Annals of Clinical Anesthesia Research

Case Report
Published: 14 Jan, 2019

A Case Report of Severe ARDS due to Falciparum Malaria: Successfully Managed with Prone Position Ventilation

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Abstract

We report a case of 34 year old man with falciparum malaria complicated with severe Acute Respiratory Distress Syndrome (ARDS) with hypoxemia refractory to conventional mechanical ventilation. We had put the patient in prone position ventilation early in the course of ARDS and continued prone ventilation for few days until the hypoxemia improved. Gradually the patient improved clinically and successfully discharged from the hospital after 32 days. Hence early implications of prone position ventilation in severe ARDS in are source limited setting can be lifesaving.

Keywords: Falciparum malaria; ARDS; Prone ventilation

Introduction

Malaria is one of the commonest parasitic infections in the developing countries. Among all the malaria species, falciparum can cause severe disease affecting almost all organs of the body within few days of presentation. The severity of the disease increases in relation to the delay between the onset of symptoms and diagnosis and its treatment should be considered an emergency, as severe complications may appear within a matter of hours. Acute Respiratory Distress Syndrome (ARDS) is the most severe form of the respiratory complications of malaria, with high mortality. The estimated incidence of ARDS in case of *P. falciparum* is 5% to 25% [1]. And with a high mortality (80%). There is no specific treatment for ARDS secondary to malaria. The lung-protective mechanical ventilation, high frequency oscillatory ventilation, nitric oxide, prone positioning, Extra Corporeal Membrane Oxygenation (ECMO) are the different strategies used for ARDS. We found only few case reports on the effect of prone positioning for ARDS secondary to falciparum malaria in adults.

Case Presentation

A 34 year old previously healthy gentleman, residence of India, admitted to our hospital with history of fever, epigastric discomfort and nausea and vomiting for 10 days. He had been to Congo (Africa) for official visit 15 days prior to his illness. Physical examination revealed clinical jaundice, BP-90/40, altered sensorium (Glasgow coma scale 10/15). His saturation was 96% on 2 litres of oxygen in nasal prong. Pupils 3 mm, equal, reacting to light, plantar down going, able to move all 4 limbs. Abdominal examination, hepatomegaly was present. Blood tests showed haemoglobin 11 g/dL, platelets 18,000 cells/dL, leukocytes 12,300 cells/dL (84% granulocytes), urea 148 mg/dL, creatinine 1.8 mg/dL, potassium 5 meq/L, sodium-137 meq/L, Lactate-7 mmol/lt, total bilirubin 16.4 mg/dL, direct bilirubin 12.4 mg/dL, Aspartate Transaminase (AST) international 61 units/L (IU/L), Alanine Transaminase (ALT) 51 IU/L, gamma-glutamyl-transpeptidase 112 IU/L, alkaline phosphatase 158 IU/L, random blood sugar 58 mg/dL and the coagulation study was within the normal range. Initial Arterial Blood Gas (ABG)-PH-7.27, PCO2-32.3, HCO3-14.8, PO2-96, SO2-97% with 40% oxygen from nasal cannula. Initial chest x-ray was normal. Non contrast CT brain was normal. Serology for dengue IgM, leptospira IgM was negative. Hepatitis was rule out as HBs Ag and anti HcM was negative. Ultrasonography of abdomen revealed only hepatosplenomegaly without any free fluid. Malaria was diagnosed by means of a Giemsa-stained blood smear, which showed *P. falciparum,* and immuno chromatographic detection of the *Plasmodium* antigen, aldolase, and histidine-rich protein 2. The parasitemia index was 30%. Initial treatment was started intravenous artesunate 2.4 mg/kg. Empirical intravenous ceftriaxone was started after sending blood and urine culture. Patient was resuscitated with 30 ml/kg of crystalloid (balanced salt solution), followed by noradrenaline infusion to maintain Mean Arterial Pressure (MAP) around 65.50% dextrose solution was given bolus for hypoglycaemia followed by 10% dextrose 20 ml/hr with continues blood sugar monitoring every 1 hourly. Platelets concentrate (1 single donor platelet) was transfused. Patient remained to

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Received Date: *09 Dec 2018*
Accepted Date: *11 Jan 2019*
Published Date: *14 Jan 2019*

Citation:
Mohanty B, Nandeeshwara K. A Case Report of Severe ARDS due to Falciparum Malaria: Successfully Managed with Prone Position Ventilation. Ann Clin Anesth Res. 2019; 3(1): 1018.

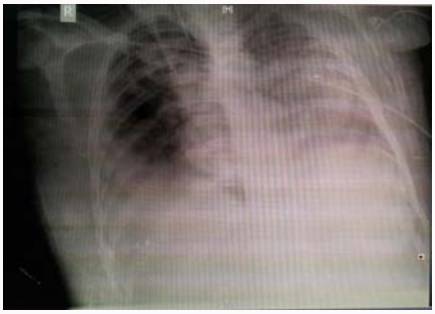

Figure 1: The repeat CXR was worsened in terms of bilateral increased homogenous opacities.

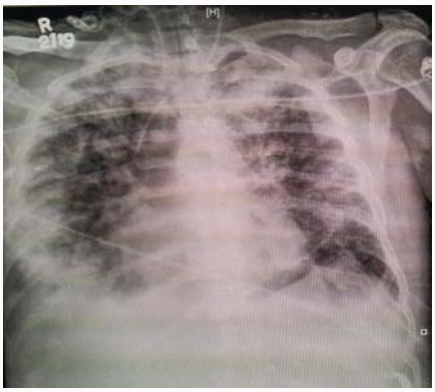

Figure 2: The chest x-ray on day 4.

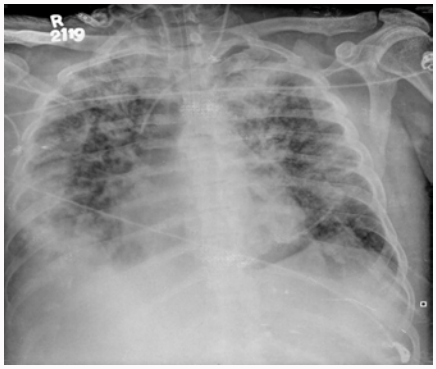

Figure 3: Patient showed a progressive clinical and very few radiological improvements.

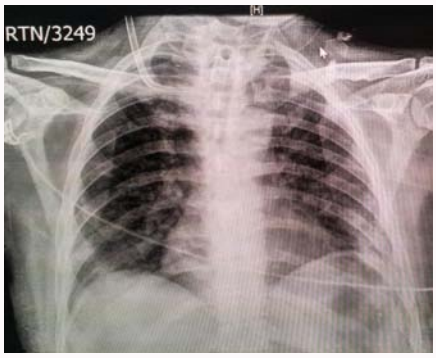

Figure 4: Tracheostomy decannulation with improved power in all 4 limbs.

be oliguric even after fluid resuscitation and vasopressors with target MAP 65. Bed side echocardiography done- Normal left ventricular systolic function, no pericardial effusion. Lung ultrasonography bed side no pleural effusion, bilateral early B lines in PLAPS [Postero Lateral Alveolar and/or Pleural Syndrome] point. Early continues venovenous hemofiltration was started for persistent acidosis. Respiratory distress developed 12 hours after admission: the patient had a respiratory rate of 45 breaths/min and progressive hypoxemia, despite oxygen via High Flow Nasal Cannula (HFNC) and Non Invasive Ventilation (NIV). The repeat CXR was worsened in terms of bilateral increased homogenous opacities (Figure 1). Patient gradually worsened in sensorium and within 16 hours of admission the patient required intubation and mechanical ventilation. Tracheal secretion was sent for culture and sensitivity. Antibiotics were upgraded to meropenem and clindamycin for worsening clinical condition of the patient and maintained for initial 7 days, when the negative results of the blood, bronchial aspirate and urine cultures were known. The mechanical ventilation was started in a pressure regulated, volume-controlled mode with tidal volume 6 mL/kg, Positive End-Expiratory Pressure (PEEP) 8 cm H_2O, respiratory frequency 32 breaths/min, and Fraction of Inspired Oxygen (FiO_2) 80%, during which blood gas values were pH 7.27, PaO_2 110 mmHg, $PaCO_2$ 46 mmHg, and bicarbonate 18 mEq/L, and PaO_2/FIO_2 was 140. Immediately after mechanical ventilation, patient maintained saturation with conventional ventilation. During the next 2 days, the hypoxemia progressively worsened, as did the radiological signs, which required increases in PEEP (to 18 cm H_2O) and Peak Inspiratory Pressure (to 40 cm H_2O). The chest x-ray on day 4 is shown in picture (Figure 2). We decided to move the patient into the prone position ventilation for severe ARDS. Prone position ventilation was started with 20 hours/day with precious care of pressure points, eyes and abdomen. After the change to prone position the patient showed a rapid improvement in oxygenation (PaO_2-180), with increased P/F ratio 240, which allowed us to rapidly decrease the peak inspiratory pressure and FIO_2. Patient made supine after 20 hrs, again developed increased oxygen requirements. So decided to again prone the position after 2 hours. In our case the patient required in total of 5 cycles of prone position ventilation, after which the patient showed a progressive clinical and very few radiological improvement (Figure 3). Tran's pyloric enteral nutrition was continued throughout the course of the illness, and it was well tolerated in both the supine and prone positions without any complications. For thromboprophylaxis, intermittent compression stocking was initiated and maintained throughout the stay in intensive care unit. Total artesunate dose was given for 7 days and repeat parasitemia index was decreasing 3%. Percutaneous tracheostomy was done on day 14 of mechanical ventilation. CRRT was stopped on day 9 of admission as the patient was off inotropes and started intermittent dialysis under guidance of nephrology. Patient started making urine on day 13 and remained dialysis free after that. Patient developed critical illness poly neuropathy which was confirmed with nerve conduction study and gradually patient recovered. Patient shifted to general ward with tracheal tube *insitu* with supplemental oxygen and discharged from hospital after 30 days after tracheostomy decannulation with improved power in all 4 limbs (Figure 4).

Discussion

Malaria is the common tropical infection in developing countries. Of the 4 types of malaria, *P. falciparum* malaria is the most severe, as it affects multiple systems. As in our case, it affects almost all systems.

Early diagnosis and treatment are essential to reduce morbidity and mortality. The incidence of pulmonary complications of malaria has increased in recent decades. It is more frequent in non immune patients between 20 and 40 years and in conditions of delay in treatment (beyond the seventh day of the onset of symptoms) [1]. In our case, though the patient was an immune adult, but due to delayed presentation, ARDS was severe. About 4% to 18% of the adult patients with *P. falciparum* malaria present with respiratory symptoms and the incidence of ARDS in case of *P. falciparum* is 5% to 25% [2]. The pathogenesis of ARDS secondary to falciparum malaria is still unclear and it may be multifactorial. These include the effects of sequestration of parasitized erythrocytes, host immunologic reactions to lung-specific sequestration or systemic malaria infection, superimposed pulmonary infections (community acquired, nosocomial, or opportunistic in immunocompromised patients), aspiration, coexistent sepsis and bacteraemia induced ARDS, or the effects of treatment such as fluid resuscitation [3]. The clinical findings of ARDS in malaria are sudden onset tachypnea, dyspnoea and cough. Life threatening hypoxemia may develop within a few hours [4]. Our case developed this clinical picture and needed mechanical ventilation within few hours after the occurrence of respiratory symptoms. Acute renal failure, hypoglycaemia, metabolic acidosis, liver derangement may accompany ARDS, which were present in our case. There are no ARDS treatment trials in malaria, so management strategies follow non malaria ARDS guidelines [3]. Mechanical ventilation strategies in malaria-associated ARDS are same as in ARDS caused by other causes, with the exception of permissive hypercapnia, since the carbon dioxide (CO_2) increases cerebral blood flow which in turns increases intracranial pressure, which has a deleterious effect on patients with malaria and altered level of consciousness [5]. For initial respiratory support oxygen therapy with FiO_2 of 0.5 to 0.6 by face mask can be used. Other measures options include mechanical ventilation or non invasive type continuous positive airway pressure. Invasive mechanical ventilation should be considered in the following cases: a) Patients with altered level of consciousness. b) Patients requiring an FiO_2 greater than 0.6 (or higher pressures than CPAP at 10 cm H_2O) to maintain PaO_2 greater than 60 mmHg [6]. Initial ventilator strategy should be the application of volume- or pressure-support ventilation with positive end-expiratory pressure, avoidance of both high tidal volumes (6 mg/kg ideal body weight) and an initial plateau pressure, 30 cm H_2O as recommended by the ARDS Net study (ARDS Network, 2000) [7]. It is recommended to maintain expiratory: inspiratory ratio of 1:1 or 2:1. The FiO_2 and Positive End-Expiratory Pressure (PEEP) must be adjusted to maintain an adequate blood oxygenation. Higher PEEP can be used initial days to improve oxygenation, but without mortality benefit [8]. Rescue therapies like recruitment manoeuvre, muscle paralysis in first 48 hour of ventilation and prone positioning are the next options of management for refractory hypoxemia after ARDS net protocol guided mechanical ventilation. Our patient was paralysed for the initial 2 days of ventilation and recruitment was tried initially for refractory hypoxemia. Patients with ARDS, especially the most severely affected, often present with refractory hypoxemia due to shunt, which require additional treatments beyond conventional mechanical ventilation, including MV in the Prone Position (PP). Several mechanisms are probably responsible for the improved gas exchange when patients with ARDS are placed in PP. These include changes in diaphragm position and/or tidal diaphragmatic motion, less cardiac-induced compression of the lungs, and increased trans-pulmonary pressure in the dorsal caudal lung facilitating alveolar recruitment [9]. Placing the patient in prone position can improve oxygenation and mortality in severe ARDS in early course of the disease. In 2013, the French multicentric RCT PROSEVA Study Group showed in patients with severe ARDS, early application of prolonged prone-positioning sessions significantly decreased 28-day and 90-day mortality [10]. In 2010, Sud et al. [11] published a systematic review and meta-analysis where they had described that prone ventilation reduces mortality in patients with severe hypoxemia. But due to its associated risks, it should not be routinely used in all acute hypoxemic respiratory failure. In another Meta analysis, Gattinoni et al., [12] found mortality differences in favor of the prone patient group with severe hypoxemia (PaO_2/FiO_2<100 mmHg). In 2014, Beitler et al., [13] published a meta-analysis, where they found that PP significantly reduces mortality in patients with ARDS when it is used with low Vt. PP may be most effective in improving oxygenation when initiated early (eg ≤ 3 d) during the exudative phase, when congestive and compressive atelectasis are predominant features, as opposed to the intermediate phase of ARDS (eg >1 week), when fibrosis and Type II cell hyperplasia are more prevalent [14]. There are a very few case reports on prone position ventilation in malaria associated ARDS. Flores et al., [15] described a case report where they have successfully managed a case of severe falciparum malaria with ARDS in a 4 year old boy with prone position ventilation. In patient's refractory hypoxemia after prone position ventilation, Extra-Corporeal Membrane Oxygenation (ECMO) is the alternative strategy. Alves et al., [16] reported a case series where they have successfully managed 1 case of falciparum malaria and 1 case of co-infection with plasmodium ovale and *p. vivax* complicated with severe ARDS unresponsive to conventional treatment with venovenous ECMO. Fluid management is crucial in patients with severe malaria. As pulmonary oedema secondary to increased pulmonary vascular permeability has been shown to be frequent, a conservative strategy of fluid management was followed in our case. Moreover, a liberal strategy of fluid management in acute lung injury has been previously associated with prolonged duration of mechanical ventilation and intensive care [17]. All patients with confirmed severe malaria should receive early parenteral anti malarial treatment. Intravenous artesunate is a drug of choice for both adults and children and in pregnant women. WHO (World Health Organisation) also recommends artesunate as a first-line treatment for severe malaria. The initial dose is 2.4 mg/kg/12 h (2 doses), followed by 2.4 mg/kg/d for total of 7 days [1].

Conclusion

Patients with severe ARDS due to falciparum malaria can be safely managed with early prone position ventilation when the conventional low volume ventilation strategy and other forms of rescue therapy do not improve hypoxemia. Early referral to an Extra Corporeal Membrane Oxygenation (ECMO) centre can be life saving in cases of refractory hypoxemia and hypercapnia not responding to any other forms of rescue therapy.

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