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Case Report

Malaria in Pregnancy

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Abstract

Malaria is a potentially life-threatening disease that is transmitted by the bite of an infected Anopheles mosquito. Five known species of genus Plasmodium infect humans: Plasmodium vivax, Plasmodium ovale, Plasmodium Knowlesi, Plasmodium Malariae and Plasmodium falciparum. Malaria infection during pregnancy is a significant public health problem with substantial risks for the pregnant woman, her fetus and the newborn child.. The symptoms and complications vary according to malaria transmission intensity in the given area and the individual's level of acquired immunity. Presented below is a case of a 26-years old primigravida, who returned to the UK from Nigeria after one week presenting with a 24 hour history of abdominal pain, nausea, vomiting and signs of sepsis. During her hospitalization, despite being treated for sepsis, the patient's overall condition did not improve, therefore suspicion for malaria became very questionable. In consideration of the patient's history and clinical presentation; a thorough investigation was to take in effect for this possible infection. Once diagnosis of malaria was confirmed, the appropriate treatment was administered.

Keywords: Malaria; Pregnancy; Plasmodium falciparum

1. Introduction

Malaria is an infectious disease caused by transmission from the infected Anophele mosquito which carries the plasmodium parasite. Once bitten by the mosquito, the parasite is released into the bloodstream causing a vicious cycle attacking hepatic and red blood cells, at times leading to fatal results if not treated adequately and promptly [1]. In endemic regions, pregnant women, children and immunosuppressed persons are the most susceptible for contracting this disease. According to WHO, there were approximately 11 million pregnant women infected with malaria in sub-Saharan Africa. Globally, malaria-related deaths in children were about 70%. Of the 5 species of malaria, plasmodium falciparum causes greater morbidity and mortality (both maternal and fetal) however, there is increasing evidence that P vivax is not as benign as previously thought [2]. Non-specific symptoms, like headaches and chills are usually caused by all plasmodium species resulting in uncomplicated malaria [3]. The adverse effects of malaria in pregnancy are caused by systemic infection (miscarriage, stillbirth, preterm birth, maternal and fetal mortality) and from paratitation (fetal growth restriction, fetal and maternal anemia, susceptibility of the infant malaria [4]. Placental parasitemia can occur in >90% of all placental red blood cells, causing parasitic sequestration and replication in the placenta. Sequestration is a characteristic feature of falciparum malaria and is not known to happen in malaria due to species of P. vivax, P. malaria, and ovale [5]. In endemic areas a high prevalence of neonatal parasitemia has been reported, with majority of the infected newborns being asymptomatic; however, the mortality was found to be higher in the infected and symptomatic newborns. Onset of symptoms such as fever, anorexia, lethargy, anemia, and hepatosplenomegaly, anywhere between day 1 of birth and months following delivery, raises concern for congenital malaria (due to transplacental contamination of the fetus frequently reported in 8-33% of pregnancies from both endemic and non-endemic areas).

As a result, this causes a decreased nutrient transport to the fetus leading to low birth weight and a higher risk for infant mortality and morbidity. Pregnant women are 3 times more likely to develop this severe disease, even if previously exposed and infected. It is also most common among nulliparous women compared to multiparous women. Diagnosis is made through clinical findings and laboratory testing. In pregnant women with pyrexia of unknown origin and history of travel to an endemic area with a high prevalence of malaria; diagnosis can be confirmed through a blood smear [6]. Once a diagnosis of malaria is confirmed, treatment with antimalarial drugs should be initiated immediately. Misdiagnosis and delay of treatment are the most common reasons mentioned for death from malaria in Europe and USA. Artesunate IV is considered first line therapy in falciparum severe malaria [7]. Uncomplicated falciparum malaria can be treated with oral quinine and clindamycin, and non-falciparum malaria with oral chloroquine [7]. Additional treatment involves supplemental oxygen, intravenous fluid hydration, blood transfusions if and when necessary [8]. Ongoing monitoring and regular antenatal care is essential, along with prophylactic measures as indicated.

2. Case Report

A 26-year-old primigravida at 35 weeks of gestation, presents with complaints of a one day history of abdominal pain and vomiting. Patient had returned to the UK from where she had an antenatal ultrasound showing a viable fetus. Initial evaluation revealed mild pallor, icterus, tachycardia (HR 120 bpm), pyrexia (TMAX 100.5^{o}F) and proteinuria (2+ on urine dipstick). Modified Early Warning Score (MEOWS) was 10. The rest of the examination was normal, her abdomen was soft and nondistended, coinciding with her gestational age. She had no signs of hemolysis, hepatomegaly or splenomegaly. Per speculum examination was normal. High vaginal swab and throat swabs were obtained and sent for testing; both resulting negative.

Laboratory investigations on admission showed hyperbilirubinemia (3.1 mg/d/l), hyperalbuminemia, elevated liver enzymes (ALT 869 U/L, Alkaline phosphatase 312 U/L), hypokalemia (3.0 mEq/L), mild hyponatremia (132 mEq/L), and increased CRP. Serum creatinine was of 52 U/L and serum uric acid levels of 325 mg/dl. Other findings included ketonuria, proteinuria, and bilirubinuria. Hemoglobin and platelets were reported as 11.7 g/dl and 204,000/µL respectively, while blood and urine cultures were negative. CTG (cardiotocography)was reassuring with Fetal Heart Rate 132 bpm, with normal variability and no deceleration. Antenatal USS showed normal amniotic fluid volume and normal doppler study of the umbilical artery. It confirmed a posteriorly located placenta not low lying. Initial treatment for suspected urosepsis was begun with evaluation for suspected acute hepatitis as well. Ultrasound of the liver was insignificant and showed two small hyperechoic lesions consistent with benign hemangiomas measuring 8mm and 3mm in the right lobe.

Over the next two days, the patient continued to have abdominal pain, then subsequently developed back pain, dyspnea, generalized headache, and vaginal pressure; with lab results showing abnormal levels of liver enzymes. Cardiotocography revealed in 2 occasions prolonged decelerations of the fetal heart rate, which quickly were returned to baseline. Subsequently, she developed very dark urine with persistent tachycardia, tachypnea, and spiking temperatures (104^{o}F). Chest X-ray showed no abnormalities. On further history, the patient revealed that she had been diagnosed and treated for malaria at 15 weeks gestation of the current pregnancy and reported a history of multiple prior malarial episodes. An immediate malarial screen was ordered, confirming falciparum malaria with parasitaeimia 5.7%.

Public Health was informed, microbiology and hematology departments were contacted. On repeated Cardiotocography, unprovoked repeated deep decelerations were traced and a decision for grade 2 emergency cesarean section was made. Oral Riamet (20 mg artemether and 120 mg lumefantrine) was administered as per advised regime 0h, 8h, 24h, 36h, 48h, and 60h till the time that intravenous artesunate would be available in the unit. Once the baby was born and diagnosed with congenital malaria treatment and plan of care were transferred to the neonatal team.Following the Cesarean section, the patient’s condition significantly improved with treatment. 24 hours later the MEOWS score was resulted as zero.

3. Discussion

The severity of the presentation of malaria depends mostly on the endemicity of infection in an area. Infants, children <5 years old, pregnant women and immunocompromised patients, non-immune migrants, mobile populations and travellers are at the greatest risk of developing severe disease usually caused by *Plasmodium falciparum.* In endemic areas, women usually develop some immunity to malaria by the time they reach reproductive age, however; there are some patients who might develop placental malaria despite the fact that the peripheral blood films are negative. This is influenced by many factors including maternal age, gravidity, using prophylaxis, nutrition, genetics, immunity to malaria, as well as parasite genetics and transmission rates [9, 10].

Patients are usually symptomatic around 10–15 days after the infective mosquito bite. They usually present with fever (most frequent), headache, and chills. These are nonspecific symptoms that make early detection of malaria a problem especially in non-endemic areas, hence the delayed diagnosis of malaria in this patient. *P. falciparum* malaria is a medical emergency since it can progress to severe illness and leading to death [9].

During pregnancy, the immune system shifts to Th2 response making pregnant women at increased risk of infection by malaria regardless of previous infections status. Moreover, malaria infected RBCs express VAR2CSA, which is a specific membrane protein that was found to enhance RBCs accumulation in the placenta. Both mechanisms were related to increased susceptibility to complications like severe anemia, acute kidney injury, consumption coagulopathy, shock, seizures, hyperparasitemia, hypoglycemia and pulmonary edema. These complications can be harmful to the fetus causing preterm labor, fetal acidosis, and intrauterine fetal demise [11, 12].

Sepsis is a complication of severe malaria esp. *P. falciparum* and is associated with increased mortality. This patient was suspected to have sepsis on presentation and treatment with antibiotics was initiated within the first hour of admission as per sepsis protocol. Some studies indicated that 2.5% of patients with *P. falciparum* infection may develop either mild liver injury or a more severe form with hepatomegaly and massive hepatic necrosis [13]. Renal failure and peripheral circulatory failure are frequent events leading to mortality in pregnant and non-pregnant patients. Renal injury could be caused by significant hemoglobinuria.

Acute pulmonary edema usually is a concerning issue occurring post-partum due to autotransfusion of placental blood rich in parasite infested red blood cells and sudden rise in peripheral vascular resistance after delivery. Acute pulmonary edema leads to fatal complications and is found to be caused by the increased capillary permeability [14]. This patient improved within 24 hours of treatment initiation. Blood glucose was monitored regularly to detect hypoglycemia occurring in malaria patients since infection symptoms can mask hypoglycemia symptoms.

The effects on infants may differ by gestational age. Studies have shown that early infection (i.e. during 1st and 2nd trimester) is more deleterious than late infection. This is thought to be due to disruption of placental development

and function.Congenital malaria is one of the rare complications that some studies reported. The mean of symptoms onset was 5.5 weeks with anemia, low platelets, hepatosplenomegaly [15]. Infant mortality could be related to low birth weight and premature delivery. Placental infection has a significant association with infant's death. About 75,000–200,000 infant deaths in the sub-Saharan region were estimated to be caused by malaria infection during pregnancy [16]. Infants born to mothers who were exposed to multiple malaria infections or had placental malaria had a higher risk of impaired growth during the first year of life. In addition, mothers who were infected once or were treated early had no significant association with impaired growth [17]. This G1P0 had a cesarean section delivery without any maternal complications. Both the mother and her baby were treated and fortunately had a positive outcome. Follow up was done as per national and regional guidelines.

4. Conclusion

Malaria should be suspected in all patients who visited or are returning from any epidemic areas during pregnancy. Early detection of malaria infection may lead to good outcomes with ample and adequate treatment; once confirmed following the CDC and WHO treatment protocols. Recommendation for prophylaxis is required for pregnant women traveling to endemic areas due to these severe manifestations. The choice of prophylaxis depends on the area where there are chloroquine-sensitive or resistant *P. falciparum* strains. Chloroquine is advised to be used for sensitive strains and mefloquine used in areas of resistant strains. Both medications were shown to be safe during pregnancy.

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