Experience in Laboratory Diagnostics of Falciparum Malaria and Dengue Co-infection with Eosinophilia: a Case Report

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Abstract

Indonesia is an archipelagic country with a tropical climate and is vulnerable to regional and global climate change impacts. Due to climatic factors, the country faces a high risk of vector-borne diseases such as malaria and dengue. Malaria and dengue are spread through vector mosquitoes. Concurrent malaria and dengue fever infections occur when these two diseases occur simultaneously in a person. There was a possible relationship between the immune response and hematological recovery after acute falciparum malaria. This case reported a patient with overlapping clinical features and the difficulties encountered in differential malaria-dengue diagnosis in a rural hospital in Jombang, East Java, Indonesia.

Keywords: *Malaria, Dengue, Eosinophilia*

Introduction

Indonesia, an archipelagic nation with diverse ecosystems and climates, is at a critical juncture in its battle against vector-borne diseases.[1] Among the most pressing health challenges are dengue fever and malaria, two infectious diseases that continue to pose significant threats to public health across the archipelago. The interplay of environmental, social, and climatic factors has fostered a persistent struggle against these diseases, which together contribute to a substantial burden on the Indonesian healthcare system.[2]

Dengue fever, caused by the dengue virus transmitted by Aedes mosquitoes, and malaria, caused by Plasmodium parasites transmitted by Anopheles mosquitoes, exhibit complex epidemiological patterns that vary across Indonesia's regions. The country's tropical climate, characterized by high temperatures and seasonal rainfall, creates optimal conditions for mosquito breeding and proliferation. Additionally, rapid urbanization, population movement, and varied public health infrastructures have further complicated control and prevention efforts.[3,4]

Both of those tropical diseases shared same manifestation, such as fever, thrombocytopenia, and elevated of liver enzyme.[3,4] However, in some rare case both of the infections caused co-infection. This present case shows the co-infection of both tropical diseases manifested in patients in our rural area in Indonesia.

Case Illustration

A 26-year-old man in the east of Java Island went to work on Kalimantan Island for a month in July 2023 and returned home in August 2023. He has been coming to our emergency department with chills and stiffness for the last three days. He didn't complain of a fever at all. A vital signs examination showed a blood pressure of 80/60 mmHg, a heart rate of 110 times per minute, a respiratory rate of 20 times per minute, and a temperature of 36^{o}C. A

physical examination showed that consciousness was still good. There was no hepatosplenomegaly; lymphadenopathy and chest and abdominal examinations were normal. There were no signs of bleeding anywhere but a positive result of the rumple leed test.

Initial laboratory values (August 27th) were Hb 9.8 mg/dL, WBC $5.9x10^3$/µL (Eos 1.6%, Baso 0.0%, Neut 62.8%, Lymp 20.4%, Mono 15.2%), and PLT $100x10^3$/µL. Serum AST, ALT, BUN, creatinine, direct bilirubin, total bilirubin, Na, K, and Cl were within the normal limit. Laboratory values four days later (31 August) showed increasing WBC $6.6x10^3$/µL (Eos 5.8%) and PLT $123x10^3$/µL, IgM and IgG anti-dengue reactive, falciparum malaria rapid diagnostic test positive, and *Plasmodium falciparum* (schizont, trophozoit ring, and gametocyte) seen on peripheral smear (parasitemia index = 0.02%). Trophozoite ring and gametocyte form were seen in Picture 1. The patient was treated by a dengue shock syndrome therapy algorithm accompanied by Dihydroartemisinin-piperaquine (DHP) 3 tablets once a day and Primaquine 1 tablet once a day.

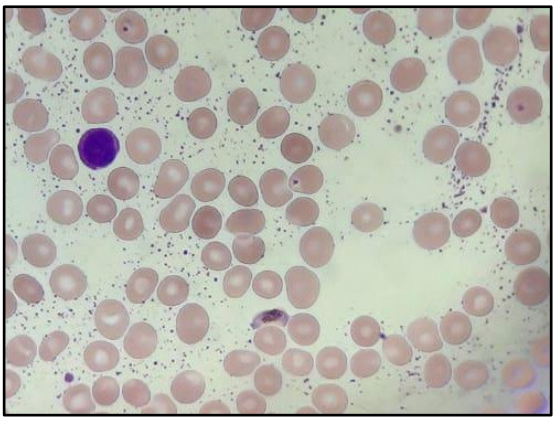

Figure 1. Plasmodium falciparum on a thin peripheral smear; a. Trophozoite ring; b. Gametocyte.

Four days later (4 September), a peripheral smear showed schizont still positive (parasitemia index = 0.01%), accompanied by an increasing WBC of 13.9x103/L (Eos 4.3%) and a normal PLT of 319x103/L. Seven days later (11 September), a peripheral smear showed malaria-negative results accompanied by a decreasing WBC of 12.9x103/µL but an increase of 5.2%. Eight days later (19 September), a peripheral smear showed malaria that was also negative, accompanied by a decreasing WBC of 9.9x103/µL, but the EOS increased by 12.4%.

WBC and EOS charts were seen in Picture 2 and Picture 3. A molecular examination for malaria and dengue was not performed on this patient due to limited resources at this hospital.

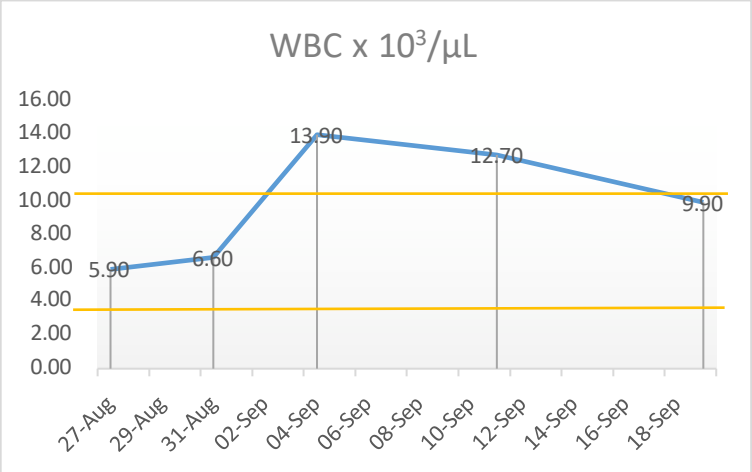

Figure 2. WBC Chart

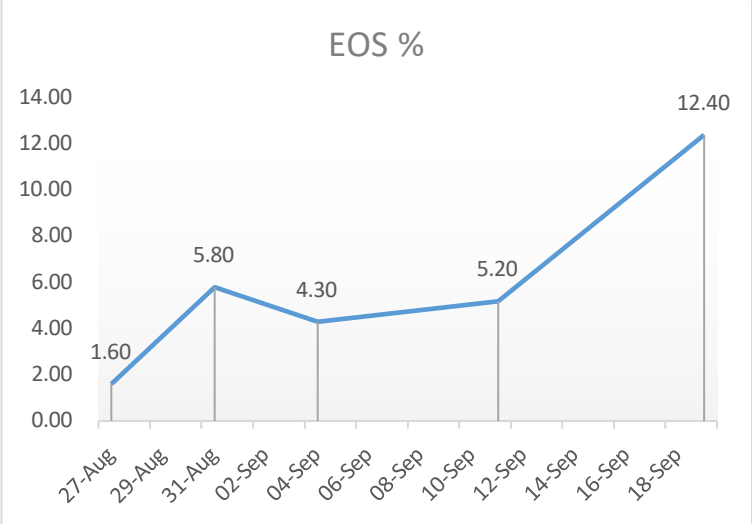

Figure 3. Eosinophil count

Discussion

Indonesia holds the second highest ranking (after India) in Southeast Asia for the highest number of malaria cases, based on the World Health Organization (WHO) report in the 2020 World Malaria Report. Even though it experienced a decline in the 2010–2014 range, the trend of malaria cases in Indonesia has been stagnant from 2014–2019.[1] Five countries (India, Indonesia, Myanmar, Sri Lanka, and Thailand) are among the 30 most highly dengue-endemic countries in the world. Despite the control efforts, there has been a significant increase in the number of dengue cases over the years, though improvements have been made in case management and the reduction of the CFR (case fatality rate) to below 0.5%. By the end of 2022, the number of dengue cases in Indonesia will reach 143,000, with the highest number of dengue cases in the provinces of West Java, East Java, and Central Java.[5]

Dengue-malaria co-infection is not uncommon. Both infections present clinically indistinguishable clinical features; early diagnosis of concurrent infections can be lifesaving.[6] The early clinical symptoms of this patient were untypical. The limitation of the basic health technology condition for the corresponding auxiliary examination led to an unclear diagnosis at the early stage of the disease and delayed timely treatment until the development of dengue shock syndrome.[7] This patient presented with chills as his main complaint and had no fever at all. The only sign of bleeding was a positive rumple-leed test. The patient was suspected of suffering from dengue fever from thrombocytopenia, so the laboratory examination was continued with the detection of anti-dengue IgM and IgG, which gave reactive results. The patient was started to be treated with the dengue shock syndrome algorithm, with a good outcome.

Even with the scarce case reports in Asia, the co-infections of malaria and dengue have recently been recognized as an important clinical problem. Considering the possibility of concurrent infection in cases of atypical clinical manifestations or acute febrile illness, an early diagnosis is essential. Therefore, the treatment regime can be lifesaving.[8] Malaria can be diagnosed using tests that determine the presence of the parasites causing the disease. There are two main types of tests: microscopic examination of blood smears and rapid diagnostic tests. Diagnostic testing enables health providers to distinguish malaria from other causes of febrile illnesses, facilitating appropriate treatment.[4] Based on suspicion of a history of travel to endemic areas, the patient was requested to have a smear and a rapid diagnostic test for malaria. Blood smear examination showed the presence of schizonts, ring trophozoites, and gametocytes of *Plasmodium falciparum* even with a low parasitemia index (0.02%).

Falciparum malaria infection is supported by rapid diagnostic test results, which provide positive results.

Acute malaria in adults with no or limited previous exposure to Plasmodium infection is usually associated with low eosinophil counts, followed by persistent eosinophilia in a proportion of patients after cure. Eosinophils might be stimulated either directly by the parasites or by cytokines or other mediators produced during the malaria attack. Eosinophils may play a role in protection against malaria by inducing parasite killing, but they may also contribute to pathology by releasing granule proteins such as eosinophil cationic protein (ECP) and eosinophil protein X/eosinophil-derived neurotoxin (EPX).[9] The increases in parasitemia are accompanied by an increase in eosinophil count; this shows that there is a high degree of relationship between malaria infection and eosinophil count.[10] This patient showed a normal eosinophil percentage in differential leukocyte counting (1.6%) at the first examination but tended to increase at subsequent examinations. The highest eosinophil percentage (12.4%) was obtained three weeks later, even though the blood smear had already shown negative results.

Conclusion

This case report and previous related studies illustrate that in endemic areas, the possibility of infection needs to be considered. Investigations into the diagnosis of the doctor treating the patient must be carried out in more detail because there are similarities in the clinical and biological characteristics of the two diseases.

Conflict of Interest

The authors affirm no conflict of interest in this study.

Acknowledgment

We would like to thank Faculty of Medicine Universitas Pembangunan Nasional Veteran Jawa Timur for supporting us in this study.

Funding Sources

None.

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