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A Triad of Sickle Cell Disease, Eclampsia and Rhesus Negativity: Case Report

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Case Report

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Abstract

Pregnancy becomes a high-risk event when it occurs in women with certain co-morbidities. High risk pregnancy requires extra medical attention for a successful delivery without any complication(s). We report a rare case of high-risk pregnancy where the patient has sickle cell disease, with Rhesus D negative blood group and had eclampsia. These were coupled with the patient being a primiparous woman. The outcome was intrauterine foetal death (IUFD), uncontrollable anaemia, persistent infection and Urethra-vaginal fistula. In a patient with multiple risk factors such as this, a more aggressive approach in medicare is recommended involving all stakeholders in healthcare delivery system. The need for special endownment for sickle cell disease patients, girl child empowerment and proper healthcare financing have been emphasized.

Keywords: Sickle Cell Disease; Eclamspsia; Rhesus Negativity; Heterozygous; Rh Isoimmunisation

Abbreviations: IUFD: Intrauterine Foetal Death; SCD: Sickle Cell Disease; RES: Reticuloendothelial System; FMH: Fetomaternal Haemorrhage; RR: Respiratory Rate; PIH: Pregnancy-Induced Hypertension; UVF: Urethra-vaginal fistula.

Introduction

Sickle Cell Disease (SCD) is a group of inherited structural disorders of haemoglobin which requires the presence of the abnormal sickle gene inherited either in a homozygous (sickle cell anaemia) or compound heterozygous fashion with a highly variable clinical spectrum. Millions of individuals are affected worldwide especially among natives from the tropics, Mediterranean as well as Afro-Americans. Recurrent pain episodes and progressive damage to vital organs such as brain, lungs, kidney and spleen characterises the majority of clinical manifestations of this disease. The disease is associated with early mortality in most patients, with unfavourable outcome in the quality of life [1,2].

Pregnancy in a woman with sickle cell disease is at a very high risk, especially among individuals with severe disease state [3]. Indeed, the risk of maternal and foetal complications is higher than in the general population. Chronic foetal hypoxia associated with decreased placental circulatory flow seems to be the most plausible explanation for this high incidence of perinatal complications such as pre-eclampsia/eclampsia observed in this group of women [4].

Pregnant women with SCD have an increased risk of developing severe pre-eclampsia, which is also a result of increased endothelial damage [5]. The identification of Rhesus (Rh) incompatibility in a pregnant woman especially at first antenatal booking is of much clinical importance [6]. The antigens which are present on the human red blood cells (RBCs) are mainly ABO (A, B, AB) antigens, rhesus D (Rh-D) antigen and infrequently other atypical antigens. Rh isoimmunisation is the development of antibodies against the Rh antigens present on the surface of RBCs [7]. Rh D antigen is the most implicated as the cause of majority of

cases of severe Rh isoimmunisation, however, the other atypical Rh antigens that bear potential to cause severe isoimmunization are c, E and Kell antigens. The remaining group of RBC antigens (Duffy, Kidd, M and S) rarely cause significant problems [7].

Rh isoimmunization in a pregnant woman may be responsible for varying severity of anaemia in the foetus and newborn [7]. Usually, its clinical manifestation is recognised in the second or subsequent pregnancies in a woman's reproductive history. In utero, the foetus will initially have foetal anaemia, which may be identified clinically as decreased foetal movements. However, with the persistence of anaemia, extramedullary erythropoiesis in the liver and spleen may be provoked. This can be seen on ultrasonography as hepatosplenomegaly. In a profoundly anaemic foetus initially there is increased cardiac output but the hypoxic heart can no longer sustain and finally culminates in heart failure. This is manifested sonographically as hydropic changes like pleural effusion, pericardial effusion, ascites, subcutaneous edema and scalp edema. To compensate for the reduced oxygen supply, the placenta also enlarges which could be seen as placentomegaly on ultrasonography.

The role of the cells of the reticuloendothelial system (RES) in mounting up immunologic response against RBCs coated with contrary antigens [8]. An individual lacks the antibodies against the antigens, which are present on his own RBCs. However, if RBCs coated with different antigens (from another individual) gain entry into the circulation, the reticuloendothelial system (RES) of the recipient identifies these antigens on RBCs as foreign and mounts immune response to eliminate these cells. A similar phenomenon occurs during Rh isoimmunization. The Rh positive RBCs of the foetus gain entry into Rh negative maternal circulation via fetomaternal hemorrhage (FMH) resulting into formation of anti-D antibodies, which in turn pass to the foetus through placental circulation and destroy foetal RBCs to produce foetal anemia. FMH occurs throughout pregnancy and the amount of this haemorrhage increases with increasing gestation. It has been found that the amount of FMH is very minute (around 0.03 mL) during first and second trimesters, however it may be as high as 25 mL during third trimester. As a way of prophylaxis, the FMH which occurs at the time of delivery is covered by prophylactic anti-D within 72 hours of birth. However, if anti-D dose is missed within 72 hours, it can be given up to 28 days of delivery with some benefit [9,10].

Each of these: Pre-eclampsia/eclampsia, Rhesus Negative blood group and Sickle cell disease confer high risk status to any pregnancy [11,12]. We are hereby reporting a rare situation where this trio were present in a single patient. Such a case is rare and has not been reported to the best of our knowledge.

Case Report

AJ was an 18 year old paraO^{+0} fashion designer who presented to the labour ward of Central Hospital Benin City, Edo State, Nigeria on 9th of April, 2020 at 12:30pm with a history of convulsion of one day duration. Her Gestational Age was 36weeks and two days. She was unsure of her last menstrual period but said sometime first week of September,2019. She was single and a known Sickle Cell Disease patient diagnosed at childhood.

She was booked in our facility for the index pregnancy at 27 weeks gestation and had three antenatal care (ANC) visits, the last visit being on the day of admission. Investigations done at booking confirmed her haemoglobin phenotype homozygous HbSS using haemoglobin electrophoresis, her blood group was A RhD negative. Virology tests for Hepatitis B surface antigen and Human Immunodeficiency Virus were negative. Random Blood glucose was 78mg/dl, VDRL was not reactive while urinalysis was normal. She had two doses of intermittent prophylactic therapy for malaria as well as 1 dose of tetanus toxoid injection. She was once admitted at the index pregnancy on account of vaso-occlusive crisis, upon which she received two units of blood transfusion and was also treated for malaria using parenteral artemether.

On clinical examination at presentation, she was very restless, afebrile, not pale, not jaundiced and there was no bilateral pitting poedal oedema. The pulse rate was 92beats per minute and Blood Pressure was 200/100 mmHg. The respiratory rate (RR) was 24cycles per minute and chest was clinically clear. The abdomen was gravidly enlarged and fundal height was 35cm corresponding with her gestational age of 36weeks 2days. . A singleton foetus was palpated, lying longitudinally and in cephalic presentation. She was having 2 in 10 uterine contractions lasting 30seconds each. There was no foetal heart sound heard. Pelvic Examination revealed a normal vulva and vagina. Cervix was 4cm dilated, soft, and central in station 0-1 with membranes bulging. An impression of active phase labour in a known Sickle Cell Disease patient with eclampsia and intrauterine foetal death was made.

She was admitted forthright, intravenous accesses secured and blood samples collected for laboratory investigations namely, Full Blood counts, Blood grouping and cross matching, Electrolytes, Urea and creatinine estimations. Her haematocrit on admission was 21% and total white cell count of 30,500 per mm^3 with differential neutrophilic leucocytosis of 87%. Urinalysis and serum electrolytes were

normal.

Intravenous Labetalol 25mg stat dose was given on account of her elevated blood pressure (200/100 mmHg). Magnesium sulphate was commenced using the Pritchard regimen: Loading Dose of 14g-4g given intravenously slowly for 10-20 minutes and then 5g into both buttocks. Maintainance dose was 5g into alternate buttocks 4 hourly until 24 hours after delivery. She was also commenced on intravenous Amoxycillin/Clavulinic acid and metronidazole 1.2g and 500mg, respectively. Intravenous Pentazocine given 6hourly provided an appreciable level of analgesia.

On further review, her blood pressure had improved to 150/90 mmHg. Artificial rupture of membranes was done and labour was closely monitored in the succeeding hours. She subsequently was delivered of a macerated stillbirth at 11am on 10/04/2020. She was then moved to maternity ward later in the day in a semi-conscious state and continued on antibiotics and other prescribed medications.

Haematologists were invited to review on 5th day on admission and four days postpartum. They recommended a hypertransfusion plan, for which the patient was to be transfused with patient's group specific (Blood group A RhD negative) donor blood instead of blood group O and the donor's blood preferably of HbAA phenotype. At 21 days on admission, she had received a total of 5 units of blood (all were blood group O RhD negative) The haematocrit was 16% and total white cell count was 17,000 per mm^3. Culture of endocervical swab and urine yielded growth of Staphyloccocus aureus and Pseudomonas species, respectively, which were sensitive to ciprofloxacillin and ofloxacin; although she had been continued on oral Cefixime and metronidazole after the initial IV preparations. In addition, patient developed urethra-vaginal fistula (UVF). She was lost to follow up in Central hospital.

Discussion

Patient is the 3rd of 4 children. She had secondary level of education and resides with her mum and four siblings in a rented apartment. Mother is separated from her father and she is a petty trader. Her consort is an artisan who had hands off her medical treatment since the first admission when she had vasoocclusive crisis.

Notable problems in this pregnant woman were her haemoglobin phenotype of sickle cell anaemia with a rhesus negative blood group and the co-morbid eclamptic state. She was also primiparous, hence increasing her pregnancy risk.

This patient was booked at 27 weeks and had three antenatal visits prior to the day of admission. At booking and antenatal visits her clinical features, blood pressure and urinalysis were devoid of signs of Pregnancy-Induced Hypertension (PIH) only for her to present with eclampsia and intra-uterine foetal death at 36 weeks. A case of atypical pre-eclampsia without elevated blood pressure and asymptomatic has been reported [13]. If this patient had elevated blood pressures during antenatal visits then the case would have been straightforward and early decision to intervene taken, this case demonstrates the need for future studies and research in this area. Our case was also similar to another case of a primiparous Japanese woman who suddenly developed convulsions and foetal death with no history of hypertension [14]. Our case apart from being primiparous, was also having sickle cell anaemia. The latter is a predisposing factor to pre-eclampsia as well as primiparity, both of which are known predisposing factors to pre-eclampsia/eclampsia [6,15-17]. In fact, some authors have dubbed pre-eclampsia a disease of ''primiparity'' [6,15].

The blood group of our patient played a very important role in her management. She was blood group A Rhesus Negative. To avoid rhesus isoimmunisation she was transfused with rhesus D Negative blood [18]. She received a total of 5 units of O rhesus D negative blood but rather than her Packed Cell Volume appreciating upwards from pretransfusion haematocrit of 21%, the haematocrit dropped to 16%. A good number of reasons could be responsible for this worsening anaemia despite blood transfusions. Whenever blood group O is transfused to non-O individuals (blood groups A,B or AB), there is possibility of the recipient's red blood cells being destroyed by immune anti-A and anti-B haemolysins in the blood group O donors. Studies by Nwagu et al. have shown that the prevalence of haemolysins among blood group O donor population in Benin City was as high as 45.2% [19]. This was the reason the haematologists recommended blood group A (the patient's blood group) should be transfused, but the blood group A RhD negative was not readily available. Another reason was the blood transfused could be anaemic and hence would not raise the haematocrit. Anaemia among blood donors has been estimated between 7.3% [20] and 31.44% [21]. About 95% of Nigeria's source of blood for transfusion is mainly from commercial donors and blood vendors [22] where blood donation criteria may not be strictly followed and adhered to.

Another reason for the persistence in anaemia could be as a result of the ongoing infections. Despite being on antibiotics for more than one week, there was laboratory evidence of ongoing infections: leucocytosis and culture of micro-organisms from specimen samples. Urine culture in this our patient yielded Staphylococcus aureus which is a gram-positive organism. There is a strong association between anaemia and gram positive organisms, [23,24] especially Staphylococcus aureus [25]. A study once showed

that among patients with *Staphylococcus aureus* infection, 56% had anaemia [25]. Our patient received 5 units of blood which were not strictly HbAA blood without HbS-gene. This could also be another contributory factor to non-correction of anaemia despite 5 blood units given. Recent study by Nwagu and Omokhua showed a more remarkable improvement in haemoglobin concentration when a sickle cell anaemia patient is transfused with HbAA blood [26].

Another unpalatable outcome in our patient is the development of obstetric fistula, Urethra-vaginal fistula (UVF) 24days post-Partum. Prolonged obstructed labour has been known to cause VVF in more than 80% of patients in Nigeria [27-30] and 94.2% in Ghana[31]. Though there was no history of prolonged labour from our patient, it is most likely she has been in labour for days at home before coming to hospital [30].

Challenges Encountered

Financial constraints were a big challenge. The needed blood group (group A RhD Negative) without Hamoglobin S gene (HbAA) were not readily available and very expensive. Unmarried status predisposes to lack of emotional support and poor or no economic status. Provision of essential medicines and blood transfusion were by good Samaritans. Prior to her pregnancy, she has not had optimal haemoglobin level.

Conclusion

High risk pregnancies are likely to result to perinatal morbidity and hence requires extra care. This patient had a combination of multiple risk factors namely, primiparity, sickle cell anaemia, rhesus D negativity and eclampsia. We have demonstrated the very poor outcome of this patient which included intrauterine fetal death, persistence of anaemia despite blood transfusions, persistence of infections despite use of antimicrobial agents and development of obstetric fistula (UVF). In patients with multiple risk factors such as this, we recommend a more aggressive approach in both antenatal care and immediate post partum period. This requires the combined efforts and cooperation of all stakeholders including the healthcare providers and caregivers, the patients and her relatives. This case brings to fore the need for a proper health care financing to be in place in Nigeria where the poorest of the poor will have access to healthcare. Foundations and special endowment is advocated for sickle cell sufferers. The need for the girl child empowerment, comprehensive adolescent sexuality education should be emphasized to stem the tide of unwanted pregnancies and its sequelae. Also embedded in this comprehensive education is the place of family planning/ contraception.

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