Coombs Negative Hemolytic Anemia of Unknown Origin in Pregnancy

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Abstract

Hemolytic anemia is very common during pregnancy especially in malaria endemic areas and it is usually an autoimmune condition. Coombs negative or idiopathic hemolytic disease during pregnancy is very rare and it has not yet been described in sub-Saharan countries.

A 34-year-old grand-multiparous woman was referred at our facility at a gestation age of 22 weeks with features of severe anemia in pregnancy, and a history of receiving a blood transfusion (seven units). Several investigations including a Coomb's test were done. However, there were hardly any derangements, except for initial low hemoglobin. Coombs negative haemolytic anaemia of unknown origin was the final concluded diagnosis. She was treated with a course of glucorticoids, hematemics and a total of 36 units of blood transfusion. She finally delivered a premature baby at 35 weeks of gestation. She recovered completely during puerperium and was discharged the seventh day postpartum with a hemoglobin of 10g/dl. She was lost to follow up.

Coombs Negative Hemolytic Anemia in pregnancy is likely to respond to blood transfusions in conjunction with glucocorticoid therapy.

Keywords: Coombs negative; Hemolytic anemia; Pregnancy

Background

Hemolytic Anemia is very common during pregnancy especially in malaria endemic areas [1]. It often associated with Tropical Splenomegaly Syndrome (now commonly known as Hyper-Reactive Malarial Splenomegaly), which is an autoimmune phenomenon that follows episodes of malaria in the past [2]. Very few cases of Coombs Negative Hemolytic Anemia have been reported in literature [3,4]. This condition has not yet been described in Sub-Saharan Africa; hence we are presenting the first such case.

Case Report

A 34-year-old grand multiparous Tanzanian woman, at 22 weeks gestation, was referred from a nearby health facility due to difficulty in breathing, awareness of heart beats, and easy fatigability for over a period of one month. She denied a history of bleeding, or ruptures of membranes, and has perceived fetal movements normally. Her past gynecologic and obstetric history was significant for a history of six previous vaginal deliveries and a Caesarean section in her last childbirth. She also gave a history of a spontaneous abortion (of a five months pregnancy) after her last childbirth, the cause of which was not established. She received seven units of blood (with no improvement) before being referred to our centre.

She denied a history of using any medications prior to illness. Family and social history was unremarkable for bleeding disorders or a history of recurrent blood transfusions.

On physical examination; she was noted to be pale and mildly jaundiced with a bilateral pitting pedal edema. There was no sternal tenderness; neither were there any skin lesions or peripheral lymphadenopathy.

Respiratory findings revealed bibasilar crackles. Her cardiovascular assessment showed a pulse rate of 78 beats per minute, a blood pressure of 110/80 mmHg, and a functional ejection systolic murmur at the apex.

Her abdomen was distended with a uterine fundus equivalent to 24 weeks gestation and a sub-umbilical midline incision scar. Hepatosplenomegaly was noted. The fetal heart rate was 134 beats per minute detected by a pinnard fetoscope.

Investigations were done and the following are the results; Hemoglobin level on admission was 2.76 g/dl.

Blood group "B", Rhesus positive.

Blood slide was negative for malarial parasites.

Her stool sample was negative for parasites and occult blood.

Urine dipstick was negative for leucocytes, red blood cells and schistosome ova.

Complete Blood Count showed hemoglobin of 4.9g/dl, packed cell volume (PCV) 16.8%, Mean Cell Volume (MCV) 87.0 fl, Mean Cell Hemoglobin (MCH) 25.7 pg, Mean Cell Hemoglobin Concentration (MCHC) 29.5 gr/dl, White Blood Cell (WBC) count of 3.5x10^9/l, with normal differentials. Platelet count (PLT) was 149x10^9/l, and Reticulocyte Count was 1.2%.

Total Bilirubin was 69.22umol/l, direct bilirubin 21.56umol/l, Lactate Dehydrogenase (LDH) 140 IU/L, Serum levels of Creatinine and Liver Transaminases were within normal range.

The Coombs Test and Rheumatoid Factor were negative.

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The APGAR score was 7 and 10 at the 1st and 5th minute respectively.

She entered labour at 35 weeks of gestation and her hemoglobin was 9 g/dl by then. She gave birth to a premature female baby of 2.2 Kg whose weight was 788 grams ±118 grams and the Gestation Age (GA) was estimated to be 25 weeks with an amniotic fluid index of 12 cm. The placenta was located high anteriorly. Sonography of the abdomen was significant for mild splenomegaly.

A later scan at 28 weeks of gestation age revealed an estimated average gestation age of 28 weeks ± 2 days. Scan at GA of 33 weeks showed an estimated fetal weight of 2.1 kg with an amniotic fluid index of 13 cm.

She was started on daily Blood transfusions for several weeks with no improvement of her hematocrit. A decision was then made to start her on oral Prednisolone. The hemoglobin started to increase with each unit of blood transfused and she gradually became free of symptoms. She entered labour at 35 weeks of gestation and her hemoglobin was 9 g/dl by then. She gave birth to a premature female baby of 2.2 Kg whose APGAR score was 7 and 10 at the 1st and 5th minute respectively.

The Peripheral Blood Smear showed spherocytes.

The Bone Marrow aspirate showed leucocytosis with normal erythroid and myeloid precursors (Figure 1).

An initial obstetric ultrasound scan revealed a single live fetus in utero with a biparietal diameter of 63mm equivalent to (25weeks ± 15 days), abdominal circumference of 208 mm equivalent to (25weeks ±15 days), femur length of 45mm (24weeks ± 15 days), the estimated fetal weight was 788 grams ±118 grams and the Gestation Age (GA) was estimated to be 25 weeks with an amniotic fluid index of 12 cm. The placenta was located high anteriorly. Sonography of the abdomen was significant for mild splenomegaly.

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The patient was re-evaluated 5 days after delivery and all biochemical tests had returned to normal. The hemoglobin level increased to 10 g/dl, and the baby was doing fine. The mother and child were both discharged after a week. From Admission to delivery, this patient had received a total of 36 units of Blood. Unfortunately she was lost to follow-up.

Discussion

Anemia is one of the leading causes of maternal and perinatal deaths in pregnancy and puerperium [5-8]. Hemolysis is one of the rare several causes of severe anemia in pregnancy worldwide [6,7].

In malaria endemic areas, hemolytic anemia can be prevalent during pregnancy, and the mechanism is thought to be related to an autoimmune response resulting into a phenomenon called the Tropical Splenomegaly Syndrome (TSS), currently referred to as Hyperactive Malarial Splenomegaly [1,2,9]. Patients will usually present with profound anemia, jaundice, a massive splenomegaly and pancytopenia with recurrent infections [2,9]. These features were present in our patient, however, a negative coombs test and the absence of massive splenomegaly and pancytopenia proved otherwise [9].

Coombs Negative Hemolytic Anemia (Idiopathic Hemolytic Anemia) is very rare in this population and its management is unclear. Although the patient presented with typical features of hemolytic anemia, other causes of anemia must be ruled out. Anemias may have a multifactorial cause at times [1,10]. A blood smear is useful to exclude malaria or even Kala-Azar while a stool analysis is used to exclude parasitic causes. Peripheral blood smear and a bone marrow aspirate/biopsy are important in ruling out myeloproliferative disorders. Complete Blood Counts (CBCs) are useful in excluding other similar conditions such as Evans Syndrome which is characterized by thrombocytopenia and autoimmune hemolysis [11].

As previously stated, management of such patients is challenging and controversial with scarce literature on the topic [3,12]. Some authors preferred steroid therapy, the mechanism being unclear [3,13]. Additionally, the role of splenectomy is also unclear as this was used in some cases related to autoimmune hemolytic disorders [2].

Multiple blood transfusion and iron supplements appeared to be an important part of the treatment [14]. Whether pregnancy has any role to play in the etiology remains unclear, however, the fact that this patient improved at the end of her pregnancy cannot be denied. A similar scenario can be seen for autoimmune related hemolysis during pregnancy, this has a better maternal outcome and usually resolves during puerperium [3,4,12,15,16].

The Preterm labour and a low birth weight are among the reported complications of severe anemia in pregnancy [14,17]. Maternal outcome is very unpredictable if the pregnant patient is allowed to go into labour with severe anemia [5,18]. Anemia may severely affect fetal outcome, hence serial obstetric ultrasound were done to monitor intrauterine growth [5,18,19].

Conclusion

Severe anemia in pregnancy requires a tireless diagnostic and treatment approach if optimum maternal-fetal outcome are to be realized. Idiopathic Hemolytic Anemias, including those with a negative Direct Antiglobulin Test, respond to gluco-corticoid therapy. Blood transfusion is mandatory in cases of severe anemia in pregnancy with unknown or known causes to improve maternal and fetal outcome.
Competing Interests

"The author(s) declare that they have no competing interests".

Authors’ Contributions

"SD received the patient and did initial work-up, did literature review, wrote the initial manuscript and reviewed all other subsequent manuscripts. JM and HJ were consulted and involved in management of this patient including obtaining biopsy, both did literature review and revised the manuscripts. AM and ANM were consulted for management of this patient and contributed to review of literature. PR performed the histological examination of the bone marrow, and contributed in writing the manuscript. All authors read and approved the final manuscript”.

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