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Plasmodium vivax Malaria: A Case Review and Therapeutic Considerations in an Adult Patient

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ABSTRACT

Plasmodium vivax malaria remains a major health problem in tropical countries due to its high relapse rate and various hematological manifestations that may worsen the patient's condition. This case report aimed to describe the clinical manifestations, laboratory findings, and evaluation of therapeutic rationality in a patient with Plasmodium vivax malaria during hospitalization. The study was conducted using a case report method involving a 22-year-old male patient who presented with periodic fever accompanied by chills for one week after traveling from a malaria-endemic area. Laboratory examination revealed microcytic hypochromic anemia, leukopenia, mild thrombocytopenia, and malaria parasites identified on peripheral blood smear examination. The patient received supportive therapy including intravenous Ringer Lactate fluid, paracetamol, omeprazole, domperidone, and ferrous sulfate, as well as definitive therapy consisting of dihydroartemisinin-piperaquine (DHP) for three days and primaquine for 14 days. The evaluation showed that most of the therapies administered were in accordance with national guidelines and WHO recommendations for uncomplicated P. vivax malaria. However, the absence of glucose-6-phosphate dehydrogenase (G6PD) enzyme activity testing prior to primaquine administration was considered one of the limitations in patient management. During hospitalization, the patient showed clinical improvement without severe complications. The management of P. vivax malaria requires a comprehensive approach including early diagnosis, rational therapy, clinical monitoring, and patient education to prevent relapse and improve therapeutic outcomes.

Keywords: Plasmodium vivax malaria; antimalarial therapy; inflammatory anemia; primaquine; case report

Introduction

Malaria remains one of the infectious diseases that contributes substantially to the global health burden, particularly in tropical and subtropical regions. The disease is caused by protozoa of the genus Plasmodium and transmitted through the bite of infected female Anopheles mosquitoes. Despite extensive global malaria elimination programs, the incidence of malaria remains relatively high, especially in

developing countries with geographical conditions that favor vector proliferation (WHO, 2023). Among the Plasmodium species infecting humans, Plasmodium vivax has the widest geographical distribution and is the predominant cause of malaria outside sub-Saharan Africa (Habtamu *et al*., 2022). Unlike Plasmodium falciparum, P. vivax is capable of forming hypnozoites, a dormant hepatic stage that may reactivate after a certain period and cause relapse. This characteristic makes P. vivax malaria more difficult to eliminate because patients may experience recurrent infections even after receiving blood-stage therapy (WHO, 2022). According to WHO reports, approximately one-third of the global population remains at risk for P. vivax malaria, and most recurrent cases are associated with hypnozoite reactivation in the liver (WHO, 2024). In addition to causing recurrent relapses, P. vivax malaria contributes to increased morbidity through anemia, reduced functional capacity, and impaired quality of life resulting from repeated infections (Phyo *et al*., 2022). Recent studies have also demonstrated that P. vivax malaria should no longer be considered a benign disease because it may lead to severe complications such as severe anemia, significant thrombocytopenia, respiratory distress, and even organ failure under certain conditions (Phyo *et al*., 2022).

In Indonesia, malaria remains a major public health challenge, particularly in endemic regions such as Papua, West Papua, East Nusa Tenggara, and Maluku. Although the national incidence has shown a declining trend, local transmission and imported malaria cases are still frequently reported due to high population mobility (Ministry of Health of the Republic of Indonesia, 2023). Consequently, malaria remains an important disease to consider, especially in patients with a history of travel to endemic areas. The clinical manifestations of P. vivax malaria are commonly characterized by periodic tertian fever occurring every 48 hours due to synchronized lysis of infected erythrocytes (White, 2018). In addition to fever, patients may experience chills, diaphoresis, headache, myalgia, fatigue, and gastrointestinal symptoms such as nausea and vomiting. Laboratory findings frequently demonstrate anemia, leukopenia, and thrombocytopenia resulting from erythrocyte hemolysis, bone marrow suppression, and systemic inflammatory responses (Douglas *et al*., 2012). The diagnosis of malaria requires a combination of clinical evaluation and laboratory examination. Peripheral blood smear examination remains the gold standard for identifying Plasmodium species and determining parasite density. However, malaria symptoms often resemble those of other tropical infectious diseases, particularly dengue fever; therefore, differential diagnosis should be carefully considered during the early phase of illness (WHO, 2022).

The management of P. vivax malaria aims to eradicate both the erythrocytic and hepatic stages of the parasite. WHO recommends the use of artemisinin-based combination therapy (ACT), including dihydroartemisinin-piperaquine (DHP), as blood-stage treatment in many malaria-endemic regions (WHO, 2022). Meanwhile, primaquine is required as radical therapy to eliminate hypnozoites and prevent relapse (WHO, 2022). However, primaquine administration requires special consideration because it may induce hemolysis in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency (WHO, 2022). In addition to definitive antimalarial therapy, supportive management also plays an important role in improving clinical

outcomes. Antipyretic agents are commonly used to control fever and improve patient comfort during acute malaria episodes. Among these agents, paracetamol has also been reported to reduce oxidative stress associated with intravascular hemolysis in certain malaria infections. (Cooper *et al*., 2018). Management of gastrointestinal symptoms, fluid correction, and monitoring of hematological parameters are also essential during hospitalization.

Cases of P. vivax malaria remain important to report due to the variability of clinical manifestations, the possibility of relapse, and the therapeutic challenges associated with the disease. Furthermore, evaluation of drug therapy in patients with P. vivax malaria is essential to assess treatment appropriateness according to current guidelines and patient clinical response. Therefore, this case report was prepared to describe the clinical course of a patient with Plasmodium vivax malaria, the hematological alterations observed, and the therapeutic considerations during hospitalization.

Methodology

Case Description

A 22-year-old male patient, referred to as Mr. A, presented to the Emergency Department of a hospital in Padang City on June 3, 2024, at 10:33 AM with chief complaints of chills and fever. History taking revealed that the symptoms had been experienced for approximately one week. The patient reported a recent travel history from North Sumatra Province one week prior to admission. The symptoms initially began with a sensation of intense coldness followed by fever reaching 39°C. The fever episodes occurred every two days during the previous week. The symptoms typically resolved after the first day and recurred on the third day. The patient stated that whenever chills and fever occurred, he took paracetamol, after which his body temperature decreased and was followed by excessive sweating that soaked his clothes. Additional complaints included generalized weakness, dizziness, dry cough, nausea, and the urge to vomit.

In the Emergency Department, the patient received oral paracetamol tablets at a dose of 500 mg twice daily. Blood samples were collected for complete blood count examination. Laboratory results revealed hemoglobin of 10.6 g/dL, leukocyte count of 4,200/mm^3, erythrocyte count of 5.74 million/mm^3, platelet count of 126,000/mm^3, hematocrit of 34.6%, MCV of 60.3 fL, MCH of 18.5 pg, MCHC of 30.6%, random blood glucose of 126 mg/dL, and negative Salmonella typhi H and O serology tests. The Emergency Department physician recommended hospitalization; however, the patient refused admission.

Two days later, on June 5, 2024, at 04:00 AM, the patient returned to the Emergency Department with complaints of chills and high fever. Initial management included intravenous paracetamol infusion at a dose of 1 g/100 mL until the patient's condition improved. Physical examination revealed a moderately ill patient with compos mentis consciousness (GCS score of 15), blood pressure of 134/76 mmHg, pulse rate of 90 beats/minute, respiratory rate of 20 breaths/minute, body temperature of 38.7°C, and oxygen saturation of 99%. Examination of the head and neck showed normocephalic findings with normal jugular venous pressure.

Ophthalmologic examination demonstrated non-anemic conjunctiva and non-icteric sclera bilaterally with isochoric pupils measuring 2 mm. Cardiovascular examination revealed no visible ictus cordis, no cardiac thrill, normal cardiac borders, regular heart sounds, and absence of murmur or gallop. Pulmonary examination showed symmetrical chest wall movement, equal fremitus bilaterally, sonorous percussion, vesicular breath sounds, and absence of rhonchi or wheezing. Abdominal examination was unremarkable with normal bowel sounds. Extremities were warm with capillary refill time <2 seconds. Genitalia and anal examinations were normal, and no localized abnormalities were identified.

At 06:06 AM on the same day, repeat laboratory examination demonstrated hemoglobin of 9 g/dL, leukocyte count of 3,100/mm^3, erythrocyte count of 4.82 million/mm^3, platelet count of 127,000/mm^3, hematocrit of 28.4%, MCV of 58.9 fL, MCH of 18.7 pg, and MCHC of 31.7%. After stabilization, the patient was admitted to the inpatient ward with a provisional diagnosis of dengue fever or malaria. During hospitalization, the patient received supportive therapy consisting of intravenous Ringer Lactate fluid administration every 8 hours, oral paracetamol 500 mg three times daily, intravenous omeprazole 40 mg once daily, oral domperidone 10 mg three times daily, and oral ferrous sulfate 200 mg twice daily. The patient was also prescribed a high-calorie, high-protein diet. At 09:14 AM, additional laboratory examinations revealed TIBC of 165, serum iron of 22, and ferritin level of 667 ng/mL. Differential leukocyte count performed at 09:16 AM showed basophils 0%, eosinophils 0%, band neutrophils 19%, segmented neutrophils 59%, lymphocytes 19%, and monocytes 3%, indicating leukopenia with neutrophilia and a left shift. Platelet count was decreased with normal morphology and distribution. Peripheral blood smear examination demonstrated microcytic hypochromic erythrocytes, polychromasia (+), schistocytes (+), cigar cells (+), and malaria parasites identified on the examined smear. The overall interpretation suggested microcytic hypochromic anemia with differential diagnosis of iron deficiency consistent with hemolytic anemia due to malaria, leukopenia with neutrophilia and left shift, and thrombocytopenia. Follow-up peripheral blood smear and Reticulocyte Hemoglobin Equivalent (Ret-He) examination were recommended. Based on these findings, the patient was diagnosed with febrile illness due to malaria and secondary diagnosis of mild microcytic hypochromic anemia with suspected iron deficiency.

On June 6, 2024, the patient continued to receive intravenous Ringer Lactate every 8 hours, oral paracetamol 500 mg three times daily, intravenous omeprazole 40 mg once daily, oral domperidone 10 mg three times daily, and oral ferrous sulfate 200 mg twice daily along with a high-calorie, high-protein diet. At 06:00 AM, dengue serology testing showed positive Anti-dengue IgG and negative Anti-dengue IgM results. On June 7, 2024, the patient continued receiving the same therapeutic regimen and dietary management. Chest radiography (posteroanterior thorax view) was performed with clinical suspicion of community-acquired pneumonia (CAP). Radiological findings showed normal heart size with cardiothoracic ratio <50%, no widening of the aorta or superior mediastinum, centrally positioned trachea, non-prominent hilar structures, and infiltrates in the left perihilar region. The diaphragmatic contours and costophrenic angles were normal, and the bony thorax

appeared intact. Based on these findings, the patient was suspected of having pneumonia.

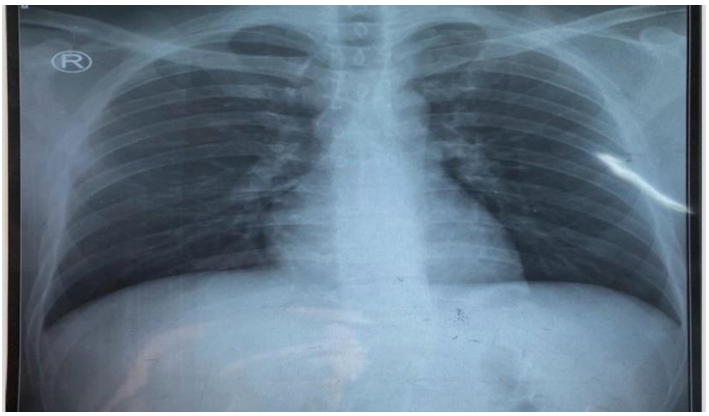

Figure 1. Thorax X-Ray (Chest X-Ray)

On June 7, 2024, at 06:00 PM, the patient was discharged from the hospital with prescribed continuation therapy consisting of dihydroartemisinin-piperaquine (DHP) at a dose of four tablets once daily for three days, primaquine one tablet once daily for 14 days, sucralfate syrup 15 mL three times daily, and lansoprazole 30 mg once daily.

Result and Discussion

Malaria remains one of the infectious diseases that contributes substantially to the health burden in tropical and subtropical countries, including Indonesia. Malaria infection is caused by protozoa of the genus Plasmodium and transmitted through the bite of infected female Anopheles mosquitoes. Among the human malaria species, Plasmodium vivax has the widest geographical distribution and continues to be a major challenge in malaria elimination programs due to its ability to form hypnozoites that can trigger relapse (Battle *et al*., 2019; Commons *et al*., 2020). In this case, the patient was diagnosed with Plasmodium vivax malaria based on characteristic clinical manifestations, travel history from an endemic area, and the identification of malaria parasites on peripheral blood smear examination.

The patient's primary clinical manifestation was periodic fever accompanied by chills occurring every two days. This fever pattern is consistent with tertian malaria caused by synchronized rupture of infected erythrocytes every 48 hours in P. vivax infection (White, 2018). The patient also experienced the classical stages of malaria attacks consisting of the cold stage, hot stage, and sweating stage. Additional systemic symptoms including weakness, headache, nausea, vomiting, and dry cough were likely associated with the release of inflammatory mediators during malaria infection (Phyo *et al*., 2022). During the first visit on June 3, 2024, laboratory examination demonstrated hemoglobin of 10.6 g/dL, leukocyte count of 4,200/mm^3, platelet count of 126,000/mm^3, hematocrit of 34.6%, MCV of 60.3 fL, MCH of 18.5 pg, and MCHC of 30.6%. These findings indicated microcytic hypochromic anemia accompanied by leukopenia and mild thrombocytopenia. Anemia in P. vivax malaria may occur due to hemolysis of both infected and non-infected erythrocytes, impaired erythropoiesis,

and increased systemic inflammatory response (Barber *et al*., 2019; Kho *et al*., 2021). However, the patient refused hospitalization and only received symptomatic treatment with oral paracetamol.

Two days later, the patient returned with high fever and chills. Repeat laboratory examination showed a decline in hemoglobin level to 9 g/dL and leukocyte count to 3,100/mm^3, indicating ongoing inflammatory and hemolytic processes. In addition, the patient continued to present with mild thrombocytopenia, with platelet counts ranging from 126,000–127,000/mm^3. Thrombocytopenia is one of the most common hematological abnormalities in P. vivax malaria and is associated with immune-mediated platelet destruction, splenic sequestration, and oxidative stress induced by parasitic infection (Naing *et al*., 2018; Kotepui *et al*., 2020). Peripheral blood smear examination revealed microcytic hypochromic erythrocytes with polychromasia (+), schistocytes (+), and cigar cells (+). Ferritin level was elevated to 667 ng/mL accompanied by low TIBC. These findings were more suggestive of inflammatory anemia rather than pure iron deficiency anemia. Ferritin is recognized as an acute-phase reactant that increases during inflammatory conditions, including malaria infection (Ganz & Nemeth, 2015). Therefore, the patient's anemia was likely influenced by systemic inflammation and hemolysis during malaria infection.

At the beginning of hospitalization, the patient was initially suspected of having dengue hemorrhagic fever because of fever and thrombocytopenia. However, Anti-dengue IgM was negative while Anti-dengue IgG was positive, suggesting previous dengue infection rather than acute dengue infection. Clinical manifestations of malaria and dengue frequently overlap, particularly during the early phase of illness; therefore, laboratory confirmation is essential to establish an accurate diagnosis (WHO, 2022; Commons *et al*., 2019). Chest radiography demonstrated infiltrates in the left perihilar region, leading to suspicion of pneumonia. Several studies have reported that P. vivax malaria should no longer be regarded as a benign disease because it may cause systemic complications, including respiratory disorders and pulmonary infiltrates due to inflammatory responses (Phyo & White, 2023). Nevertheless, the patient did not exhibit severe respiratory manifestations such as dyspnea or decreased oxygen saturation; therefore, the pulmonary condition could still be managed conservatively with close clinical observation.

During hospitalization, the patient received supportive therapy consisting of intravenous Ringer Lactate fluid, paracetamol, omeprazole, domperidone, and ferrous sulfate. Administration of intravenous Ringer Lactate at one bottle every eight hours was considered appropriate because the patient experienced high fever and excessive diaphoresis that increased the risk of dehydration. WHO recommends careful fluid administration in malaria patients to maintain tissue perfusion and fluid balance while avoiding fluid overload (WHO, 2022). The patient received oral paracetamol 500 mg three times daily and intravenous paracetamol 1 g/100 mL upon arrival at the Emergency Department with high fever. These doses were within the recommended therapeutic range for adults, namely 500–1000 mg every 4–6 hours with a maximum daily dose of 4 grams (Dipiro *et al*., 2020). Paracetamol administration was considered appropriate as antipyretic therapy to control fever and improve patient comfort during the acute phase of illness. Cooper et al. (2018)

also reported that paracetamol may reduce oxidative stress associated with intravascular hemolysis in malaria infection. The major adverse effect of paracetamol is hepatotoxicity, particularly with excessive or prolonged use; however, no signs of liver dysfunction were observed in this patient.

Intravenous omeprazole was administered at a dose of 40 mg once daily, which was within the recommended dosing range for adult patients (Dipiro *et al*., 2020). Although proton pump inhibitors are not routinely recommended for uncomplicated malaria, they may be considered in patients with gastrointestinal complaints, particularly nausea and reduced oral intake. In the present case, the patient experienced nausea during the acute phase of illness. The choice of omeprazole over other proton pump inhibitors, including lansoprazole, was likely related to hospital formulary availability and the treating physician's clinical judgment rather than evidence of superior efficacy. Nevertheless, the need for proton pump inhibitor therapy in this patient should be interpreted cautiously because no documented history of peptic disease or gastrointestinal bleeding risk factors was identified. Common adverse effects of omeprazole include headache, nausea, and diarrhea, whereas prolonged use may increase the risk of hypomagnesemia and vitamin B12 deficiency.

The patient also received oral domperidone 10 mg three times daily for nausea and vomiting. This dosage was in accordance with standard adult recommendations of 10 mg three times daily before meals (Dipiro *et al*., 2020). Domperidone acts as a peripheral dopamine antagonist that enhances gastrointestinal motility and accelerates gastric emptying. Its administration was considered rational because the patient experienced nausea during the acute phase of illness. Potential adverse effects include QT interval prolongation, especially at high doses or prolonged use; however, no cardiovascular abnormalities were observed during hospitalization.Ferrous sulfate was administered at a dose of 200 mg twice daily as supportive therapy for anemia. The use of ferrous sulfate was based on findings of microcytic hypochromic anemia on complete blood count examination. Nevertheless, elevated ferritin and low TIBC were more suggestive of inflammatory anemia rather than pure iron deficiency anemia. Previous literature has indicated that iron supplementation during acute infection should be considered cautiously because inflammation may increase hepcidin levels and inhibit iron utilization (Ganz & Nemeth, 2015). Therefore, ferrous sulfate administration in this patient could still be considered supportive therapy, although further evaluation of iron status would be necessary after resolution of the acute infection. Common adverse effects of ferrous sulfate include constipation, epigastric pain, nausea, and dark-colored stools.

After malaria diagnosis was established, the patient received definitive antimalarial therapy consisting of dihydroartemisinin-piperaquine (DHP) for three days and primaquine for 14 days. According to the Indonesian national malaria guideline, DHP is the first-line artemisinin-based combination therapy (ACT) for uncomplicated P. vivax malaria in adults (Ministry of Health of the Republic of Indonesia, 2023). Dihydroartemisinin rapidly eliminates erythrocytic-stage parasites, while piperaquine has a long half-life that helps prevent early recurrence (Price *et al*., 2020). Potential adverse effects of DHP include nausea, vomiting,

dizziness, and QT interval prolongation; therefore, clinical monitoring remains necessary during therapy.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article

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