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CASE REPORT

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Preterm management of sickle cell crisis in a twin pregnancy with suboptimal antenatal care in a primary healthcare facility: A case report from Cameroon and literature review

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Key Clinical Message

Twin pregnancies in homozygous sickle cell patients are not only uncommon in our setting but are most often associated with adverse maternal–fetal outcomes especially in primary healthcare facilities where most of these cases initially present due to financial constraints, though lacking the necessary technical platform (including blood banks) to properly manage them.

Abstract

We are reporting the case of the preterm management of sickle cell crises in a twin pregnancy with poor antenatal care uptake in a primary healthcare facility devoid of a blood bank in Cameroon. Ngungi Fely, a 21-year-old HbSS patient, of the Bakweri tribe G3P0020, blood group O rhesus positive, was admitted at our health facility at 33 3/7 weeks' gestation with twin pregnancy, clinical anemia (hemoglobin 3.3 g/dL), the pulse rate of 123 beats/min, the respiratory rate of 38 breaths per min, the temperature of 39.2°C, and altered state of consciousness. She has a history of two spontaneous abortions (16 and 18 weeks' gestation) and has attended three antenatal care (ANC) visits (18, 24, and 28 weeks' gestation) for the index pregnancy. She underwent cesarean delivery of two live-born babies at 35 4/7 weeks' gestation and received 9 units of compatible blood (before, during, and after the cesarean) partly with the help of the "Blood Track Program" (which uses text messages to seek blood donors). The babies were referred to a secondary healthcare facility and the mother and babies' outcomes were uneventful. Sickle cell disease (SCD) in pregnancy is difficult to manage in primary care settings in Cameroon because of a poor technical platform. A multidisciplinary approach to the management of SCD in pregnancy is the mainstay in secondary and tertiary healthcare centers. The "Blood Track Program" is a good initiative that should be extended nationwide in Cameroon to reduce the burden of acquiring blood for transfusion, particularly in primary care centers devoid of blood banks.

KEYWORDS
anemia, blood track program, blood transfusion, case report, pregnancy, sickle cell, twin

1 | INTRODUCTION

Sickle cell disease (SCD) is the most common inherited disorder worldwide, being associated in pregnancy with a high risk of maternal and perinatal adverse outcomes, especially in low-resource settings.[1] The incidence of SCD in low-resource settings like Nigeria is up to 3% of the population, and unfortunately, Nigeria together with other sub-Saharan countries like Cameroon has a high prevalence of SCD and reported rates of maternal mortality due to SCD exceeding 9%.[2] This is because the management of SCD in pregnancy is difficult in low-resource settings where human, diagnostic, and therapeutic resources are less developed, limited, or unavailable.[1] We are reporting a case of the preterm management of sickle cell crises in a twin pregnancy with poor antenatal care uptake in a primary healthcare facility devoid of a blood bank in Cameroon.

2 | CASE HISTORY

2.1 | Patient information

She is a 21-year-old HbSS pregnant woman, of the Bakweri tribe, G3P0020, blood group O rhesus positive, who presented at 33 3/7 weeks' gestation with respiratory distress and an altered state of consciousness. She had intermittent fever with chills, generalized severe throbbing joint pains, and prostration of 2 days duration before presentation.

She is a known sickler on routine 5 mg of folic acid daily. She has a history of two spontaneous abortions at 16- and 18-week gestation. For the index pregnancy, her booking visit was at 18 weeks' gestation and she had three antenatal care (ANC) visits (18, 24 and 28 weeks' gestation) before coming to our health facility. At the booking visit, her hemoglobin level was 7.0 g/dL and she started taking 1.6 mg of folic acid daily and 240 mg of elemental iron daily. An ultrasound scan on November 02, 2021 reported a normally evolving dichorionic diamniotic twin pregnancy at 24 weeks' gestation. She received 3 doses of sulfadoxine–pyrimethamine for malaria prevention. Her partner's hemoglobin electrophoresis and blood group are unknown to the patient and relatives.

2.2 | Clinical findings

On physical examination, she appeared pale and prostrated. She was conscious, diaphoretic, and dyspneic. Her blood pressure was 100/58 mmHg, pulse rate of 126 beats per min, respiratory rate, was 38 breaths per min, oxygen saturation (SaO_2) was 96%, and axillary temperature, was 39.2°C. Her conjunctivae were pale and the sclerae icteric. There was a systolic murmur on cardiac auscultation. Her lungs were clear. Her abdomen was distended with a gravid uterus, which was discordant with the gestational age (higher than the period of amenorrhea). Two fetal heart rates were recorded (FHR1 = 166 bpm and FHR2 = 140 bpm). The cervix was posterior, long, and closed.

2.3 | Diagnostic assessment

Entry-level investigations were as follows: hemoglobin level of 3.3 g/dL (NV level = 11.6–15.1 g/dL), a positive malaria rapid diagnostic test (mRDT), 2-plus albumin on urinalysis and a serum creatinine level of 3.849 mg/dL (NV = 0.6–1.1 mg/dL).

2.4 | Diagnosis

Severe malaria (with acute kidney injury as severity criterion) and sickle cell crises (acute chest syndrome, vaso-occlusive and hemolytic crises) complicated by severe anemia in an SCD patient with a twin pregnancy.

2.5 | Timeline of the current episode

She was admitted, positioned in left lateral decubitus, and placed on 4 L of oxygen per min. Seven units of packed blood cells were requested from the laboratory, and 1 unit (500 mL) was transfused immediately. Intravenous (IV) fluids 2500 mL/24 h; analgesics (Nefopam 20 mg every 12 h (IV) and Metamizole 500 mg/12 hourly (IV) for 3 days); antimalarials (Artesunate 180 mg H0, H12, H24, and H48 slow IV injection); Antibiotics for acute chest syndrome (Ceftriaxone 1 g/12 hourly (IV) for 5 days) were given. Folic acid 5 mg daily was continued. FHRs were monitored every 3 h, vital signs every 4 h, and urine output twice daily. The following day, she was fully conscious and her vital signs were reassuring. She had received 3 units of compatible blood, and the fetal heart rate and fetal kick count were regularly felt and recorded. By Day 6 of admission, she had received 4 units of packed blood

cells in total, her hemoglobin level was 8.3 g/dL, her creatinine level had normalized, and both mother and fetus were doing well.

2.6 | Therapeutic interventions

Following clinical and haemodynamic stabilization with reassuring fetal activity, she was then counseled for elective cesarean delivery at 36 weeks' gestation for the following reasons: poor obstetrical history and twin pregnancy (high-risk pregnancy) in an SCD patient. She refused the referral to the Buea Regional Hospital (BRH) (a secondary care health facility and referral hospital for the southwest region of Cameroon) reason being her lack of finances. The pediatrician of the BRH was informed of the case and the search for more compatible blood was launched. Before the surgery, 3 compatible blood units were secured with the help of the "Blood Track Program" and 2 other units by the family. However, she went into spontaneous labor at 35 4/7 weeks' gestation prompting an earlier cesarean section than initially planned. She eventually gave birth by cesarean section to two heterozygous live fetuses weighing 2100 g (male) and 1900 g (female) with a 5-min Apgar score of 7/10 and 8/10, respectively, at 35 4/7 weeks' gestation. She received 3 units of blood on the eve of the surgery and 2 other units during and after the cesarean birth.

2.7 | Follow-up and outcome of interventions

The babies were referred to the BRH for specialist care at the neonatal intensive care unit. Maternal milk letdown was effective, but expressed milk was transported to the BRH (a distance of about 20 km) to feed the babies. By postoperative Day 7, she had sustained clinical improvement and was discharged, reuniting with babies later that day. Mother and babies were together in the Kangaroo Mother Care (KMC) unit of the BRH. The babies were feeding well and weighed 2210 g and 2010 g for the first and second twins, respectively.

3 | DISCUSSION

The twin pregnancy on the SCD background accounts for the high-risk nature of this gestation, and the poor obstetric history accounts for the delicate nature of the case. When coupled with the emergency presentation of the patient, the poor ANC uptake and follow-up, the lack of a technical platform, and the financial constraint of the patient, it worsens the prognosis of this already seemingly hopeless case. Nevertheless, with more donor tracking programs and a multidisciplinary approach to management, they stand a better chance of both maternal and fetal survival.

4 | SICKLE CELL DISEASE AND SUB-FERTILITY

A study in Nigeria comparing the mean ± SD of serum anti-Mullerian hormone (AMH) levels reported diminished ovarian reserve in women with Hb SS (AMH 3.64 ± 0.65 ng/mL) when compared with age-matched women with HB AA (AMH 7.35 ± 1.19 ng/mL.[3] The diminished ovarian reserve and other SCD-mediated ovarian damage could eventually result in the impairment of ovulation, fertilization, and implantation, thereby causing subfertility.[3] Furthermore, a study in Ghana reported a SCD miscarriage rate of up to 37.2%, which is nearly twice the miscarriage rates reported in non-SCD pregnant women in other sub-Saharan African countries.[4] This highlights the fact that SCD patients have a decreased ability to conceive and a high chance of having a miscarriage after a successful conception. It also highlights how rare it is to have pregnant SCD patients, especially those with multiple pregnancies successfully going through the entire gestation to term and later delivery without adverse outcomes.[4] This was the case of the index patient, who had two previous miscarriages and had a twin pregnancy.

5 | SICKLE CELL DISEASE, MALARIA, AND ANEMIA IN PREGNANCY

The reported prevalence of anemia in pregnancy in Buea, Cameroon in 2021 is 68.4%, which is higher than the national prevalence of 44.4% recorded in 2019.[5] In the same study, malaria infestation and gravidity were significantly associated with anemia in pregnancy (AOR: 9.47, $p < 0.001$ and AOR: 1.98, $p = 0.04$,4 respectively), with a strong negative correlation between malaria parasitemia and hemoglobin concentration ($r = -0.5816$, $p < 0.001$).[5] Pregnant women with multiple gestations and malaria in pregnancy like the index case were, therefore, almost 10 times more likely to suffer from anemia, especially severe anemia.[5] Furthermore, there is a reportedly higher risk of maternal deaths among SCD pregnant women with multiple gestations compared to non-SCD pregnant women in low-resource settings (OR: 22.8; 95% CI: 14.7–35.5, $p < 0.001$).[5] Data from Cameroon shows a similar incidence.[6]

6 | PREGNANCY, SICKLE CELL DISEASE, BLOOD TRANSFUSIONS, AND A LACK OF FUNDING FOR TRANSFUSION PROGRAMS

The National Blood Transfusion Program (NBTP) was launched in Cameroon in 2013 by the Ministry of Health (MoH) and the Centre for Disease Control President's Emergency Plan for AIDS Relief (CDC/PEPFAR) to support blood transfusion activities all across the country. Through this program, blood banks were established in 10 secondary healthcare facilities nationwide, and blood transfusion screening procedures were subsidized but not fully endorsed.[7] This left a void at the primary level of care, where the majority of patients in need are received. Furthermore, the blood units still have to be purchased or replaced with blood from voluntary donors, taking into consideration the cost of transportation to obtain the blood units. In other words, financial constraints may prove detrimental to patients. In addition, the availability of donors in times of need and without delay for areas without a blood bank-containing health facility remains a great challenge for caregivers.[7] There is a dire need for blood tracking programs (that search for blood donors when needed) in Cameroon. There are only a few such programs worldwide that have been reported in the literature such as the drone delivery of blood products in the rural areas of Rwanda.[8] The "Blood Track Program" is an initiative of alumni of the Faculty of Health Sciences of the University of Buea, Cameroon (since 2016), where short message service (SMS) text messages are sent out informing the general public of the urgent need for compatible blood donors at various locations, the number of units needed, and the health facility requesting for the blood. We secured 3 units of compatible blood using the "Blood Track Program" for the patient's surgery. Unfortunately, the "Blood Track Program" is only limited to the southwest region of Cameroon. Therefore, if stakeholders could make the "Blood Track Program" nationwide in Cameroon, including subsidies for blood transfusion procedures, this could greatly reduce mortality rates due to anemia.

7 | SICKLE CELL DISEASE IN PREGNANCY AND PERINATAL MORBIDITY AND MORTALITY FACTORS

The association between maternal anemia, IUGR, preterm delivery, and low birth weight has been reported previously.[9] However, the babies in the index case weighed 2100 g and 1900 g, respectively, at 35 3/7 weeks' gestation. This was slightly less than the average twin weight reported in other studies[9] for non-SCD twin pregnancy (2470+/−480 g). However, these neonates were in chronic fetal distress during their intrauterine life. Therefore, a specialist (pediatrician/neonatologist) is primordial to care for these neonates in their early extrauterine life to ensure good neonatal outcomes. However, neonatologists are seldom available at the primary level of care in Cameroon and most low-income countries, and referrals to other hospitals are most often not possible due to financial difficulties.

8 | SICKLE CELL DISEASE IN PREGNANCY AND CESAREAN SECTION

A study in Nigeria reported a greater rate of perinatal complications associated with the vaginal delivery of twins in SCD women than in non-SCD women and that 28.7% of SCD women with twin pregnancies eligible for vaginal delivery ended up undergoing a cesarean delivery.[10] Cesarean delivery, therefore, remains the preferred option for such patients despite its inherent risks. Spinal anesthesia has long been used to improve the maternal and fetal outcomes during cesarean delivery. Therefore, spinal anesthesia should preferably be done by a specialist anesthesiologist, but they are not usually present at the primary level of care in Cameroon.[11] However, general anesthesia was used in the index case, despite its reported risk among SCD patients. This trend is consistent in low-resource settings and at the primary level of care because of its availability and ease of use compared to spinal anesthesia.[11]

9 | SICKLE CELL DISEASE IN PREGNANCY AND ANTENATAL CARE (ANC)

SCD in pregnancy is a high-risk gestation, requiring close follow-up by an obstetrician as well as a proper technical platform for its management.[6] These are seldom present at the primary level of care. They also require early, consistent, and frequent ANC consultations where they are also required to take a recommended dose of 5 mg of folate daily periconceptually and throughout the pregnancy.[6,9] The index patient, however, started antenatal care visits with nurses/midwives at 18 weeks' gestation and had 3 ANC contacts with a suboptimal follow-up. This is consistent with Halle-Ekane et al. (2015) who

reported a mean gestational age at the start of ANC of 19.2 ± 4.2 weeks (range: 8–31 weeks) and the number of visits done as well as follow-up was substandard in a semi-urban area in Fako Division, Cameroon.[12] These highlight gaps in the ANC follow-up both quantitatively and qualitatively, which is usually the trend in primary healthcare settings in Cameroon.

10 | CONCLUSION

SCD in pregnancy is difficult to manage in a primary healthcare setting in Cameroon because of the lack of an appropriate technical platform (human, financial, and material resources), the suboptimal ANC uptake, quality and follow-up, and the delicate nature of the condition keeping in mind that many have poor obstetrical histories and fertility records. A multidisciplinary approach is thus most appropriate for the management of SCD in pregnancy; therefore, referral of cases to tertiary care centers is the mainstay, though frequently denied by patients for financial reasons. The "Blood Track Program" is a good initiative that should be extended nationwide in Cameroon to reduce the burden of acquiring blood for transfusion, particularly in primary care centers devoid of blood banks. In such patients, quick and effective access to blood when required, as well as the presence of an adequate technical platform could greatly the maternofetal outcomes of such patients and encourage more of them to conceive without fear.

AUTHOR CONTRIBUTIONS

William Ntchompbopughu Tih: Conceptualization; resources; writing – original draft. **William Ako Takang:** Writing – review and editing. **Thomas Obinchemti Egbe:** Supervision; validation; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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