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Case Study

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COMPLICATED MALARIA: RAPID PARASITEMIA A RARE PHENOMENON

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INTRODUCTION

Malaria, a severe disease transmitted to humans by the bite of female mosquitoes infected with parasites of the genus *Plasmodium,* has been reported to affect around 219 million people and cause 435,000 deaths in 2017 worldwide.[1] Globally, its mortality rate ranges from 0.3%-2.2%, with most commonly encountered fatal outcomes (11%-30%) in regions with tropical climate.[2] The severity of the disease rests on several factors like microvascular occlusion, acidosis, and other metabolic derangements, leading to severe manifestations of malaria in the form of acute respiratory distress syndrome, renal insufficiency, and cerebral malaria. We report one such case of sever malaria, with the patient landing up into concomitant septic shock, severe hepatic dysfunction, rhabdomyolysis, and renal dysfunction.

CASE REPORT

A previously healthy 45-year-old Indian male was admitted to the emergency room with high fever (39.5-41°C), shivering and confusion. Our physical examination revealed a pulse of 152/min and a systolic blood pressure of 98 mm Hg, respiratory of 24/min. Auscultation of the chest revealed ubiquitous wheezing and normal heart sounds without presence of murmurs. The skin was dry, but with no erythema. The abdomen was soft with no rebound tenderness. The liver was not enlarged and the spleen was not palpable. Neurological examination showed no focal neurological signs and no signs indicative of meningitis. The Glasgow Coma Scale was 11. Laboratory evaluation revealed a hemoglobin of 11gm/dl, total bilirubin of 15 mg/dl and lactate dehydrogenase of 310 unit/l, indicative of ongoing hemolysis. Procalcitonin and C-reactive protein (CRP) were markedly elevated, and the patient showed a severe thrombocytopenia. Lactate was 7.5 mmol/l, base excess-4.5 mmol/l, anion gap 16.6 mEq/l and pH 7.43, indicative of a compensated metabolic acidosis. The presence of malaria falciparum parasites could be detected by microscopical examination of a thick blood film. The chest X-ray was normal. The patient received 500 ml of crystalloids and 1 gm paracetamol intravenously and was admitted to the intensive care unit (ICU).

The patient received colloids, crystalloids and a continuous infusion of glucose 10% under concurrent laboratory control of glucose, arterial blood gases, lactate and electrolytes every 4 hours. Two units of platelets were transfused. Quinine was administered intravenously, starting with a bolus injection followed by continuous infusion over 24 hours under regular control of quinine blood levels. Additionally, doxycycline was given orally. The first hemodynamic measurement revealed a central venous pressure (CVP) of 12 mmHg, cardiac output of 6.2 l/min and a systemic vascular resistance (SVR) of 709 dynes*s/cm2. CVP was measured every 4 hours.

During the first 24 hours in the ICU, the overall fluid administration was 4.9 l and diuresis was 3.2 l, resulting in positive fluid balance of 1.7 l. The heart rate decreased to 110 beats/min and the systolic blood pressure (SBP) increased to 100 mmHg with a mean arterial blood pressure (MAP) of 70 mmHg. The next day, the parasite load of 25.5% on admission increased to 36.7%. A second venous catheter was inserted into the right femoral vein and a red cell exchange with a cell separator. A 1.5-fold blood volume red cell exchange was performed with 20 units of packed red blood cells. The procedure was well tolerated and no bleeding occurred. The parasite load dropped to 16%. The following day the hemodynamic status of the patient destabilized with a drop of SBP to 80 mmHg and of the MAP to 45 mmHg, respectively. The heart rate increased to 180 beats/min and the CVP was 3 mmHg. The respiratory rate was 25/min under supplementation of 10 l O2 given via venturi face mask. Laboratory data showed a peak lactate level of 21.4 mmol/l, a base excess of -16.4 mmol/l and a pH of 7.24. The patient showed severe agitation. A mechanical ventilation was immediately initiated under analgesia and sedation with propofol and sufentanil. The patient was breathing spontaneously by means of pressure support of 15 to 20 mmHg and a positive end expiratory pressure of 6

mmHg. The shock was treated with fluid resuscitation according to the concept of early goal directed therapy. During the next 6 hours, administration of 2 liters of crystalloids and 1 liter of colloids was required to increase the CVP. Increase of MAP over 65 mmHg and a sufficient central oxygen venous saturation could only be reached by means of dobutamine and norepinephrine. After hemodynamic stabilization, CVP was around 12 mmHg. Lactate levels fell gradually to 5.5 mmol/l and the pH normalized. The net fluid balance was 5.3 l. Because of the high parasite load of 16%, a second red blood cell exchange via cell separation was undertaken with 13 units of packed red blood cells. The parasite load decreased to 2% the next day. The patient remained hemodynamically stable during the procedure with no need for increased doses of catecholamines. A CT scan of the brain showed no signs of bleeding, ischemia or edema. Due to increased myoglobin levels and the subsequently developed renal failure, renal replacement therapy was initiated via continuous Veno-venous hemodiafiltration (CVVHDF). Although the thrombocyte count remained low, administration of heparin was initiated at 200 i.u. per hour in order to prevent clotting of the dialysis machine and provide prophylaxis against deep vein thrombosis. As a consequence of the shock, the patient developed a severe hepatic dysfunction with a massive increase of liver enzymes and bilirubin and a decrease of albumin to one third of normal levels. Furthermore, the patient developed rhabdomyolysis.

With a positive fluid balance of almost 4 liters the fourth day, the patient remained hemodynamically stable. Thereafter, dobutamine could be stopped and norepinephrine slightly reduced. With a CVP between 9 and 13 the patient developed no pulmonary edema and all respiratory parameters remained stable. On the fifth day C-reactive protein (CRP) and leucocyte count increased, but temperature remained stable between 38 and 39°C. Cultures from blood, respiratory secretions and urine were performed and the patient was given antimicrobial treatment with a fixed preparation of combined piperacillin and tazobactam. All cultures remained negative.

During the following days norepinephrine was further decreased based under hemodynamic status and was finally discontinued on the seventh day. Based on CVP measurements, the net fluid balance was negative from day 5 on until discharge from the ICU. Mechanical ventilation was discontinued on day 7, and continuous dialysis was replaced by intermittent dialysis. The extremely high scores (Acute Physiology and Chronic Health Evaluation II, Simplified Acute Physiology Score II, Sequential Organ Failure Assessment) on the day of the shock improved gradually. Hepatic dysfunction and rhabdomyolysis dissolved, but the patient remained in renal failure. Thrombocytes and leucocytes returned to normal values. After extubation the patient's confusion improved slowly. At discharge from the ICU on day 12, there was sufficient orientation in time and person, but not in situation. The patient remained hospitalized for a further period of three weeks. During this time, he regained full orientation. At the time of discharge creatinine level was 1.8 mg/dl, renal function had been resumed and thus there was no need for further dialysis.

DISCUSSION

In this case, the patient had severe shivering and confusion when he reported to the emergency room, and was not comatosed, with a stable hemodynamic and respiratory status for the first 48 hours. However, his microbiological and biochemical features like constantly increasing parasitic load, hyperbilirubinemia, and hyperlactemia were the issues of concern. Although the parasite load of 25.5% on admission that increased to 36.7% the next day dropped to 16% in 48 hours, the patient landed up in septic shock. As per the reported cases in the literature, a 7.7% frequency of development of shock has been encountered in patients on admission with severe anemia[3] and 21.5% in the ICUs specialized for infectious disease treatment.[4] Tran TH et al (1996) reported an overall mortality of 14.8% in patients with severe falciparum malaria complicated with septic shock, with 10% of the patients succumbing to intractable shock.[3] Bruneel et al (1997) reported 28% of the patients of severe malaria to be developing shock and 14% dying of it. They opined that once shock precipitates in a patient with severe malaria, the mortality rate increases to 50%-67.5%.[5]

As a general finding, disagreements persist in the treatment approaches toward such cases of severe malaria complicated by shock among the specialists in the treatment of tropical diseases and those in intensive care medicine. However, literature encompasses data guiding treatment plans with most promising outcomes.

Focusing on the treatment of severe malaria, fluid replacement cautioned for the prevention of both underhydration and overhydration is recommended. It has been emphasized that inadvertent or excessive intravenous fluid replacement leading to circulatory overload might lead to pulmonary edema and successive acute respiratory failure. Thus, the recommendation is avoiding the central venous pressure (CVP) from exceeding 5 cm of water, and in case of persistent hypotension, dopamine be the drug of choice.[6]

Focusing on the treatment of sepsis, reversal of tissue hypoperfusion is mandated by fluid resuscitation at the first sign of development of shock. This aims at CVP being achieved between 8 and 12 mmHg, MAP above 65 mmHg, and central venous oxygen saturation above 70%. In mechanically ventilated patients, the targets CVP must be between 12 and 15 mmHg. Further aid can be obtained by transfusion of packed red blood cells and dobutamine administration to increase the cardia output.[7,8]

Generally, bacterial infections lead to septic shock. However, our case of malaria also showed similar laboratory and hemodynamic changes as evident in septic shock. Septic shock leads to tissue hypoxia, multiorgan failure, and subsequent death of the patient.[9] The hypoxia in turn leads to endothelial activation and homeostatic imbalance, with disrupted vascular permeability and tone. The effects are also evident in the lungs, leading to acute respiratory distress syndrome due to lung injury. Thus, it was decided to treat the case as per the early-goal directed strategy and the surviving sepsis campaign guidelines. The former includes rapid fluid resuscitation that helps restoring oxygen delivery. However, the "malaria recommendations" directs to refrain from aggressive fluid resuscitation to avoid pulmonary edema.[10] Gachot et al (1995) reported that acute lung injury is the most common phenomenon in multiple organ dysfunction syndrome in cases of severe falciparum malaria.[11] Thus, weighing the risk of lung injury due to sepsis against the risk of respiratory failure due to volume overload, we adopted fluid resuscitation. Moreover, Maitland et al (2005) demonstrated that volume resuscitation does not lead to an increased risk of pulmonary edema and commented that the fear of inducing pulmonary edema from overhydration is just an exaggerated concept.[12]

CONCLUSION

Considering the data on the treatment protocols for patients with severe malaria complicated with shock, we treated our patient following the sepsis guidelines. Despite the development of multiorgan failure as a result of the shock followed by parasitic overload, the patient survived. Our approach was backed up by the understanding of the pathophysiological mechanisms and the evidential literature.

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