risk never experienced an adverse outcome and those predicted to be at low risk developed severe conditions later in life. Sickle cell dactylitis in infants and young children is believed to be due to infarction or tissue necrosis at metacarpals, metatarsals, and phalanges, resulting from sickling of RBCs in the capillary beds and eventually blocking the vessels at these sites.[13] Histologically, extensive infarction of inner layer of the cortical bone, Dactylitis: A Complication in Patients With Sickle Cell Disease American Research Journal of Hematology Page 3 medullary trabeculae, and the marrow results in enhanced erythropoiesis (production of erythrocytes or RBCs), sub-periosteal new bone formation, and bone marrow expansion of the hand and feet, causing swelling, tenderness, redness, and hyperthermia of the affected limb or digit.[1, 6] In fact, capillary blockage by abnormal sickle RBCs causes infarction in both the diaphysis and epiphysis of long tubular bones, leading to medullary infarcts and the appearances of a vascular necrosis respectively. Due to the impediment of blood through the bones and tissues, excruciating pain occurs, which is considered to be the classical painful bone crisis.[1] Furthermore, prolonged ischemia or infarction often led to bony destruction of the terminal phalanges and metacarpals. In addition to the abnormal shape of RBC, there are several other factors affecting the blood flow in the vessels, which include viscosity of blood, the diameter of blood vessels, and various blood constituents. In general, SCD patients are prone to have increased blood viscosity that results in decreased flow of blood, which in turn hinders oxygen distribution to the essential areas of the body.[1] This tissue anoxia due to capillary stasis resulting from viscous blood is presumed to be another possible cause of sickle cell dactylitis.[3] Furthermore, swelling of soft tissue during dactylitis occurs due to the reparative response of hyperemia adjacent to the infarcted area and as the swelling subsides new periosteal bone is formed either through incorporation in to existing cortical bone or through layered deposits along the inner surface of the cortex.[3] This clinical condition is mostly observed in homozygous HbS disease, sickle cell hemoglobin C disease and sickle cell β- thal-assemia.[3]





Due to diagnostic imprecisions, management of these conditions sometimes becomes difficult. Standard Radiography is usually performed to detect the disease. Radiographs are generally normal during the acute phase of vaso-occlusive crisis. However, the radiological changes could be observed 10 to 15 days after the onset of the syndrome.[7] Conservative treatment is considered to be the best treatment option for dactylitis, since symptoms generally subside by one to two weeks. In general, treatment is directed towards management and prevention of acute manifestations. Treatment involves bed rest, immobilization, use of topical heat pack to ease the discomfort and swelling. However, the use of cold or icepack should be avoided in order to prevent vaso-occlusive crisis. [7] The mainstay treatment for dactylitis includes use of oral or parenteral analgesics such as dipyrone, paracetamol, non-steroidal anti-inflam-matory drugs for moderate pain and opioid derivatives for extreme painful crises. A previous study had also reported a significant reduction of dactylitis in very young children after the use of hydroxycarbamide.

[1] Additionally, the use of hydxoyurea is highly recommended for pediatric SCD patients suffering from severe pain. Hydroxyurea stimulates the production of Hbf in blood. Hbf prevents sickling of the RBCs which is quite useful for SCD patients. Besides Hbf production, hydoxyurea has several other benefits such as it decreases vasoocclusive episodes and painful crises, increases the interval between the episodes of pain, and thus reduces the need for hospitalization or blood transfusion.[6] However, the response of hydroxyurea is varies from patient to patient and thus is unpredictable. As a preventive measure, children suffering from dactylitis should avoid exposure to extreme cold and heat, especially cold, since severe cold causes peripheral vasoconstriction, and thus reduces the flow of blood through tissue vasculature and induces vaso-occlusive crisis.[8] It has also been noticed that administration of malarial prophylaxis could reduce both malaria as well as dactylitis episodes.[1]

SUMMARY

SCD is a genetic disorder which involves multiple organs. Skeletal changes in SCD mainly results from hyperplasia of the bone marrow and vascular insufficiency resulting in thrombosis in microcirculation, which eventually leads to infarction and secondary infection. Dactylitis or hand-foot syndrome is a condition that causes tenderness, swelling, redness, and warmth of the affected hand or foot in infants and young children. This is the earliest musculoskeletal manifestation of SCD. The main radiological changes observed in bones are due to hyperplasia of the marrow and osteonecrosis. Although, dactylitis symptoms in some cases were misdiagnosed with arthritis or osteomyelitis, yet recent advancement in the diagnostic modalities are quite helpful in obtaining proper diagnosis. In addition, improvement of medical management is beneficial in reducing acute pain and swelling which in turn minimizes the morbidity in these patients.

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