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Multi-organ dysfunction in Sickle Cell Disease: a rare presentation and its management in resource-limited setting.

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Abstract

Introduction: Chronic end-organ damage among the sicklers is frequently diagnosed in Tanzania, but rarely involves multiple organs in a single patient.

Case report: A 26-year-old Tanzanian black-sickler woman presented with features related to avascular necrosis of the right hip, left ventricular hypertrophy, pulmonary hypertension, Chronic Kidney Disease and Cholelithiasis. Despite the management given, her condition is still deteriorating.

Conclusion: Prevention of these complications through screening and early diagnosis with a concurrent timely treatment should be advocated by all health-care providers.

Key words:

Sickle cell disease, avascular necrosis, LV hypertrophy, pulmonary hypertension, chronic kidney disease, cholelithiasis

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Introduction

Long term complications of sickle cell disease (SCD) which usually result from vaso-occlusive phenomena and hemolysis have been attributed to early deaths and/or serious end organ dysfunction (EOD) with permanent disabilities. Diagnosis of chronic EOD among sicklers is frequently delayed until adolescence/early adulthood where manifestations of previous asymptomatic complications usually occur as majority of patients survive beyond childhood (1). Concurrent involvement of multiple organs in one patient is infrequent but when happens, it may result into life-threatening condition (2). Its management is challenging especially in a resource-limited settings where most of the patients present to the health facilities in an advanced stage of the disease. In our center, we have never seen a patient with multiple major organs dysfunction related to SCD, neither has it been reported anywhere in the country.

Case report

We are reporting a 26-year old black African Sickler (SS) female, a well-established patient with several painful vaso-occlusive crises and anemia presentations since the age of 5 years. Ever since, she has been followed-up in a district hospital where she had received multiple blood transfusions and continuously being given Folic acid and Chloquine for Malaria prophylaxis. The sequence of complications started at the age of 19 when she first presented in our facility with severe progressive right hip joint pain with limited movement. An X-ray of the right hip joint showed a narrowing of the space with alternating regions of sclerosis and lucency on the superior aspect with the crescent sign. These findings are consistent with the diagnosis of avascular necrosis of the right femur. **(Figure 1).** She was managed conservatively with analgesics and no surgical intervention was done. Three-years later, she presented to our clinic with progressive features of heart failure; orthopnea, lower limbs swelling and features suggestive of pulmonary edema. The chest X-ray showed cardiomegaly, poor defined interstitial infiltrate in the right lower zone and congested pulmonary vasculature **(Figure 2).**

Echocardiogram revealed left ventricular hypertrophy, normal ejection fraction (51%), elevated pulmonary arterial pressure (PAP) (38mmHg) with the right atrial straining (tricuspid regurgitant jet of 2.7m/s). A minimal bilateral pleural effusion was also evidenced. Sonographically,

congestive hepatomegaly, moderate ascites and dilated thoracic inferior vena cava were evidenced. Multiple bright echogenic foci mobile cast shadowing were incidentally seen in the gall bladder and the spleen was shrunken. Serological examinations for Hepatitis B, Hepatitis C, Alanine transferases (ALTs), Bilirubin and HIV were repeatedly found to be negative. The diagnoses of Congestive Heart Failure (CHF) with pulmonary edema, Severe Pulmonary Arterial Hypertension (PAH) and multiple gall stones were established. We treated this patient with Captopril 12.5mg 12 hourly and Furosemide 40mg 12 hourly for her heart failure. As regards to gall stones, no intervention was done at this stage as the stones were insignificantly small and asymptomatic. Despite of multiple 'controlled' blood transfusions (BTs) and Folic acid supplements, correction of anemia was not achieved with the hemoglobin (HB) ranging from (3.0-7.6)g/dl displaying microcytic-hypochromic picture. Other hematological parameters were insignificant. A year later, during the clinic follow-up, a progressive deterioration of the renal function was noted with an estimated Glomerular Filtration Rate (eGFR) ranging from 71-13 (normal range 90-120) mL/min/1.73m^2 over the ensuing ten-month period. Other parameters recorded includes blood urea nitrogen (BUN): 26-75.5 (normal range 6-20) mg/dL calcium: 0.9 - 2.20Mmol/l (normal range 2.1-2.8) Mmol/L and potassium: 4- 7 (3.5-5.5) Mmol/L. Urinalysis revealed proteinuria 3+ equivalent to 300mg/dl. Renal ultrasound showed both kidneys are small (6 X 7) cm with bilateral complete loss of cortico-medullary differentiation. A diagnosis of End Stage Renal Disease (ESRD) was established. Renal biopsy was not done due to limited capacity of our Center. Hemodialysis was started through the right internal jugular temporary dialysis catheter which was later replaced by a permanent catheter. She is currently on hemodialysis thrice a week; an ultrafiltration of 1500-2000mls for 4 hours with a urea reduction rate of 70-80%. To-date, our patient has already undergone more than 15 hemodialysis sessions with moderate improvement. She still requires BT at least twice a month with erythropoietin (EPO) after every dialysis session. The girl is in the kidney transplant waiting list.

Discussion

The chronic complications of SCD can affect any organ and their presentations is quite diverse, ranging from asymptomatic to severe illness depending on the type of complication, age, sub-type of SCD and the degree of expression of fetal Hemoglobin (HbF) by an individual (3). According to the recent recommended definitions of sickle cell complications (4), at least five

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co-existing chronic complications (Avascular necrosis, LV hypertrophy, pulmonary hypertension, chronic kidney disease and cholelithiasis) were diagnosed in the index patient.

Avascular necrosis (AVN)

AVN of the head of femur is the most frequently encountered musculo-skeletal complication in people with SCD (5). The overall prevalence of AVN in SCD is estimated to be up to 50% by the age of 33 years in patients with SS Hb (6). Our patient presented to the hospital in an advanced stage of the disease (Stage III- Ficat and Steinberg classification). An effective recommended management for a significant pain relief and restoration of function is a total hip replacement (THR) (7). This procedure was not done due to lack of supportive equipment.

Left ventricular hypertrophy and pulmonary hypertension

Cardiovascular complications are important cause of morbidity and mortality among patients with SCD. Diastolic dysfunction secondary to Left ventricular (LV) remodeling due to chronic anemia or systemic vasculopathy is the most commonly cardiac complication in SCD (8). CHF with diastolic LV dysfunction which was poorly responding to standard treatment was diagnosed in the index case. However, hypertensive heart disease in this patient cannot be ruled out as a cause of LV hypertrophy. Most recent studies suggest that the SCD patients with high PAP and low HB form a subset of those having multiple other sequelae like high hemolytic rates, proteinuria, low glomerular filtration rate (GFR) and LV dysfunction (9,10). Both of these were observed in our patient.

Chronic kidney disease

CKD is common amongst SCD patients and the prevalence and intensity increases with age. As compared to non-Sicklers, the progression to ESRD is significantly faster in CKD-SCD patients (average of 5 years) (11). A very rapid progression (<1year) to ESRD was observed in the index patient. Co-existence of other nephropathic conditions, such as hypertension and CHF might have contributed to her accelerated clinical downfall. Nonetheless, despite of the clinical improvement following hemodialysis, she still stands a poor prognosis as it has been observed in several studies (12). Among patients with ESRD, kidney transplantation offers the best outcome

though it is still very difficult option to practice in resource-limited setting like ours. This patient is currently in the kidney transplant list, awaiting for her prospective donor's matching and typing results from abroad.

Cholelithiasis

The occurrence of cholelithiasis in Sicklers usually follows an excessive production of bilirubin from chronic hemolysis. Asymptomatic gall stones affects up to to 45% of adolescents and young adults. It is still controversial to whether cholecystectomy should be done in these patients as conservative management has not been associated with increased risk of complications (13, 14). Cholecystectomy was not done in the index case, and a close follow-up is being carried out for development of cholecystitis and/or increasing size of the stones.

Conclusion

Many chronic complications of SCD which can lead to severe life-threatening conditions can be delayed or prevented if a timely diagnosis and intervention is done. Screening, monitoring and supportive care to SCD patients as recommended in the World Health Organization guidelines are the key preventive measures. This case is perhaps a tip of an iceberg out of many Sicklers in the country who are either not attending the health facilities or else face a situation of health-care facility constrains that are important for proper diagnosis, and appropriate treatment of the complications.

Competing interests

Authors declare that they have no competing interests

Author's contributions

FAB, SBK, DWG managed the patient and collected clinical information; FAB, SBK, DWG and ERS searched the literature and wrote the manuscript.

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Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The CUHAS /BMC ethics review board provided the approval to publish this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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Figures

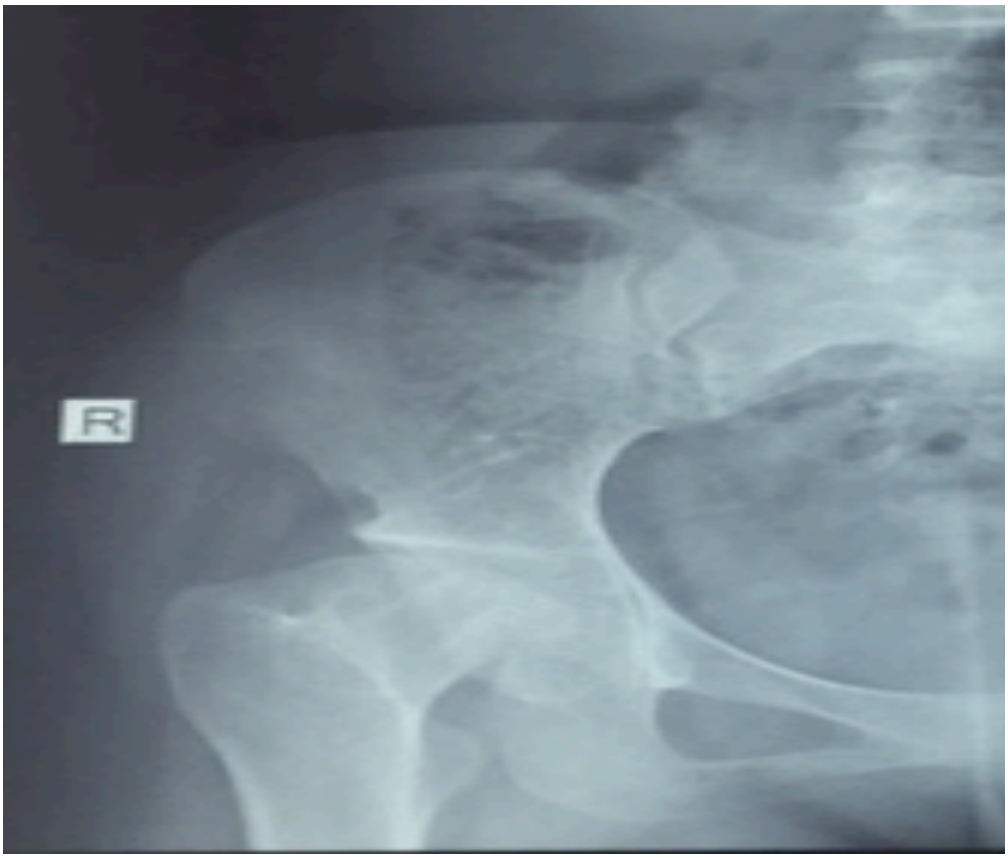

Figure 1: AP view X-ray of the right hip showing avascular necrosis of the head of femur.

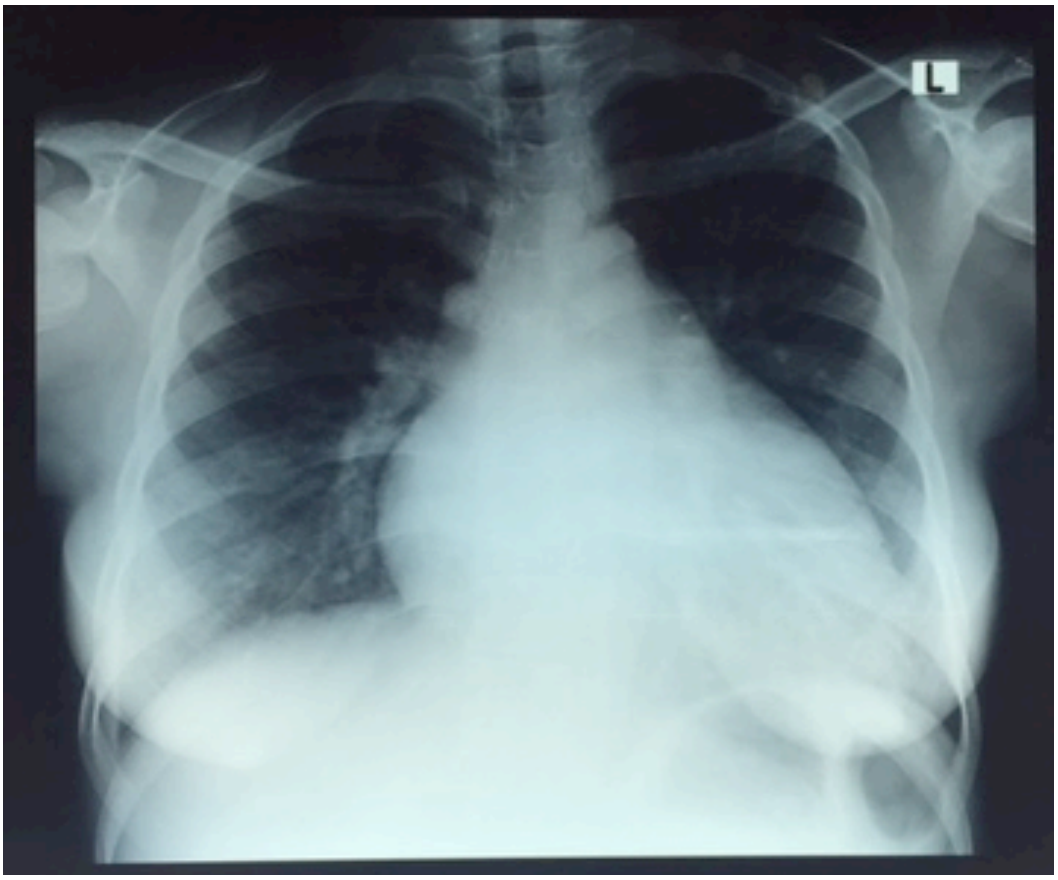

Figure 2: A postero-anterior chest X-ray