Two Cases Of Severe “Traveler’s Falciparum Malaria “ With Improved Conditions After Administration Of Quinine Oral

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Abstract:
Traveler’s Malaria is a new emerging health problem in the whole world due to (1) the increasing mobility of international traveler and (2) The recurrent of the disease in the areas those once partially or fully freed from the disease.
We are reporting 2 cases of severe ‘traveler’s malaria’ found attacked a man from Greece and a man from Philippine with the age of 54. Both of the patients are ship captains. On the first case found acute kidney failure with anuria and lung oedema, pneumonia and a progressive declining of haemoglobin concentration. With the second cases we found declining of consciousness, disorder of liver function with icterus, disorder of kidney function, bleeding of upper digestive tract, pneumonia and severe anemia, signs of DIC (Disseminated Intra-vascular Coagulation) and admission in ICU (Intensive Care Unit). Both of cases are assumed having resistance to Chloroquine and Fansidar. Both of them were treated with Quinine Sulphate by mouth (we hardly can find Quinine injection in Medan). With such treatment for a seven day duration we saw a significant clinical and laboratory improvement. The evidence were the disappearance of asexual parasite from peripheral blood. During the hospitalization both of the patients required PRC (blood) transfusion to overcome the tendency of progressive declining of haemoglobin. With the disappearance of parasite from blood, the disorder of the suffered organs mentioned above, gradually become normal. The condition of the patients showed a satisfactory improvement either.

Keywords: Severe – Traveler’s Malaria – Complication – Quinine Sulphate

INTRODUCTION:
The disease of malaria still creates problem both in developing and developed countries. This phenomenon is signed by still increasing number of incidence of the disease in recent time. The verdicts are assumed as:
1. The increasing of malaria parasite resistance to the available chemotherapeutical medicines.
2. The increasing of Anopheles mosquito resistance to the currently used insecticides.
3. The significant change of climate and echo-system
4. The increasing number of international travelers
Malaria Import is an emerging problem happens in the whole world. A part of the cause is the increasing mobility of the international travelers and the other is due to the reappearance of the disease from the past-freed endemic areas. The evidence of malaria to suffer the international travelers is significantly increased within past two decades. East Africa, especially Kenya, is the infection source of malaria falciparum for the people of America and Switzerland who traveled to the country. Indonesia is still a country with a high transmitting potential to be the source of the disease especially the other island exclude Java, Madura and Bali. It is not uncommon evidence to find malaria import cases in Jakarta, imported from the endemic areas in of the other islands of Lampung, East Timor and Papua.

In the following part we are reporting about 2 severe Traveler’s Falciparum Malaria cases whose recently were treated in a private hospital in Medan, Indonesia.

**THE FIRST CASE:**

Male, 54, Greece, Occupation : Ship Captain, admission to hospital on 7\textsuperscript{th} of March 2001 with main complaints : fever, weak and pale. The condition has been experienced in a week with a special pattern of up and down fever alternated by normal condition. There were severe headache and shaking chill, nausea and vomiting. On the primary physical examination we found normal consciousness; Blood Pressure (BP) : 100/70 mmHg; Pulse : 100 per minute and regular; respiration : 20 per minute and body temperature 39\textdegree C.

**In further physical examination:** Head , eyes : anemic (+). Neck : no any defect found; Thorax : Heart and Lung in the normal limit; Abdominal : within a normal limit; Extremities : within a normal limit.

**Laboratory investigation results:** Red Blood Cell (RBC) : 8.5 gr % ; White Blood Cell (WBC) : 11,400/mm\textsuperscript{3} ; Blood Sedimentation Rate (BSR) : 20 mm/hrs; Haematocryte (Ht) : 44 %; WBC differential telling : 3/0/63/30/3/1; Thrombocyte : 196,000/mm\textsuperscript{3}; Urinalysis within normal limit; Blood Sugar : 89 mg% ; Liver Function Test : Bilirubin Total : 1.3 mg/dL; Direct : 0.54 mg/dL; SGOT : 156 u/dL; SGPT : 128 u/dL; Alkaline Phosphatase : 53 u/dL; Blood Ureum : 89 mg/dL; Creatinin : 4.2 mg/dL; Peripheral blood : found asexual form Trophozoite and ringform of Plasmodium falciparum.

**Working diagnosis :**
Malaria Falciparum with Insufficiency Kidney Function

**Treatment :**
The treatment had been given : Bed rest, regular diet, Intravenous fluid drips Ringer solution 20 drops / minute. Chloroquine 250 mg tablet with ‘ 4 – 2 – 2 – 2’ schedule by mouth.

After 2 days treatment, the patient still had fever, coughing and experienced shortness of breath. On physical examination we found there was wet rales in lower part of the left lung.

**Working diagnosis and further treatment**
Severe malaria with Acute Kidney Failure + Pneumonitis. The list of medicines added with Cefobid 1 Gr per 12 hours (IV) and Fansidar 3 tablet at once.
On the 5th day of hospitalization the patient suffered from more intensity of shortness of breath. No urine by 12 hours, the body temperature 37.6 °C. Auscultation on chest signed more severe wet rales. Blood Urea : 201 mg/dL, Creatinine : 5.8 mg/dL, WBC : 12,300/mm²
The treatment was added with Lasix injection per 8 hours IV, Essential Amino Acid Solutions (EAS) 2 bottles per day.
On the 6th day : The shortness of breath reduced, urine output 850 cc per 24 hours, Hb : 6.2 gram %, Thrombocyte 48,000/mm³, WBC : 19,600/mm³, Ureum : 177 mg/dL, Creatinine : 5.6 mg/dL. Examination of the parasites density gave the figure of 1060 ring forms and 1060 Gametocytes per mm³ of blood. Thorax X-ray showed Pneumonia in lower part of right lung. From this point the treatment continued with Quinine Sulfate 222 tablet with the dosage of 3 tablets 3 times per day.
On the 7th day : Hb : 5.8 gr %. Given 500 cc Packed Red Cell (PRC) transfusion.
On the 8th day : Hb (post blood transfusion) 10.3 gr %. Urine volume : 3180 cc per 24 hours.
On the 10th day, we conducted Ultrasonography (USG) upon kidneys and KUB (Kidney, Ureter, Bladder) X-Ray. The result showed the normal kidney. Urine production was 2100 cc per 24 hours. Chest X-Ray was repeated. The result showed normal lung. No more fever, vital signs were within normal limit.
On the laboratory examination found Ureum : 141 mg/dL, Creatinine : 3.6 mg/dL; No ring form of malaria found but ‘Gametocytes’ with the figure of 775 per mm³ of blood.
On the 12th day The general condition of the patient was improved. Malaria was negative. Ureum : 75 mg/dL, Creatinine : 2.2 mg/dL. Treatment : Multivitamins orally.
On the 20th day the patient was allowed to go home.

THE SECOND CASE :
Male, 54, Philippine, Occupation : Ship Captain, admission to hospital 7th of March 2001 with main complaints: fever, weak and jaundice. The condition had been experienced by the case for 11 days. There were trembling chill followed by intensive perspiration and headache. On the primary physical examination we found somnolent consciousness; BP : 90/70 mm Hg; Pulse : 116 per minute and regular; respiration : 20 per minute and body temperature 38.6 °C.

In further physical examination : Head, eyes : jaundice (+). Neck : no any defect found; Thorax : Heart : heart rate 116 per minute, regular beat; intensity was fair, Lungs : found wet rales on both lungs. Abdominal palpation : liver, kidney and spleen were unpalpable (should be within a normal limit); Extremities : no any sign of abnormality.
Laboratory investigation results : Hb. : 5 gr % ; WBC : 12,700/mm³ ; Erythrocyte : 1.59 x 10⁶, Thrombocyte : 326,000 per mm³ ; BSR : 20 mm hrs; Ht : 44 %; Blood Ureum : 176 mg/dL; Creatinine : 3.3 mg/dL; Na : 128 meq/dL; K : 4.4 meq/dL; Cl 103 meq/dL; Total Billirubin : 6.20 mg/dL; Direct Billirubin : 2.69 mg/dL; SGOT : 84 u/dL; SGPT : 57 u/dL; Alkaline Phosphatase : 68 w/dL; yGT :
159 u/dL, HbsAg (negative); Peripheral blood sample: Found Trophozoite and the ring form Plasmodium falciparum.

**Urinalysis**: Protein (+); Sugar Reduction (-); Urobilinogen positive, Billirubin (+); Sediment: WBC: 5 to 10 per filed; Erythrocytes: > 100 per field and Epithelial cell: 1 to 2 per field.

**Analysis of arterial blood gas**
Analysis of arterial blood gas showed: pH: 7.203; pCO₂ mmHg: 26.5 mmHg; pO₂: 122.6; BE: -16.1; Bicarbonate: 10.2 mmol/dL; Total CO₂: 11.2 mmol/dL; Saturated O₂: 97.3%.

**Working diagnose**: 
1. Severe Malaria Falciparum with severe anemia 
2. Acute Kidney Failure 
3. Metabolic Acidosis

**Treatment**: 
Intravenous fluid drips Ringer Solution 10 drops per minute, injection of Cefobid 1 Gr per 12 hours by intravenous. Fansidar 3 tablets at one dosage, Chloroquine 250 mg tablet with '4 – 2 – 2 – 2' schedule by mouth, Injection of Lasix 1 vial per 12 hours. The case was admitted in the Intensive Care Unit (ICU).

On the 3rd day the patient was still in fever, Blood Pressure 80/50 mmHg. We gave Dopamin 200 mg diluted in 100 cc of Dextrose 5% solution by intravenous drip with the rate of 5 drops per minute, Quinine Sulphate 3 tablets three times per day, and 500 cc PRC transfusion.

On the 4th day: Hb post transfusion: 6.8 gr%; Parasite count: Ring-form 1290 per mm3; Gametocyte: 1290 per mm³; Albumin 2.07 gr%, Na: 128 meq/dL; DDimer: 1000 u/dL. The patient was given NaCl 0.9% 20 drops / minute, 100 cc of Albumin Substitution 25%. The amount of urine was 1300 cc per 24 hours.

On the 5th day we conducted chest x-ray. The reading was within normal limit. USG reading on kidneys also gave a normal result. Urine protein per 24 hours: 23 mg. Patient vomited blood (haematemesis) about 100 cc. The medicines was added with the injection of Teranexamic acid 1 vial per 6 hours, Injection of Losec 1 vial per day.

On the 7th day: The upper GI tracts bleeding was stopped. The general condition of the patient gradually becomes normal. Fever disappeared. The amount of urine produced 2000 cc per 24 hours. Na: 144 meq/dL; K: 3.6 meq/dL; Cl: 98 meq/dL; Hb: 6.6 gr%; Ht 21.3%. On a repeated blood examination for malaria: Ring-form was negative; Gametocytes was 373 per mm².

On the 10th day: Patient was moved from ICU to an ordinary bedroom. Blood ureum: 43; Creatinine 1.1; Thrombocyte: 215,000 per mm3. Lasix was stopped. Multivitamins orally were given.

On the 14th day. The general condition of the patients was improved very well, fever absolutely disappeared but Hb concentration still low, 6 gr%. The other 500-cc PRC transfusion was administered. Peripheral blood examination for malaria found negative of parasite form.

On the 17th day the Hb concentration increased to 10.5 gr%. Malaria parasite was absent on a repeated peripheral blood examination.
On the 20\textsuperscript{th} day of admission the patients is allowed to go home.

**DISCUSSION:**
Severe Malaria always affects certain number of organs at once, therefore, the handling of the case requires serious attention and proper follow up. Treatment options depends on whether the parasite is susceptible to Chloroquine. This information is available from periodic reports that describe Chloroquine resistance patterns throughout the world. If this information is not available, the infection should be considered Chloroquine resistant.\textsuperscript{3}

The definition of severe malaria itself must be made to include the conditions mentioned below:

**Clinical criteria:**\textsuperscript{4}

1. Cerebral malaria
2. Severe anemia (Hct < 15 %)
3. Renal failure (no urine or urine out put < 400 ml in 24 hours, or 12 ml/Kg/24 hours after rehydration, or serum creatinine > 3 mg %)
4. Pulmonary edema or adult respiratory distress syndrome
5. Hypoglycemia (blood sugar < 40 mg %)
6. Shock (systolic BP < 70 mmHg in adult or < 50 mmHg in children age 1 - 5 years)
7. Spontaneous bleeding and disseminated intravascular coagulation
8. Repeated convulsions
9. Acidosis (arterial pH < 7.25 or plasma HCO\textsubscript{3} < 15)
10. Macroscopic haemoglobinuria
11. Hyperparasitemia (>5 % parasitemia in non-immune)
12. Hepatic dysfunction
13. Hyperpyrexia (persistance of rectal temperature > 40 degree C

On both cases we just mentioned previously, all the parameters found showed the signs and symptoms of Severe Malaria Falciparum with severe anemia acute kidney failure and pneumonia complication. The second case showed the bleeding of the upper part of gastro intestinal tract (upper digestive tract), thrombocytopenia with increasing D-Dimer. This case proofed the signs of DIC (Disseminated Intravascular Coagulation). The DIC itself was not handled for this case because the bleeding fairly was stopped with only hemodynamic intervention.

Acute kidney failure is known as a killer attributed to the severe malaria case. Before the invention of hemodialysis, the death rate attributed to the complication of severe malaria was approximately 10 to 20 %.\textsuperscript{1}

In both cases we found there were acute kidney failure sign by oliguri, signs of metabolic acidosis, and the elevated level of blood ureum and creatinine. The administration of Lasix via injection and also the intervention to the acidosis condition, monitored continuously via the proper intake & output procedure, the condition of kidney gradually back to normal. Both of the patients did not need any hemodialysis procedure.
It is said in the literature that the proper treatment for severe malaria is the continuous administration of Quinine by intravenous injection or giving of Artemisin as the faster alternative to sweep malaria parasite out from blood circulation.\textsuperscript{2,3}

We did not give Quinine Infusion nor Artemisin or Artesunat for both cases we treated because neither of mentioned medicines available in Medan market. We only gave Quinine Sulfate orally.

There is a strong suspicion that there are sure resistances to either Chloroquine or Fansidar happen in both patients we treated. After administration of both medicines there were still clinical fever and in the examination of the peripheral blood there were found malaria parasites in a significant figure after 6\textsuperscript{th} day for the first case and after 4\textsuperscript{th} day of the second. With the administration of Quinine Sulfate, there were a reducing number of parasites and a fully swept out from blood after 2 weeks of treatment.

The blood transfusion with PRC administered to both patient were decided because there were a real tendency of declining the Hb concentration along the treatment days and there were certain hemodynamic disorder monitored.

**CONCLUSION:**

We have reported about 2 cases of Severe Malaria falciparum suffered by 2 foreigners who came from Philippine and Greece. Both of the were suspected a resistance to Chloroquine and Fansidar. With the treatment using Quinine Sulfate orally and also the proper care to eliminate the complication as well as the administration PRC (blood) transfusion, fluid balance and administration of diuretic to maintain renal function, antibiotic to secondary infection, both of the patients were cured in the sense of clinic and laboratory.

It is suggested to guide any foreigner who comes with fever or jaundice to have a proper examination for malaria disease. It just proofed that at the moment time, the cases of malaria are increasing, so we are recommended not to delay the handling because of the delayed diagnose. Quinine Sulfate is still the drug of choice for malaria cases as yet, at least it is true in Indonesia.

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