CASE REPORT

Plasmodium ovale Malaria and Dengue Co-infection in a Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency Patient : A Case Study

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ABSTRACT

Malaria and dengue are among the most important public health threats in Malaysia. These two-arthropod borne diseases have overlapping mosquito biotopes and clinical manifestations, and co-infections have been associated with increased severity notably on the haematological abnormalities. Dengue caused by four dengue virus (DENV) serotypes has been highly endemic in Malaysia. However, malaria due to *Plasmodium ovale (P. ovale)* has been rarely reported among Malaysian population. Nonetheless, climate change and increased influx of international travellers and migrants have shifted the parasite boundaries to non-endemic countries. Thus, diagnosis and management of imported malarial infections should rely on the geographical knowledge on the origin of potential *Plasmodium* species, prompt laboratory testing and public health intervention. Moreover, it would be difficult to clinically differentiate dengue fever (DF) with a potential relapse or partially treated case of P. ovale, and there is absolutely no transmission of this Plasmodium species in our country. Hence, we believed that this case deserved to be reported.

Keywords: *Plasmodium ovale,* Malaria, Dengue, Co-infection

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INTRODUCTION

Malaria and dengue fever are the most prevalent arthropod-borne diseases in tropical countries and represent major public health problems due to high morbidity and mortality. To the authors' knowledge, concurrent infections of *Plasmodium* species and dengue virus (DENV) has been rarely documented in Malaysia. The only available data was on case series of *Plasmodium knowlesi* malaria and dengue co-infection, which was published in 2016 (1). Malaria due to *P. ovale* has usually remained localised to tropical Africa and the Middle East regions. However, increased international travels for commercial and non-commercial purposes would pose substantial risks to local health and ecosystem (2). Moreover, dengue virus is known to initiate massive inflammatory reaction in hepatocytes which in turn could trigger the release of *P. ovale* parasites into the blood circulation (relapse) (3). Herein, we describe a possibly relapse case of *P. ovale* malaria which could be triggered by dengue infection in an international student.

CASE REPORT

A 32-year-old Nigerian student presented with high-grade fever associated with chills, rigors, arthralgia, myalgia, and headache of five days' duration. He also had other constitutional symptoms such as nausea, vomiting and loose stools of similar duration.

He denied history of recent travelling or jungle exposure or swimming in the river or contact with dengue patients. However, he claimed that he had been staying with her brother in a dengue-prone area when he came to Malaysia two weeks ago prior to the onset of the presenting complaints. On past medical history, he admitted that he was treated for malaria a few days prior to his visit to Malaysia.

On admission, he was febrile (39°C) with normal vital signs and good peripheral perfusion. The cardiovascular, respiratory, abdominal and nervous

system examination was unremarkable.

His full blood count showed thrombocytopenia (platelet count of 75 x10^9/L) with normal white cell count and haematocrit level. Dengue Duo (Standard Diagnostics, Republic of Korea) was positive for both Dengue IgM and IgG antibody with negative NS1 antigen at day five of illness.

In view of past medical history of malaria, blood film for malarial parasite (BFMP) was performed and demonstrated the presence of asexual and sexual stages of *Plasmodium ovale* with the density of 5200 /uL and 1000 /uL, respectively (Please refer to Figure I). He was then diagnosed with dengue fever with no warning signs and coinfected with uncomplicated *P. ovale* malaria. Patient was treated symptomatically for dengue infection and was well tolerated orally. Oral Artemether 20mg/Lumefantrine 20mg (4 tablets) was commenced stat and 6 hours later, then 4 tablets 6 hourly for two days. Daily monitoring of haematological parameters and BFMP was done with no signs of liver failure and gradual clearance of parasites was noted. His hospital stay was uneventful, and he was discharged from the ward with an adjusted dose of oral primaquine 45mg stat and once a week for 8 weeks as he had Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency.

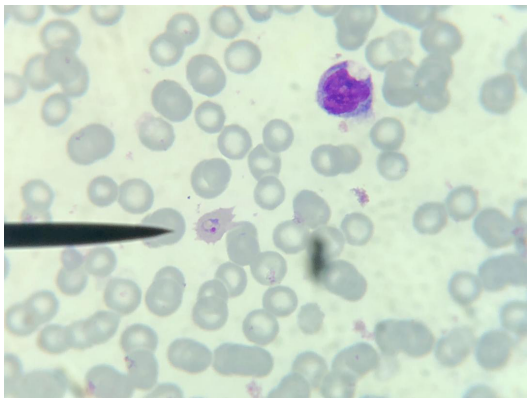

Figure 1 : A sexual phase (ring trophozoite) of Plasmodium ovale in thin smear (100x high power field)
Note : The fimbriated borders of an infected red blood cell are observed as the characteristic feature of P. ovale (black pointer)

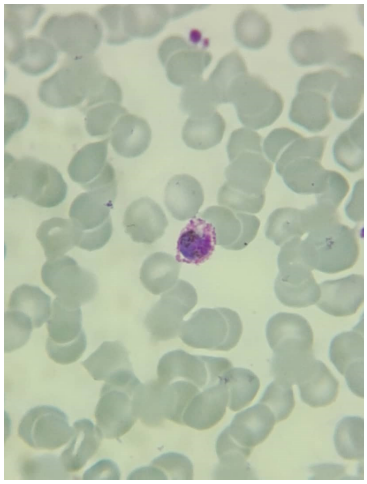

Figure 2 : Sexual stage (gametocyte) of *Plasmodium ovale* in thin smear (100x high power field)
Note: Dark Schüffner's granules in an infected red blood cell. The fimbriated border is not apparent in this case.

DISCUSSION

Malaria and dengue fever are well known to be endemic in Malaysia. According to World Health Organization (WHO), Malaysia has recorded a tremendous drop in the number of reported indigenous human malaria case from 5000 in 2010 to zero case in 2018 (2). However, imported case of malaria has become the national major concern as there were 478 cases reported in 2018 (2). There are several contributing factors for the emergence of imported malaria cases. Increased influx of foreign workers and immigrants, as well as travelling to endemic countries for commercial and non-commercial purposes have been shown to play significant roles (2). Meanwhile, dengue fever remains the most endemic disease in Malaysia. It has been reported that the cumulative number of dengue cases has increased from 53,872 cases with 88 deaths in 2018 to 98,184 cases with 143 deaths in 2019 (4). As for this case, concurrent infection by DENV and *P. ovale* has been rarely reported in Malaysia. As there is no autochthonous *P. ovale* malaria in our region, the detection of this parasite may be contributed to the migration of travellers (international student in this case) from *P. ovale* endemic region that is Nigeria. This can also be explained by a stress response due to massive inflammatory reaction by DENV, which could have triggered the release of *P. ovale* in the blood circulation (3). Moreover, relapses of *P. ovale* usually begin as early as 14 days following effective therapy (3), which could be observed in this patient.

Co-infection by these two different pathogens could pose a challenge for the accurate diagnosis of the aetiological agents due to overlapping clinical symptoms. It is therefore difficult to discriminate this co-infection based on the clinical signs and symptoms alone. More worryingly, malaria and dengue co-infection is more severe than mono-infection in which bleeding, severe thrombocytopaenia and anaemia are frequently encountered in the former (5). In our uncomplicated dengue patient, *P. ovale* is considered benign and it only affects young erythrocytes, thus, severity of co-infection is not apparent. . As for the diagnosis of dengue, no molecular confirmation was performed thus one could question whether serological evidence of dengue may be influenced by malaria as false positive results (1). Malaria parasites have been recognized to be a mitotic agent that can initiate the polyclonal activation of B-lymphocytes. Nonetheless, the antibody titres

would be very low and will decrease early after malaria treatment (6). In our case, both dengue IgG and IgM were detected, which could strongly support the diagnosis. However, a repeat serum sample for dengue was not requested. Absence of NS1 is expected in this case as this biological marker is more apparent at Day 3 of dengue fever although it may last up to Day 5 of fever. With regard to malaria treatment in G6PD patients, the dose of primaquine should be used in great caution. In non-G6PD patients, oral primaquine is given for 14 days as recommended by WHO but it must be adjusted in G6PD deficiency patients as seen in this case to avoid haemolysis.

CONCLUSION

Although dengue infection is highly prevalent in our country, any cases of acute febrile syndrome should raise a high index of suspicion for clinicians on travellers who come from malaria-endemic regions. Close monitoring on patients with malaria-dengue co-infection is needed regardless of the types of *Plasmodium* species as bleeding and hepatic complications may occur. Continuous laboratory training for malaria diagnosis is useful for the detection of *P. ovale* that is not prevalent in our country.

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