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Case Report

Obstetrics and Gynaecology Section

Plasmodium vivax Induced Acute Respiratory Distress Syndrome – A Diagnostic and Therapeutic Dilemma in Preeclampsia

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ABSTRACT

Malaria during pregnancy can cause various feto-maternal complications. Life threatening respiratory involvement is rare with vivax malaria but common with *Plasmodium falciparum*. In most of the cases severe respiratory involvement occurs, after beginning of anti-malarial treatment. We are reporting a case which involved a diagnostic and therapeutic challenge, as the pregnant woman with severe preeclampsia developed acute respiratory distress, actually caused by *Plasmodium vivax*.

Keywords: Complicated malaria, Diagnostic dilemma, Therapeutic challenge

CASE REPORT

A 27-year-old woman, G2P1L1 at 36 weeks gestation presented to our hospital with complaints of fever with chills and rigor since five days. There was no prior history of any obstetric or medical problems. She underwent lower segment caesarean section four years back for breech presentation.

On examination, she was conscious and oriented, having mild pallor and icterus. Her temperature was 102.6°F, PR 128 bpm, RR 18/min, BP 146/94 mmHg, O_2 saturation 100% at room air. Chest was clear with normal vesicular breathing and cardiovascular system. There was no hepatosplenomegaly and fundal height was 36 weeks, cephalic relaxed and fetal heart rate was 140 bpm regular. Laboratory investigation were – Hb 10.2 g%, TLC 8400, platelet count 1.2 L, random blood sugar was 84 mg/dl, serum electrolytes Na^+ 136 and K^+ 3.8 mg, total serum bilirubin was 2.82, indirect 2.14 and direct 0.68, SGOT/PT 69/60, blood urea 18 mg/dl and serum creatinine 0.7 mg/dl. Dipstick showed 1+ albuminuria. Viral markers, peripheral smear for malarial parasite and dengue serology were negative. Although widal was positive in titres of 1:160, urine and blood culture reported no growth. Ultrasound whole abdomen revealed mild splenomegaly. Provisional diagnosis of non severe preeclampsia with typhoid fever was made.

She was started on injection monocef 1 g IV 12 hourly and tablet paracetamol, after 24 hours patient became afebrile. Her blood pressure increased (SBP 160-150 mmHg/DBP 100-90 mmHg). After two days she had an episode of acute breathlessness and tachypnea with RR=32/min and tachycardia 110/bpm, BP was 150/90 mmHg, bilateral chest showing coarse crepitation. She developed hypoxemia with O_2 saturation of 82% at room air. Patient was intubated, given injection furosemide and was taken for emergency caesarean in view of term pregnancy with previous Lower Segment Cesarian Section (LSCS) and preeclampsia with Acute Respiratory Distress Syndrome (ARDS).

Caesarean section was done under general anaesthesia and was uneventful. A live male baby of 2.9 kg was born. Postoperatively patient's chest condition was poor and she could not maintain oxygen saturation, so she was sent to Intensive care unit and kept on ventilator. Chest X-ray show infiltration in all lung fields and ECHO showed normal cardiac chambers with normal functioning.

On postoperative day two her Hb was 6 gm and platelet count was 20000, total serum bilirubin was 5.4 and direct was 3.4, SGOT / PT -96/70. Renal function test were normal. As her Hb and platelet counts were persistently low, she received four units red cell concentrates and 16 units of platelet transfusion. Third day onwards patient again developed fever between 100^{0}F to 101^{0}F. Repeat fever profile was sent and her smear now showed presence of trophozoite of *Plasmodium vivax* only. Co-infection with *Plasmodium falciparum* was ruled out by histidine protein-2 antigen testing.

Fourth postoperative day onwards, she was started on antimalarial artiplus-CD. Patient showed dramatic improvement, she became afebrile, there was increase in platelet count from 7000 to 1.2 lacs and TLC also increased from 2800 to 6200 after three days of treatment. Her chest condition improved and became clear. From fifth day tablet primaquine 15 mg once a day was added and was continued for 14 days. Rest of the postoperative period was uneventful. Patient was discharged in satisfactory condition with healthy baby. She was followed up after two weeks; her BP was normal and had no complaints.

DISCUSSION

The incidence of malaria in India accounts for 58% of cases in the South East Asia Regions and World Health Organisation (2014) reported the existence of 0.7–1.6 million confirmed malaria cases and 400-1,000 deaths annually [1]. Pregnant women are more susceptible to have severe manifestation of malaria, since there are changes in maternal immune system and presence of new organ (placenta) with new places for parasites to bind. Non immune primigravida are more susceptible [2].

During pregnancy malaria can cause hyperpyrexia, maternal anaemia, hypoglycaemia, pulmonary edema, cerebral malaria and even puerperial sepsis. Mortality can occur from haemorrhage and severe infection. Maternal complications of malaria can adversely affect the fetus and lead to abortions, preterm labour, fetal growth restriction, low birth weight fetal heart abnormalities [3,4]. Congenital malaria can occur due to transplacental spread. Prenatal and neonatal mortality can be 15.7% in *P.vivax* and 33% in *P.falciparum* [5].

Life threatening respiratory involvement is rare with vivax malaria but common with *Plasmodium falciparum* infection. In most of the cases severe respiratory involvement occur, after beginning of anti-malarial treatment [6,7]. Here we report a case where acute respiratory distress caused by *P.vivax* occurred in a preeclamptic women and it was a diagnostic and therapeutic dilemma as she did not improve after her delivery until antimalarial therapy was started.

Malaria has various typical and atypical presentations, which mainly depends upon the type of parasite, racial and regional characteristics. The main clinical manifestation of severe malaria caused by *P. falciparum* includes severe anaemia, jaundice, renal failure, cerebral malaria and ARDS have also been reported in vivax malaria [8].

Physiological, hormonal, haematological and immunological changes that occur during pregnancy can lead to various atypical manifestations of malaria. Parasitemia tends to be 10 times higher and therefore malarial infection is more severe and fatal. Maternal mortality is double (13%) during pregnancy and 6.5% in non pregnant population [5].

Pulmonary manifestation of falciparum, vivax and ovale malaria occurs due to altered pulmonary physiology, which includes obstruction in airways, altered gas exchange and ventilation, exaggerated phagocytic activity and accumulation of monocytes in the pulmonary compartment. This leads to intravascular inflammatory response.

Severe pulmonary manifestation of *Plasmodium vivax* usually occurs after six hours to eight days after the initiation of antimalarials, when the gas transfer is progressively reduced due to interstitial and alveolar oedema. Respiratory distress can also occur due to soluble mediators causing endothelial damage, hypoxia, systemic shock leading to diffuse alveolar capillary damage [9]. This could be the reason in our patient who presented with severe pulmonary symptoms before the diagnosis was made and anti-malarial treatment was started.

In falciparum malaria and not *Plasmodium* vivax, there is sequestration of parasitized erythrocytes which elicit a sequence of immune and physical response [10].

McGready R et al., reported that *Plasmodium falciparum* associated maternal mortality was 1% [6]. They followed up 48,983 antenatal women prospectively and observed 12 *P. falciparum* and 1 *P.vivax* related maternal deaths and concluded that each species could lead to at least one ARDS death. Malaria associated maternal deaths, *caused by P.falciparum was* 2.89 per 1,000 and *Plasmodium vivax was* 0.23 per 1,000 (p-value = 0.003). ARDS related mortality was not significantly different for *Plasmodium falciparum* 0.24 per 1,000 and for *Plasmodium vivax* 0.23 per 1,000 (p-value = 1.000).

Our case was unique in three ways firstly, maternal acute respiratory distress due to *Plasmodium vivax* occurred before the initiation of antimalarial drugs. Secondly respiratory distress caused by malaria was confused with the pulmonary symptoms of severe preeclampsia, since initially the diagnosis could not be made because peripheral smear was negative for malaria. Thirdly, although ARDS associated with malaria has high mortality rate especially in pregnant women, our patient survived due to timely ventilator support, diagnosis, delivery, transfusion of blood products and initiation of antimalarials has not been described in the literature.

Treatment of malaria during pregnancy consist of tablet chloroquine 500 mg weekly as suppressive chemoprophylaxis that prevents the vivax hypnozoites from reactivation in liver and causing relapses, until delivery because primaquine is contraindicated during pregnancy. Then a complete treatment with full therapeutic dose of chloroquine and primaquine should be given.

WHO recommends quinine and clindamycin for the treatment of malaria in the first trimester of pregnancy and artemether in second and third trimester of pregnancy [1]. Artemether, an artemisinin compound are potent, safe, rapidly eliminate parasitemia and is given in combination with other longer half life antimalarials. Inadvertent exposure of Artemisinin in first trimester does not increase the rates of abortion, stillbirth, congenital anomalies and preterm birth [11,12].

CONCLUSION

Malaria should always be suspected until proved otherwise in a patient belonging to endemic regions with acute febrile episodes and severe respiratory symptoms and even if test results are negative.

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