A case of imported Plasmodium Falciparum chloroquine and Sulfadoxine-Pyrimethamine sensitive in a Finland male presentation

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A case of imported *Plasmodium Falciparum* chloroquine and Sulfadoxine-Pyrimethamine sensitive in a Finland male presentation

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Abstract. Travellers in tropical countries are to get various infections including malaria. Severe or complicated malaria mostly caused by plasmodium falciparum. We reported uncomplicated malaria case in travellers caused by P. Falciparum who remain sensitive to chloroquine and sulfadoxine-pyrimethamine according to PCR result. The malarial diagnosis was confirmed with a microscopic test, RDT and PCR. The patient was treated with fixed- dose artemisinin-combination therapy and primaquine. Early treatment failure was not found based on clinical finding or microscopic test. The patient was discharged on the day 5th of treatment.

1. Introduction

Malaria in which the human red blood cell is infected by the parasite of the Plasmodium genus remains a global health problem worldwide.[1] Malaria has been recognized as a major cause of death and illness in children and adults, especially in tropical countries [2]. Indonesia is one of the topical country in which 230 million of people are exposed to malaria infection [3]. In general, the annual parasite incidence (API) of malaria in Indonesia has been reported to be decrease form 1.8/1000 populations in 2009 to 0.86/1000 population in 2016 [4]. Several areas have been categorized as a red zone area of malaria such as East Nusa Tenggara, West Nusa Tenggara, Maluku, North Maluku, Central Borneo, Central Sulawesi, West Sulawesi, Gorontalo and others [5]. It has been well recognized that Indonesia poses over 20 species of Anopheles mosquitoes. This malaria vector transmits the Plasmodium thoroughly its bite, which mainly bites human between sunset and sunrise (night time). The incubation period is 7 days or longer [1,2].

The most first symptoms of malaria are nonspecific, comprises of a headache, lassitude, muscles and joint pain, abdominal discomfort and followed by fever, chills, nausea, vomiting, perspiration and may develop jaundice[6]. Those cases without any features of severe malaria manifestation termed uncomplicated malaria. Severe (complicated) malaria manifest as one of the following: coma (cerebral malaria), acute kidney injury, black water fever, severe anemia, metabolic acidosis, hypoglycemia or acute lung edema [7]. To confirm the diagnosis of malaria all cases of suspected malaria should have a parasitological test (microscopy or rapid malaria diagnostic test/RDT) [6]. Malaria diagnosis with Polymerase Chain Reaction is used as a confirmatory diagnostic tool in assessing malaria [8]. The

treatment of uncomplicated malaria (except pregnant women in the first semester) is emisinin-combination therapy (ACT). The ACT has been successfully replaced the using of first-line anti-malarial drugs such as chloroquine or sulfadoxine-pyrimethamine due to a rapid growth of resistance to the oldest drugs. Chloroquine resistance has been reported from all areas of Indonesia where the studies to this were conducted [9].

Malaria in developing countries is one of the major threats to traveler that mostly from non-immune areas or developed countries [10]. The outcome of malarial infection may be fatal such as an immune compromise patient from non-immune area [11]. Bali is one of the most popular tourist destinations which are not malarial endemic area. Some imported cases in Bali were reported of the travelers after visiting endemic areas particularly Eastern Indonesia. Herein, we reported a traveler infected with Plasmodium Falciparum following travel to malaria endemic area in East Indonesia in which the malarial molecular finding was remains sensitive to chloroquine and sulfadoxine-pyrimethamine.

2. Case report

A 46 years old male from Finland was admitted at Kasih Ibu Hospital with fever nausea, and vomiting on 6th December 2018. The fever was for 3 days prior to admission and continuous fever, mostly high-grade fever (39.5-400C) with a presentation of chills prior to the fever. In addition to fever, the patient also suffers from a headache as well as joint pain, followed by vomiting and diarrhea. There was no episode of loss consciousness. There was no jaundice or bleeding reported. He went to Bangkok on 7th November 2018 for 8 days. He also was traveling to Sumbawa Island on 17th November 2018 for 6 days, than Gorontalo and Sulawesi for one day. He did not take malaria prophylaxis. This patient was fully alert with Glasgow Coma scale 15 and normal vital sign except the temperature. There was no jaundice or anemic found in his eyes. Heart and lungs sound was normal. There was no hepatomegaly or splenomegaly. On admission, the NS1 test result was negative. The results of the blood test for 5 days are list as table 1. Blood smear and PCR result revealed for Plasmodium falciparum. The blood sample was sent to Eijkman Institute for Biology Molecular Jakarta for further molecular diagnostic. PCR Result and Blood smear is presented in figure 1 and figure 2.

Table 1. Characteristic of laboratories finding.

	Day 1	Day 2	Day 3	Day 4	Day 5
NS1	negative				
WBC	3.03	2.8	2.40		3.69
Lymphocytes absolute	0.77	1.00	1.14		2.53
Monocyte	0.31	0.22	0.37		0.47
Eosinophil	0.00	0.01	0.03		0.07
Basophile	0.00	0.00	0.00		0.00
Neutrophil	1.95	0.95	0.59		0.62
HGB	15.40	14.30	14.60	14.3	13.70
MCV	88.1	85.9	84.70	84.3	85.7
MCH	29.3	29.0	29.30	29.5	28.70
HCT	45.20	41.9	42.20	40.9	40.9
PLT	102	75	42	64	105
RDT Mal	positive *P. falciparum*				
IgM Den					positive
IgG Den					positive

Diagnosis of malaria also confirms by molecular test through PCR according to the previous study with the primer targeting the Plasmodium spp 18S sRNA genes [8]. The primer for P. falciparum are Plasmodium sp. rPLU5 CCTGTTGTTGCCTTAAACTTC and rPLU6 TTAAAATTGTTGCAGTTAAAACG. The PCR reveal the finding of Plasmodium falciparum. We then analyzed the polymorphism on the gene dihydrofolate reductase gene (dhfr), dihydropteroate

synthase gene (dhps), P. falciparum chloroquine resistance transporter (pfcrt) gene and MDR1 gene. The results reveal that the P. falciparum remains sensitive to chloroquine and sulfadoxine-pyrimethamine.

Since the patient presentation was mild malaria, the treatment of this patient with oral fixed-dose ACT comprising of 40 mg dihydroartemisinin and 320 mg piperaquine for each tablet. This regimen was used for 3 days (D1, D2 and D3), 3 tablet daily due to 86 kg of the patient weight. Primaquine 45 mg single dose was administered in order to eliminate the gametocyte. We monitor the possibility of early resistance by monitoring the clinical manifestation and microscopic test at D1 of treatment and followed with D3 and D7 monitoring. There is no sign of treatment failure whether clinically or even microscopically. In addition, there were no complications such as severe anemia, malaria biliosa, backwater fever, acute kidney injury or other severe malaria symptoms found in the case. There was no identification of late treatment failure because the patient has returned to his country before the time of follow-up (on the 28th days post-treatment).

Figure 1. PCR test.

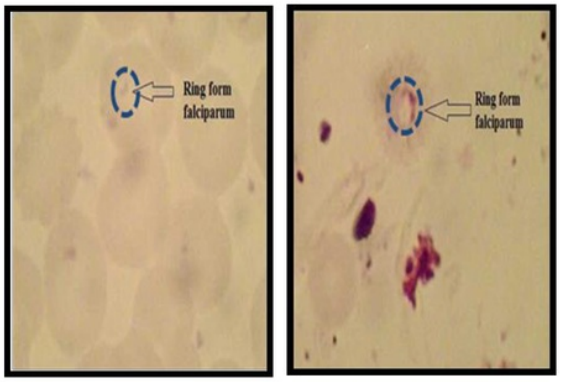

Figure 2. Blood smear test.

3. Discussion

Contracting with an infection during travelers is common between the travelers to the tropical countries. Dengue infection among the returning travellers [12, 13], diarrhea in the tourism area [14], or malaria [15-17] has been reported as the risk of travel. The life threatening malaria infection threats not only the

resident in the tropical countries but also the traveller from non-tropical countries. Plasmodium falciparum and P. vivak are the most prevalent plasmodium genus found elsewhere. Another genus of plasmodium are P. ovale, P malariae and the most recent monkey malaria parasite P. knowlesi are being reported from forested region around Borneo island. The API of Bali was 0.00 in 2016, but it does not reveal that there is no malaria case in Bali [3]. The most malaria cases in Bali are mostly imported case from the people who visiting malaria endemic area prior malaria symptoms development.

In this patient, before visiting Bali, he has travelled to an endemic malaria area, Sumbawa Island for 7 days and followed to visit Gorontalo City for 2 days, the areas where the malaria cases routinely reported, before his visiting to Bali. It than assume that he got the parasite in the endemic areas of Indonesia. He did not take the malaria prevention as the best method to prevent such infection. The symptoms of the case were compatible with the un-complicated or non-severe malaria clinical manifestation with fever as the main symptom, followed by a headache, weakness, bone and joint pain, nausea or vomiting. Laboratory finding also supports the malaria diagnosis, which positive of RDT, microscopic and PCR test. Although the result of PCR did not find any sign of CQ + SP resistance as the WHO guiding of ACT based for malaria treatment the patient has been treated with fixed-dose dihydroartemisinin plus piperaquine and a single dose of primaquine as a gametocide drug. Unfortunately, there is no tool to evaluate the parasite density to define the response to malaria treatment. We use clinical response and microscopic test to assessing the possibility of treatment failure. The patient was discharged after 5 days of treatment without any sign of treatment failure until the 7th day of treatment. We suggest reviewing the late treatment failure with his internist in his country.

The current case presents with un-complicated malaria manifestation may related with the infecting parasite is still sensitive to the former first-line anti-malarial drugs or due to the immunocompetent status of the case. However, another immunocompetent malarial case has been reported co-infection with invasive pulmonary aspergillosis [18]. The previous case report did not evaluate the genotype of the Plasmodium.

Infection by Plasmodium falciparum is the most common malarial infection in the world, not only in a local but also among international travellers traveling to tropical or sub-tropical areas [19]. In Europe, malaria has been eradicated since 1970s through successfully combining of insecticide spraying, drug therapy and environmental engineering. Massive travel has reported as the cause of occurrence of imported malaria cases in Europe [20]. Plasmodium falciparum was also reported as the most cause of malarial infection among European travellers returning from countries of endemicity [21]. Meanwhile, Plasmodium vivax reported as the most cause of malarial infection in Australian travellers returning from Asia-Pacific region [22].

The current case assumes that the malaria infection is import case from Sumbawa or Gorontalo City, since Bali's API is zero. Similar cases were reported among travellers in Bali on their returning from journey to Lombok Island or Gili Trawangan/Gili Meno (unpublished data).

4. Conclusion

In conclusion, this case report has reported a case of uncomplicated malaria caused by P. falciparum that remains sensitive to CQ + SP. Prompt diagnosis and treatment may provide malaria outcome.

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