CASE REPORT

PERIPHERAL GANGRENE IN SICKLE CELL DISEASE- A RARE BUT DREADED COMPLICATION

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Abstract

Sickle cell disease (SCD) is a very common condition in central India affecting a large number of pediatric population. The acute painful sickle cell episode (painful crisis) resulting due to vaso-occlusion is the hallmark of sickle cell disease. Pain usually involves the low back, joints, bones of extremities, chest, and abdomen in decreasing order of frequency. Other major complications include infection, acute splenic sequestration crisis, aplastic crisis, acute chest syndrome, stroke, cholelithiasis and renal disease in children. Vascular thrombosis with gangrene is rare. We present a 9-year-old male with SCD who developed peripheral gangrene of digits of upper limb and lower limb along with pain in extremities.

Introduction

Sickle cell disease (SCD) is a blood disorder caused due to homozygosity of the sickle – cell allele β s at the β –globin gene locus resulting in the replacement of glutamic acid by a valine in the expressed proteins at the sixth position of the b chain of haemoglobin. (1,2) At low oxygen tension, the mutant sickle hemoglobin, polymerizes inside the red blood cells into a gel or further into fibres leading to the red cell deformability. As a result, micro-vascular occlusion arises which may lead to serious, sometimes fatal, crises. Hyper-coagulability is also described in these children. The reasons being decreased level of Protein C, S, increased fibrinogen, platelet aggregation and activation, vascular endothelial dysfunction and also cellular inflammation. (3) These factors increase thrombotic events and if in the peripheral vessels can cause gangrene. So far only four cases of SCD with peripheral gangrene have been reported. (4-7) In this report we present a case of a child with sickle cell disease who presented with the pain in extremities and gangrene.

Case Report

A 9-years-old male child, suffering from sickle cell disease presented with pain in the extremities and bluish black discoloration of index and middle finger of right hand and great toes of both feet. He was diagnosed to have SCD at 18 months of age. He had no past history of sickle cell crises. One year ago, he was given packed red blood cells (PRBCs) transfusion for anemia. On presentation, he had pallor and jaundice. There was black discoloration of the tip of the index finger of right hand and toes of both feet along with tenderness and swelling of these digits (Figures 1,2). His peripheral pulses were felt. He had hepatosplenomegaly (liver span 15cm and spleen 3 cm below costal margin). Lower limb arterial doppler showed small vessel end arterial vasculitis. Large vessels were normal. Hemoglobin was 9.3gm%, rest of hemogram including platelets were normal. Liver and kidney function tests were normal. Blood levels for protein C antigen was 32 IU/dl (normal ranges from 64 – 125 IU/dl), free protein S was 48 IU/dl (normal ranges from 64 – 154 IU/dl). Protein C and S activity, Antiphospholipid antibodies, anticardiolipin antibodies, antithrombin activity, concentrations of clottable fibrinogen, activities of coagulation factors VIIIC and XII, anti-cytoplasmic antibodies, antinuclear antibodies could not be done due to un-affordability. The surgical team was consulted and they suggested no active intervention and advised dry dressing of the affected area and medical management with close follow up. Amputation is planned once the progress has stopped. He was given PRBCs and a short course of steroids 40mg once a day initially (in view of suspected vasculitis) along with pentoxyfilline 200mg three times a day for 8 weeks.

Figure 1. The ventral aspect of the tip of right index finger.

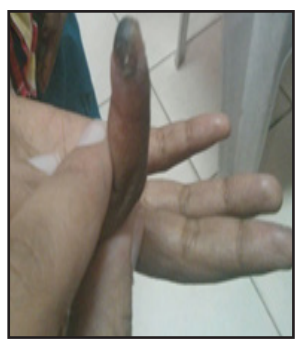
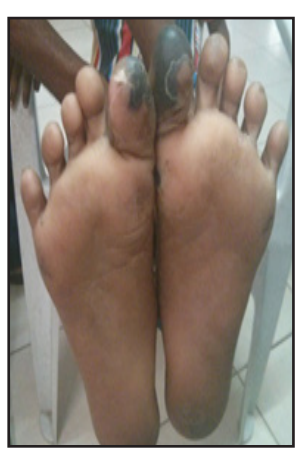


Figure 2. The blue discoloration of great toes of both lower extremities, showing gangrene



Discussion

When a child of sickle cell disease presents with painful and discoloured extremities, vaso-occlusive crises or dactylitis is suspected but gangrene is a rare and devastating complication of dactylitis. Home remedies like dipping the limb in cold water might increase the chances of gangrene. (6) In a retrospective study of 316 children (122 females and 194 males) with sickle cell anemia, 282 patients were hospitalized for 1725 times in a follow up for 5.8±5.7 years but none had the vasculopathic presentation

which is considered as number one criteria to define severe disease. (8) This should alarm the physicians that each and every case is different and should be evaluated thoroughly and completely for complications. In sickle cell crises the organs most commonly affected are lungs, spleen and brain. Thus it is possible that complications like gangrene mimicking dactylitis can be completely overlooked leading to devastating sequelae. Elsharawy et al reported a 14 years old boy with peripheral gangrene, he did not have peripheral pulses and X-ray of extremities showed extensive calcifications. (5) This indicates definite involvement of major vessels in some patients though our patient had palpable pulsations and major vessels were not involved on doppler.

Many studies are being done to find the reason for hypercoagulability. Reduced levels of anticoagulant protein C and S have been shown both in steady state and also in crises. Endothelial activation markers and CRP was high also in both the states indicating role of endothelial damage. (3)

Gangrene in sickle cell disease once set in has rarely been managed by embolectomy or revascularisation leaving amputation as the only choice. (4,5) Pentoxifylline is a methylxanthine derivative with potent hemorrheologic properties - increases red blood cell deformability, decreases blood viscosity by decreasing plasma fibrinogen concentrations, inhibits spontaneous platelet aggregation via thromboxane synthesis and increased prostacyclin synthesis thus resulting in significant increase in peripheral blood flow. (9) Hypercoagulable states improve through decreased platelet aggregation and adhesion, increased plasminogen activator, increased plasmin, increased antithrombin III, decreased fibrinogen, decreased α2-antiplasmin, decreased α1-antitrypsin, and decreased α2-macroglobulin. (10) Thus we suggest the use of pentoxifylline whenever the patient has an ongoing crisis to prevent progression to peripheral arteries although more research is required in support of this mode of treatment.

Regular thrombophilia testing should be done at-least every yearly. Monitoring of peripheral pulses, colour changes in extremities, local temperature and pain should be done in every sickle cell clinic visit. Once these signs are noticed, long term low molecular weight heparin or anti platelet drugs can be started to prevent extension to major vessels. Measures like cold water dipping or limb elevation which will further worsen the ischemia must be deferred. The parents should be educated and made aware regarding these complications.

Conclusion

A complete thrombophilia screening should be recommended in patients with SCD. Peripheral arterial assessment with the help of arterial doppler in low resource settings or digital subtraction angiography wherever possible must be done at regular intervals for these children. Long term and frequent PRBC transfusions are indispensable to prevent progression.

Contributor Statement

KK drafted the case report, did literature review, final approval of work and agreement to be accountable for all parts of the work. BLB did critical revision for important intellectual content, final approval of the version to be published, agreement for accountability for all aspects of this paper.

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