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Mobile Worker Coming Back From Myanmar–India Border Presented With Septic Shock, High Fever, Confusion, Prostration, Anemia, Thrombocytopenia, Acute Kidney Injury and Transaminitis Due to Complicated Falciparum Malaria, Successfully Treated With Parenteral Artemisinin Followed By Artemisinin–Piperaquine Combination Therapy: COVID–19 Pandemics and Malaria Elimination

Case Report

Khin Phyu Pyar[1,*] Soe Win Hlaing[2], Soe Min Aung[2], Zar Ni Htet Aung[2], Nyan Lin Maung[2], Aung Phyoe Kyaw[2], Kaung Myat[2], Thein Soe Tun[2], Hein Hlaing Soe[2], Han Lin Aung[3], Myo Thant Kyaw[3], Zay Phyo Aung[3], Kyaw Thuyein Lwin[4], Ye Htut Maung[4], Lynn Htet Aung[5], Lay Maung Maung[5], Ye Min Hein[5], Moe Tun Zaw[5], Myo Maung Maung[5], Sai Aik Hla[2] & Swan Htet[6]

[1]Professor and Head/Senior Consultant Physician, Department of Medicine/ Department of Nephrology, Defence Services Medical Academy/ No.(1) Defence Services General Hospital (1000–Bedded), Myanmar.

[2]Consultant Physician, No. (1) Defence Services General Hospital (1000–Bedded), Myanmar.

[3]Assistant Lecturer / Consultant physician, Defence Services Medical Academy, Myanmar.

[4]Consultant Nephrologist, No. (1) Defence Services General Hospital (1000–Bedded), Myanmar.

[5]Nephrology Fellow, No. (1) Defence Services General Hospital (1000–Bedded), Myanmar.

[6]Consultant Microbiologist, No. (1) Defence Services General Hospital (1000–Bedded), Myanmar.

***Corresponding author**

Khin Phyu Pyar,
Professor and Head/Senior Consultant Physician,
Department of Medicine/ Department of Nephrology,
Defence Services Medical Academy/ No.(1) Defence Services General Hospital (1000–Bedded),
Myanmar;
Email: khinphyupyar@gmail.com.

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Abstract

A 49 year old mobile worker was brought to hospital in state of shock following high fever with chills. He was drowsy; dehydrated; high fever of 104ºF; hypotension; and tachycardia. He was initially treated as a case of septic shock with parenteral fluids, inotropes, and, antibiotics (meropenum and levofloxacin). Blood tests revealed anemia (haemoglobin 6.1 gm%); normal total WBC count; thrombocytopenia; raised serum creatinine (2.4 mg%); and, transaminitis (SGOT 80 IU/L and SGPT 100 IU/L). He came back from Myanmar–India border, malaria endemic

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area and peripheral blood film revealed ring form of plasmodium falciparum (count 1273/HPF) with gametocytes. Thus, parenteral artemether followed by 3 days course of dihydro–artemisinin piperaquine combination were prescribed. The clearance time for fever was 96 hours; parasite clearance time was 72 hours. To cut transmission chain, eradication treatment was given; primaquine. Liver enzymes became normal by 2 weeks; acute kidney injury recovered with conservative treatment. The patient did not have recrudescence of fever as well as parasite in peripheral blood film till 42 days after artemisinin combination therapy.

Keywords: Mobile Worker; Myanmar India Border; Septic Shock; Confusion; Prostration; Anemia, Thrombocytopenia; Acute Kidney Injury; Transaminitis; Complicated Falciparum Malaria.

Introduction

Malaria is caused by Plasmodium species; severe clinical manifestation is commonly seen with *Plasmodium falciparum* and extremely rare with *Plasmodium vivax*. The Greater Mekong region (GMS) as well as Myanmar National Malaria Control Program have been trying for malaria eradication; falciparum free by 2025 and total malaria free by 2030. Despite the emergence of the COVID–19 pandemic, all countries of The Greater Mekong subregion (GMS) have continued to achieve great progress towards the malaria elimination targets outlined in the GMS strategy. According to record from Mekong Malaria Elimination Program, 12,454 malaria cases were reported from April 2020 to June 2021 in the GMS (Mekong Malaria Elimination Program, 2021 October). In Myanmar, the prevalence of malaria has dropped dramatically since 2017 [1]. In 2020, both cases of Plasmodium falciparum and mixed cases dropped nearly 70%; likewise, Plasmodium vivax cases reduced by one third.

In view of drug resistance, artemisinin resistance has been noticed not only in Myanmar [2–4] but also in the GMS [5] since 2009. Artemisinin resistance is a major threat to global malaria control and elimination efforts. Thus, various efforts to combat resistance to antimalarial drugs have been done; artemisinin combination therapy has been recommended in treatment guideline of both WHO and Myanmar. Artemisinin combination therapy currently available in Myanmar are artemether–lumefantrine, dihydro–artemisinin piperaquine, and artesunate mefloquine.

The possibility of extended drug resistance to artemisinin combination therapy is worrisome as newer drugs are under trial [6–8]. In fighting malaria, there are several limitations faced by countries in the GMS particularly in border areas; and, the dominant species differ too. In the China–Myanmar border area, *P. vivax* was the predominant species [9]. The emergence and spread of Plasmodium falciparum and Plasmodium vivax multidrug resistance (MDR) malaria on Thailand–Myanmar and Thailand–Cambodia borders were highlighted [10]. Every GMS country faces difficulties in both elimination and control among mobile/migrant workers [11,12].

Case presentation

A 49 year old man was brought to hospital in early October 2021 as he had cold and clammy extremities following high fever with chills for two days. His Glasgow Coma Scale was 14/15; dehydrated; and, temperature was 104ºF. He had anemia but no jaundice. No features of meningeal irritation. Sa O2 was 94% on air. Blood pressure was 70/50 mmHg; pulse rate was 140/min. He was treated as a case of septic shock with parenteral fluids, inotropes, meropenum and levofloxacin.

He came back from Nu Bu Unit, Palatwa township where malaria is still endemic; Nu Bu Unit is 2 days walking distance from Myanmar–India border. (Figure 1) Therefore, blood for rapid test for malaria was done and it was positive for falciparum malaria. Peripheral blood film revealed ring form of plasmodium falciparum (count 13924/HPF) with gametocytes. Total WBC

Figure 1: Geographical distribution of Nu Bu Unit, Palatwa township.

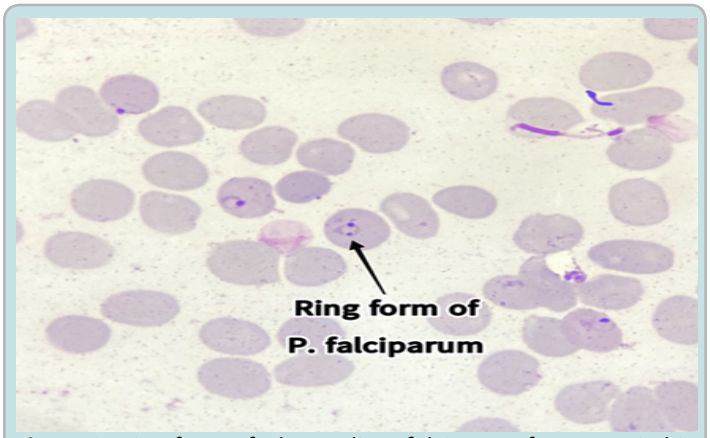

Figure 2: Ring form of *Plasmodium falciparum* from Day 0 thin blood film.

count was 8.0 × 10^9/L with normal differential count, hemoglobin 6.1 gm%, Hct 50% and platelet count was 51 × 10^9/L. Serum creatinine was 2.4 mg% and electrolytes were normal. Liver enzymes were raised; SGOT 80 IU/L and SGPT 100 IU/L. Blood for Widal test was negative. Blood for Dengue serology was negative. Nasopharyngeal swab for COVID–19 was negative. Chest radiograph was normal; ultrasound abdomen was normal. Blood culture was sterile.

Thus, parenteral artesunate was given for three days; it was followed by 3 days course of oral dihydro–artemisinin piperaquine combination. Blood for malaria parasite was checked 6–hourly. Seventy–two hours later, there was no more ring form in blood film and only gametocytes were seen (Figure 3 & 4).

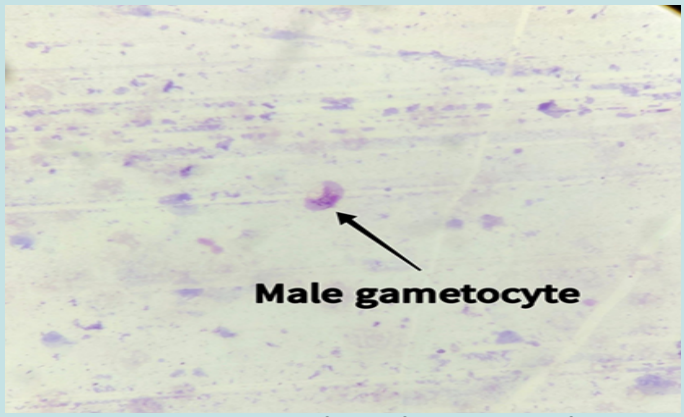

Figure 3: Male gametocyte form of *Plasmodium falciparum* from Day 3 thin blood film.

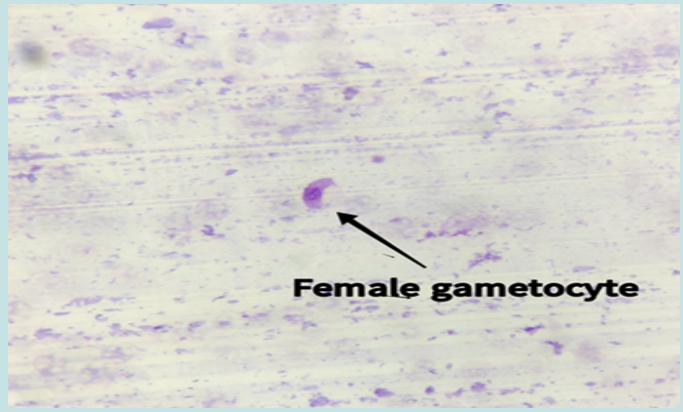

Figure 4: Female gametocyte form of *Plasmodium falciparum* from Day 3 thin blood film.

Fever clearance time was 96 hours. To prevent transmission, eradication treatment was given; primaquine. Liver enzymes became normal by 2 weeks. Acute kidney injury recovered with fluid therapy. Anemia was corrected with packed cell transfusion. Weekly blood film for malaria was negative till 6 weeks after artemisinin combination therapy. There was no recrudescence of fever till 6 weeks. Therefore, he had excellent 42 days adequate clinical and parasitological response; there was no evidence of artemisinin–piperaquine resistance.

Discussion

Malaria is one of the major public health problems in Myanmar. Myanmar adopted the goal of eliminating malaria by 2030 and aims to eliminate *P. falciparum* malaria by 2025 in line with the Greater Mekong Sub–region Malaria Elimination Strategy.Significant progress has been made over recent years in reducing malaria morbidity and mortality in Myanmar. According to report from National Malaria Control Program, falling incidence of falciparum malaria and relatively high incidence of vivax malaria has been reported since 2017. In our tertiary hospital, we did not come across complicated falciparum malaria for almost 4 years; this is the first reason for presenting rare case.

Typical complicated falciparum malaria case may have multi–system involvement: (1) cerebral manifestation which varies from confusion to coma or fits; (2) pulmonary manifestation like acute pulmonary oedema or ARDS; (3) renal manifestation in form of acute kidney injury; (4) hematological manifestation like severe anemia, thrombocytopenia and disseminated intravascular coagulation; (5) liver manifestation like jaundice and transaminitis; (6) gastro–intestinal manifestation like diarrhea and dysentery; (7) severe intra–vascular hemolysis leading to black water fever; (8) algid malaria or septic shock; (9) prostration; (10) Non–per–os state; (11) hyperpyrexia; (12) hyper–parasitemia; (13) metabolic acidosis/ lactic acidosis; and (14) hypoglycemia (WHO treatment guideline). In this case, he had multi–organ failure–7 manifestations: septic shock, confusion, prostration, severe anaemia, thrombocytopenia, acute kidney injury and transaminitis. It is very rare to see complicated malaria with multi–organ failure; important reason for sharing case story.

Thirdly, in the era of malaria elimination, having only one case of severe falciparum malaria is extremely important from public health point of view because this case may be one of the ice–berg phenomena. Malaria control and elimination plan in both GMS subregion and Myanmar National Malaria Control Program may find more ways in Palatwa township which has been known as hotspot for several years.

Moreover, this case also highlighted the situation of Myanmar India border malaria as he probably acquired falciparum malaria in Na Bu Unit, 2 days walking distance to India border. From Palatwa township to Na Bu Unit, it takes 10 days by walking. Thick jungle of bamboo trees occupies the whole area– Na Bu Unit; a very hard to reach area. Several reports explained the difficulties in doing control of malaria at hard–to–reach area [9].

Fifthly, this case gave excellent information to GMS region. The emergence and spread of Plasmodium falciparum and Plasmodium vivax multidrug resistance (MDR) malaria on Thailand–Myanmar and Thailand–Cambodia borders was reported previously [10]. As West Pacific region is afraid of spread of artemisinin resistant malaria from Asia, having good adequate clinical and parasitological response for 42 days in this case proved that there was no evidence of artemisinin–piperaquine resistance in Myanmar–India border. However, pharmacokinetics and molecular study should have done in this case to give more precise information.

Moreover, this case again highlighted to consider malaria prophylaxis in special situation like crowds of mobile workers going to malaria endemic area because pocket treatment would not save patient with complicated malaria.

Finally, this case also reminded us to revise the strategy to control/eliminate malaria in COVID–19 pandemic era in order to achieve malaria free by 2030. Regarding the behavior, the patient did not use bed nets and he lived in huts; the predicting factor for acquiring malaria. It confirmed previous report by [13]; the predicting factors for positive rapid test in malaria endemic area were people living in huts; with non–septic toilets; possessing farm animals; presenting with fever; having a malaria episode in the last year; traveling to any outside village in the last 14 days; and, not using bed nets in high burden area [13].

Conclusion

To avoid fatal complication, early diagnosis and treatment of complicated malaria is essential. Therefore, clinical awareness is extremely important although the prevalence of malaria is very low particularly in malaria elimination era. The clinician should have high index of suspicion in mobile/migrant population particularly returning back from malaria endemic area. Control of malaria in border area particularly in mobile/migrant population is still challenging from public health point of view. Adequate clinical and parasitological clearance for 42 days with dihydro–artemisinin piperaquine combination therapy generally indicated that the resistance to dihydro–artemisinin piperaquine in Myanmar–India border is unlikely.

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Declaration of conflict of interest

The authors declared no potential conflicts of interests with respect to authorship and publication of this article.

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Our institution does not require ethical approval for reporting cases.

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Informed consent

The informed consent for publication in this article was obtained from patient.

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