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Case Report

HELLP syndrome presenting as malaria in a post-menopausal Invitro fertilisation conceived pregnancy - A Case Report

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ABSTRACT

HELLP syndrome is a pregnancy disorder associated with severe maternal morbidity and mortality. The syndrome can present nonspecific symptoms and the diagnosis may be difficult to be established, resulting in delay of treatment. We present a 57-year-old postmenopausal, chronic hepatitis B positive woman, who achieved live birth of twins following donor-oocyte in vitro fertilization (IVF). She had preeclampsia complicated with Haemolysis, Elevated Liver enzymes, and Low Platelet count (HELLP) syndrome, which masqueraded as malaria in pregnancy. HELLP syndrome may present as malaria in pregnancy especially in malaria endemic areas; so as high index of suspicion and proper laboratory investigations will usually confirm the diagnosis so as to prevent unnecessary delay in management.

Key words: in vitro fertilisation, post-menopause, HELLP syndrome, malaria.

Introduction

HELLP syndrome is a clinical condition that leads to hemolysis, elevated liver enzymes and low platelets, associated with preeclampsia in a pregnant woman. The syndrome frequency varies from 0.5 to 0.9% pregnancies and manifests preferentially between the 27th and 37th week of gestation.[1]

The pathogenesis of the syndrome is unclear but classical presentation include pain in the right upper quadrant of the abdomen or epigastric pain, nausea and vomiting. However, this syndrome can present nonspecific symptoms and the diagnosis may be difficult to be established. Laboratory tests and imaging exams are essential for differential diagnosis with other clinical conditions.[2]

Our patient presented with symptoms of malaria and the diagnosis was only made after laboratory test results revealed the condition.

Case report

Mrs. A. A. was a 57-year-old G3P1+1(1A), 13 years post-menopausal, chronic hepatitis B positive woman, who registered for antenatal care at the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Nigeria, at an estimated gestational age of 14 weeks. Her last confinement was in 1998. She had a complete spontaneous miscarriage in 2000. Prior to attaining menopause in 2007, she had a seven-year history of secondary infertility. She had conceived index pregnancy via IVF of her husband's sperm with anonymous donor oocytes, at a private hospital in Nigeria. Three embryos were transferred into her endometrial cavity on the 13th of August 2019. Pregnancy was diagnosed by a positive serum beta human chorionic gonadotrophin (β-hCG) two weeks after embryo transfer. Pelvic ultrasound scan done at estimated gestational age of seven weeks showed two gestational sacs. Her expected date of confinement was on the 6th of May 2020. She had luteal phase support with dydrogesterone (Duphaston®).

At booking, her blood pressure was 110/60 mmHg and urinalysis was negative for protein. Hepatitis B surface antigen (HBsAg) test was positive. She had been diagnosed hepatitis B positive during evaluation for IVF. Hepatitis B panel done was suggestive of a chronic hepatitis B infection. She was negative for the hepatitis B envelope antigen (HBeAg). Other booking investigations and clinical examination findings were within normal limits. Ultrasound scan revealed a dichorionic diamniotic twin gestation. She was commenced on daily low dose aspirin for prevention of preeclampsia.

Except for threatened miscarriage at 13 weeks' gestational age, her pregnancy was uneventful, with normal blood pressure and urinalysis, until an estimated gestational age of 36 weeks plus two days, when she presented with fever, headaches, body pains and abdominal pains, which was suggestive of malaria. A malaria blood smear was performed and was positive for *Plasmodium falciparum*. Her blood pressure at presentation was 120/80mmHg. She was admitted and commenced on antimalarial, without significant improvement of her symptoms and clinical condition.

Further evaluation however revealed 2+ of protein on urinalysis. A complete blood count revealed a packed cell volume of 33% and platelet count of 56,000 cells/mm^3. Liver function tests revealed elevated liver enzymes with AST of 68IU/L and ALT of 49IU/L. Both of these were suggestive of HELLP syndrome.

Her blood pressure remained within normal limits until about 24 hour prior to delivery when it became elevated. A repeat platelet count after transfusion with two units of platelet concentrate was 71,000 cells/mm^3. Obstetric ultrasound scan was normal and fetal monitoring detected no signs of distress. Patient was reviewed by the haematologist and anaesthesiologist.

She subsequently had Caesarean section under general anaesthesia and endotracheal intubation, with rapid sequence induction, and was delivered of live male twins, weighing 2.12kg and 2.45kg respectively, with Apgar scores of 5 and 6 respectively at the first minute, and 8 for both babies at the fifth minute. The babies were admitted into the neonatal intensive care unit (NICU) on account of moderate and mild birth asphyxia respectively and low birth weights. Hepatitis B immunoglobulin (HBIg) and hepatitis B vaccine were given to the neonates within 12 hours of delivery.

Intra-operatively, following delivery of the babies, despite 100 mcg of intravenous carbetocin, she had uterine atony and suffered primary postpartum haemorrhage, with estimated blood loss of 1,300 ml, necessitating a subtotal hysterectomy, which was performed promptly. She had two units of platelet concentrate and a unit of whole blood transfused intra-operatively. A repeat CBC on the first postoperative day revealed a packed cell volume of 34% and platelet count of 91,000 cells/mm^3. Repeat clotting profile was normal. By the third postoperative day the platelet count had normalized at 163,000cells/mm^3, the liver

enzymes were also within normal limits and she was discharged on the fourth postoperative day in clinically stable condition. Her babies were also doing well.

Discussion

Our patient was 57 years old and her pregnancy was complicated by preeclampsia with HELLP syndrome, necessitating Caesarean delivery of low birth weight babies with mild/moderate birth asphyxia. She also suffered primary postpartum haemorrhage resulting in a prompt and life-saving subtotal hysterectomy.

The HELLP syndrome in our patient was not typical. She presented at 36 weeks' gestational age with malarial symptoms and normal blood pressure. Her blood pressure and urinalysis had remained normal since she booked pregnancy at 14 weeks' gestational age. Although HELLP syndrome is most frequently associated with severe preeclampsia, about 15-20% of patients (like our patient) with HELLP syndrome do not have antecedent hypertension or proteinuria.[3] Our patient's malaria blood smear was positive for Plasmodium falciparum, and she was commenced on antimalarial drugs. Further evaluation on admission however revealed thrombocytopenia and elevated liver enzymes, both features of HELLP syndrome. Whereas there are reports of malaria masquerading as HELLP syndrome,[3,4] in these cases the HELLP-like syndrome resolved following the successful treatment of the malaria but in our patient, HELLP syndrome masqueraded as malaria with the condition persisting until the delivery of the woman despite antimalarial therapy. This case also documented the fact that women getting pregnant in advanced age may not present in the typical way when affected by known pregnancy complications, hence, a high index of suspicion is needed.

In Africa, the consequences of infertility is so grave that women would do anything in order to have a child.[5] Assisted reproductive technology was hitherto unavailable to women in Africa due to the cost implication,[6] but it is now widely becoming available and older women are accessing care with the associated complications. Our patient was a 57-year-old woman.

A study that stratified maternal age demonstrated that mothers older than 49 years had statistically significant more maternal morbidity, including risk of diabetes, cardiac disease, and preeclampsia, as well as increased neonatal mortality and morbidity, compared to their younger cohort who are 49 years or younger.[7] Other risks include higher rate of miscarriages, fetal abnormality, preterm delivery, lower birth weight, higher rate of Caesarean sections and even maternal death.[8]

As recommended in guidelines by the United Kingdom's National Institute of Health and Clinical Excellence (NICE), the American Society for Reproductive Medicine and the European Society of Human Reproduction and Embryology (ESHRE), infertile couples seeking assisted reproduction treatment should be checked for hepatitis B virus (HBV) serostatus.[9,10] Reasons for baseline screening in these cohorts are for the prevention of vertical transmission and laboratory safety. Between 80% and 90% of children born to mothers who are both HBsAg and HBeAg positive will become infected. Transmission falls to less than 25% if HBeAg is negative,[11] like in our patient. Administering HBIg and hepatitis B vaccine within 12-24 hours of delivery to babies born to HBsAg-positive mothers is 85-95% effective in preventing both HBV infection and the chronic carrier state.[11,12] Our patients' babies were administered HBIg and hepatitis B vaccine within 12 hours of delivery.

From an ethical point of view, there is no sound reason to advise against IVF treatment in a woman chronically infected with HBV, since in similar circumstances, a spontaneous pregnancy is thought to be acceptable. Hepatitis B infection is therefore not a contraindication to IVF.[7] It is for this reason that our patient, who was diagnosed HBsAg positive while being evaluated for IVF was not denied IVF treatment. Pregnancy and live birth rates following IVF treatment in HBV-seropositive women are not significantly different from those of their negative counterparts.[10] Our patient despite being chronically infected with hepatitis B had a

successful pregnancy which terminated in live births following IVF treatment.

Conclusion

Pregnancies in advanced age is associated with a myriad of medical, social and ethical concerns. The medical complications may not present in the typical fashion, complicating the management of such cases. The Association for Fertility and Reproductive Health (AFRH) recommends a maximum age of 54 years for women undergoing assisted reproduction procedures[13] but this is yet to be generally accepted by practitioners. Women aged 40 years and above should be properly counselled on the associated risks and possible complications of pregnancy at advanced age. In the event of life threatening complications as was the case in our patient, a multidisciplinary approach with timely interventions is lifesaving even in resource-constrained settings like ours. Adherence to regulatory guidelines by practitioners would guarantee optimal maternal and fetal outcomes following IVF.

Consent

The patient's written consent was obtained for publication of this case report after she was assured that the publication will be anonymous with no direct link to her.

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