Unusual co-infection of severe malaria by *Plasmodium vivax* and dengue virus in Mexico

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ABSTRACT

Malaria and dengue fever are among the most common mosquito-borne diseases worldwide; however, reports of coinfection are rare. We present a case of severe malaria and dengue coinfection in a 16-year-old female patient presenting with fever, thrombocytopenia, pleural effusion, myopericarditis, and acute respiratory distress syndrome. Dengue infection was confirmed by the presence of immunoglobulin M antibodies and nonstructural protein 1, while malaria was confirmed by the presence of *Plasmodium vivax* in thick and thin blood smears. This is the first report of a dengue/malaria coinfection in Mexico.

Keywords: Co-infection; Dengue; Malaria.

INTRODUCTION

Malaria and dengue fever are the most important mosquito-borne diseases in endemic areas of Central and South America; they significantly affect public health due to their high morbidity and mortality (Wiwanitkit, 2011). Dengue is a viral infection that is prevalent in Mexico and other Latin American countries, including Brazil, Honduras, and Colombia (Arredondo-García *et al.*, 2018). Despite vector prevention and control efforts, the persistence of dengue viral outbreaks makes it a major public health concern in Mexico (Organización Panamericana de la Salud, 2008). Malaria is a parasitic disease caused by several *Plasmodium* species. In 2018, there were 614 cases of malaria caused by *Plasmodium vivax* in Mexico, three of which occurred in the state of Campeche, specifically in the municipalities of Candelaria, Escárcega, and Campeche. In 2019, Mexico reported 618 cases of malaria caused by *P. vivax*, two of which occurred in Candelaria (Sistema Estatal de Vigilancia Epidemiológica, 2019).

Although cases of coinfection with malaria and dengue have been reported, they are rare (Carme *et al.*, 2009; Chong *et al.*, 2017). A comprehensive literature review confirmed that this is the first case report of *P. vivax* and dengue virus coinfection in Mexico.

CASE PRESENTATION

A 16-year-old female Guatemalan patient residing in Candelaria, Campeche, Mexico, was admitted to the Hospital of Candelaria on March 13, 2021, reporting 3 days of symptom evolution involving headaches, myalgia, and fever. Although the patient had no relevant medical history, she referred to a trip to a refugee camp at the Guatemala-Mexico border 7 days before the symptoms developed. During the general physical examination, the patient had signs of mosquito bites in multiple anatomical areas. She was conscious, drowsy, and tachycardic (151 bpm), with a blood pressure of 85/58 mmHg and abdominal pain upon hypogastrium palpation. Blood test results revealed anemia (hemoglobin 11.6 g/dL, normal values 12.0 a 16.0 g/dL) and thrombocytopenia (platelet count 68 × 10^3/µL, normal values 150 a 450 × 10^3/µL), suggesting dengue virus infection. As the patient presented clinically in a shock state, she was initially treated with crystalloids and antipyretics according to guidelines for dengue treatment; however, as there was no improvement, she was transferred to the General Hospital of Specialties of Campeche 3 days after admission to Candelaria Hospital. Given the persistence of fever, headache, abdominal pain, and cough, follow-up controls with complete blood count were performed. The results of the laboratory tests again showed anemia (hemoglobin 10.8 g/dL, normal values 12.0 a 16.0 g/dL), a hematocrit of 31.16% (normal values 38 a 48%), severe thrombocytopenia (platelet count 32.2 × 10^9/L, normal values 150 a 450 × 10^3/µL), and a normal leukocyte count (white blood cell count 8.3 × 10^3/µL, normal values 5.0 a 10.0 × 10^3/µL). Normal renal function was observed, with an urea of 17.1 mg/dL (normal values 0.60 a 1.10 mg/dL), a serum creatinine of 0.61 mg/dL (normal values 0.60 a 1.10 mg/dL), and a serum creatinine of 0.61 mg/dL (normal values 0.60 a 1.10 mg/dL). Liver function was mildly impaired, with a total bilirubin of 1.3 mg/dL (normal values until 1.10 mg/dL), direct bilirubin of 0.9 mg/dL (normal values until 0.25 mg/dL), and alanine aminotransferase (ALT) of 49 U/L (normal values 0.60 a 1.10 mg/dL), and alanine aminotransferase (ALT) of 49 U/L (normal values 0.60 a 1.10 mg/dL), and alanine aminotransferase (ALT) of 49 U/L (normal values 0.60 a 1.10 mg/dL), and alanine aminotransferase (ALT) of 49 U/L (normal values 0.60 a 1.10 mg/dL), and alanine aminotransferase (ALT) of 49 U/L (normal values 0.60 a 1.10 mg/dL).
Chest computed tomography demonstrates smooth... (2018). However, there is likely a prevalence of work center on the publication of patient data. The authors declare that they have followed the protocols of their Confidentiality of the data

dL, total bilirubin of 1.3 mg/dL, ALT of 22 U/L and AST of 29 U/L. Hematocrit of 35.2%, platelet count of 60.16 × 10^9/L, leukocyte count of 6.936 × 10^3/µL, creatinine of 0.57 mg/dL, urea of 42.8 mg/dL, total bilirubin of 1.3 mg/dL, ALT of 22 U/L and AST of 29 U/L.

DISCUSSION

There have been few reports on malaria and dengue coinfection since the publication of the first case by Charrel et al. (2005) and Bygbjerg et al. (2018). However, there is likely a prevalence of coinfection in tropical environments that is not being reported despite the presence of both infectious agents (Carme et al., 2009). Our case involved a patient living in a tropical region where dengue
virus and *Plasmodium* coexist. Fever, headache, fatigue, and joint pain are common symptoms of both infections (Gupta et al., 2017). Diagnosis of coinfection based solely on clinical presentation is difficult due to the similar clinical features of these diseases, which may account for the lack of reports on coinfections (Bygbjerg et al., 2018). Another factor contributing to the underreporting of coinfections could be the differential distribution of the *Aedes* and *Anopheles* mosquitoes. As the species are not expected to be found together, infection by the distinct pathogens is rarely assumed (Wiwanitkit, 2011).

Laboratory tests are necessary for definitive diagnosis. In our patient, dengue-specific IgM antibodies and NS1 were detected on the sixth day after symptom onset. NS1 detection suggested a recent infection (Suleman et al., 2016). In addition, the patient reported having a fever 3 days prior to admission and demonstrated a lack of IgG reactivity, indicating that she had not been previously infected. Severe dengue fever was suspected as the primary diagnosis; over the course of clinical development, the patient’s fever persisted even after the assumed critical period, and respiratory deterioration and hemolysis were observed. Malaria was suspected due to the periodicity of the fever and epidemiological associations, and the diagnosis was confirmed by the presence of *P. vivax*.

Malaria infections can range from non-severe to severe, with an increasing risk of serious complications, including cerebral malaria, severe anemia, respiratory distress, and kidney failure (Cabezón-Estévez & Hernández-Mora, 2016). In this case, the patient presented with pleural effusion and acute respiratory distress syndrome, which occur in 1–10% of cases infected with *P. vivax*. This severe presentation of malaria is uncommon, with pulmonary symptoms more often observed in pediatric patients (Taylor et al., 2012). The malaria parasite has tropism for myocardial tissue and has been reported to cause myocardial dysfunction. Cardiovascular complications can coincide with other fatal complications, including pulmonary manifestations and circulatory collapse. Severe malaria can lead to specific cardiac complications, with reports describing conduction disorders, arrhythmias, myocarditis, pericarditis, cardiogenic shock, and heart failure (Gupta et al., 2021). Increased severity is associated with *Plasmodium falciparum* infection but has also been reported for *P. vivax* (Maguire et al., 2007; Bustos et al., 2014), such as the case described in this report. The pathogenic mechanisms differ between the two infections; malaria is primarily characterized by anemia due to significant intravascular hemolysis (Mendonça et al., 2015), while thrombocytopenia and fluid leakage are the major features of dengue fever. Notably, coinfections increase the incidence of severe thrombocytopenia, as observed in our patient (Epelboin et al., 2012; Mendonça et al., 2015). In this case, both pathologies were characterized as serious due to the clinical manifestations and laboratory findings, which included shock, lung involvement, prostration, myopericarditis, anemia, and thrombocytopenia (PAHO, 2022; WHO, 2022).

Other studies on dengue and severe malaria coinfection reported a low hematocrit value, similar to what was found in our clinical case. An alarm sign for severe dengue fever is a high hematocrit value, which can be confusing when establishing criteria for severe dengue (Magalhães et al., 2014). However, in this type of coinfection, patients present with anemia, which is observed in malaria but not in dengue fever. Therefore, the anemia caused by *P. vivax* explains the low hematocrit concentration. It is difficult to diagnose the severity of dengue fever due to its clinical manifestations, which have been reported to be similar in both concurrent infection and mono-infection (Aruchana et al., 2016). No specific treatment is recommended for patients with concurrent infection. Moreover, there is no specific treatment for severe dengue fever (PAHO, 2022; WHO, 2022). Otherwise, specific treatment for pleural effusion due to plasma leakage is only preventive, supportive with positive pressure, or in case of respiratory deterioration, pleural puncture is considered.

Patients with dengue fever are treated based on their symptoms, and antimalarial drugs are prescribed according to the parasite species and the disease severity. In this case, the antimalarial regimen recommended by the guidelines of the National Center of Preventive Programs and Disease Control in Mexico were followed.

Due to a high prevalence of dengue in this area, dengue virus infection was initially suspected. However, coinfection with dengue virus and *Plasmodium* species may frequently occur in tropical and subtropical areas where these diseases coexist. In such regions, both pathologies should be considered to ensure timely diagnosis and treatment.

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**Conflict of interest**

The authors declare no conflict of interest for the publication of this manuscript.

**REFERENCES**


